"Non-Gonococcal Urethritis in the Male."

by

S/Ldr J. Norrie Swanson M.B., Ch.B., R.A.F.V.R.
"All that runs is not necessarily gonorrhea."

Henry Morrise.

"Whatever be the degree of cleanliness, the apparent health, the presumed virtue, the real virtue, even virginity of any woman, she may have a leucorrhoeal discharge from some cause.......... she is in a condition to transmit a discharge to a man having intercourse with her."

Monsieur Diday.
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An introduction, like an overture which hints at melodies to come, should give some indication to the reader of what may be expected in the pages that follow; it is hoped that this introduction will be not without success in fulfilling this function, and will at the same time afford an opportunity for giving some few explanations that are best made at the start.

While reading over what had been written, it was realised how much the thesis differed from its original design, the first intention having been to put forward evidence for the belief that there was a type of urinary infection, contracted during coitus, which might be found in the Medical wards presenting as a so-called Abacterial Pyuria or as Reiter's Disease, or in the Special Treatment Department as a non-gonococcal urethritis. For this purpose, details of all cases which came to the hospital - The Royal Air Force Hospital, Ely, Cambridgeshire - complaining of a discharge, had been collected. But it was then found that the intention of confining the investigation to this one type of infection had been submerged in a growing interest in the whole subject of non-gonococcal discharges, which at that time comprised as many as 50% of all the cases of urethritis. It was therefore decided, since there was material available
to make a study of the whole of this subject, and not just one type of urethritis.

A routine plan for questioning and investigating each case was worked out, so that comparison could be made between them; details of this plan are given immediately after this introduction. The results of the investigation are then described in sections dealing with the salient features of the history, the various symptoms, the complications encountered and the several forms of treatment that were tried. These findings are then discussed and interpreted, still in sections, along with the relevant literature; wherever possible, there is a summary at the end of the section giving any conclusions that have been reached. There is also at the end, a summary of all the conclusions reached, and this is followed by a Bibliography and two appendices.

Before proceeding to outline the methods of investigation, there are a few remarks to be made by way of explanation. Firstly, the terms non-gonococcal and non-specific urethritis are used here as synonyms; even those discharges whose aetiology is certain (e.g. from an intra-meatal syphilitic chancre or from urinary tuberculosis,) are considered here to be non-specific, as they stand in that relation to gonorrhea which is the one specific discharge for the purposes of this thesis.

Secondly, although/
a total of 120 cases have been analysed, it must be added that there were a few more which were not suitable for analysis; this was either because these men had very great difficulty in making themselves understood in English, or their mental capacity was so low that they were unable to give an intelligent statement of the sequence of events concerning their trouble; these cases, were reluctantly omitted from this series.

Thirdly, it was very fortunate that there were some German Prisoners of War working in the hospital as their help in translating some of the German literature was invaluable, and saved many hours of work.

One final comment: if it be considered that too much effort has been expended reiterating and labouring some points, for all the results that have been achieved, that after mountainous labour only the ridiculous mouse has been begot, it is hoped that it will be remembered that the mouse it was who set the lion free by nibbling at the imprisoning net, that the apparent smallness of the results does not detract from their importance. It is believed that the conclusions reached are a summary of what is known about non-gonococcal urethritis at the present time; and it is regretted that this knowledge is not more widely spread amongst both doctors and laymen. Too often
a doctor may not recognise the simple nature of a discharge, so that a happily married man may suffer doubts and suspicions concerning his domestic life, perhaps even becoming involved in litigation, all because the label of gonorrhcea has been carelessly applied.

It is hoped that more attention will be paid in the future to the non-gonococcal forms of urethritis than is at present, and that efforts will be made to improve the techniques of diagnosis and treatment of these conditions.

**METHODS OF INVESTIGATION.**

**History.**

A very careful history was taken from every case, whether new, or coming for observation or continuation of treatment.

Special note was made of the following points:
Interval between intercourse and onset of symptoms. (= Incubation Period.)

Any mechanical or chemical contraceptive used and if any, which.

Any Early Treatment, such as that recommended in the Services.

Any auto-medication attempted.

The amount, if any, of alcohol taken at the time of coitus, and also on the day or two preceding the onset of the symptoms.

Any other details about the duration of coitus, whether coitus interruptus had been practised, and whether any difficulty of penetration had been encountered. (These questions were only asked when the confidence of the patient had been gained. Occasionally, too, there was opportunity to ask about masturbation, but usually there was doubt about the veracity of the answers to questions of this kind.)

Whether, as far as the man knew, the coitus took place just before, during or just after a menstrual period; whether the woman had reported with a discharge since the intercourse. (This latter sometimes happened, but unfortunately, it was never possible to investigate these cases.)

A detailed description of how the symptoms started; which came first, and how long an interval there was/
there was between them; whether the discharge was in
the morning only or all day; whether it was profuse or
slight, white or watery or greeny-yellow; just a stick-
liness or a dampness.

Whether dysuria was felt near the tip of the
glans, the frenum, along the urethra or at the root
of the penis; whether it was felt before, during, to-
wards the end of, after, or unrelated to micturition.

Whether pain was also felt in the loins, flanks
lower part of the abdomen, rectum or back.

Whether there was any frequency by day or by
night; whether there was any haematuria, dribbling,
urgency or change in the stream volume.

Whether there were any toxic symptoms of mal-
aise, headache, anorexia or pyrexia.

Whether there were any joint pains or swellings.

Whether there were any eye symptoms.

In certain cases, questions were also asked
about food habits and drugs to see if there was any
idiosyncracy present.

Any previous history of venereal infection with
the treatment given and any relapse that occurred;
previous personal or family history of kidney trouble.

Examination.

The general condition of the pat-
ient was noted, particular attention being paid, of
course, to the external genitalia: the size of the ur-
inary meatus and the presence or absence of balanitis,
chancre, warts or other skin affections; the size of
the/
testes, epididymes, and spermatic cords. In cases where there was no acute urethritis, the prostate was palpated and massaged.

Laboratory Investigations.

1. A slide was made from the discharge and stained with Gram's stain to exclude any gonococci, and to show whether there were any pus cells or organisms. (Most cases which were gonorrheas were eliminated at this stage.)

2. A wet film was examined immediately on a warm stage for trichomonas vaginalis.

3. A Chocolate Agar plate was inoculated and incubated in a 5% CO₂ atmosphere to try and grow any gonococci which had been missed in (1).

4. Water was passed as for the Two Glass Test, and if there were threads in either, and sometimes in their absence, the urine was centrifuged and the deposit examined microscopically for cells and organisms; Blood Agar and McConkey's media were inoculated with the deposit to grow any organisms present.

5. After urine had been passed, and the anterior urethra had thereby been cleared of pus, a platinum loop was inserted as far as possible and drawn backwards and forwards two or three times to obtain epithelial scrapings. Slides of these scrapings were sent to London, and were examined for virus inclusion bodies by Dr Henderson Begg of the Wellcome Foundation, and Dr Meenan of The London School of Hygiene and Tropical Medicine/
Medicine, under the direction of Dr A.J. Rhodes.

6. If there was only a very little discharge, or if the prostate was suspected of being chronically infected, prostatic massage was done and the resultant fluid examined as in (1), (2), and (3). If however, the prostate was found to be enlarged or tender, it was left entirely alone.

7. In persistent cases, urethral sounds of increasing calibre were passed to ascertain whether there was either folliculitis or stricture present.

8. Blood was taken for Wassermann, Kahn, and GCFT tests.

9. In selected cases, admission to hospital was arranged and the following further investigations carried out:— (i) Three 24 hour specimens were examined for tubercle bacilli microscopically, and at the pathologist's discretion, culture and guinea pig inoculation were performed.

(ii) Intravenous pyelograms were taken to disclose any congenital or infective disorder in the urinary tract.

(iii) Anterior Urethroscopy and Cystoscopy were done to see whether any urethral, trigonal or bladder pathology were visible. Unfortunately, no posterior urethroscope was available.

10. Hoffman-Frei Antigen to eliminate Lymphogranuloma Inguinale was not available; attempts were made to/
to obtain some from New York and fly it back, but they were unsuccessful, the official reason being shortage of dollars.

11. "Sloppy Agar" for growing L organisms was not able to be made owing to difficulties of obtaining certain of the ingredients, and also because the staff in the Laboratory at Ely was so over-worked.

RESULTS AND ANALYSIS OF INVESTIGATIONS.

Age Incidence.

With only 7 exceptions, all the cases were of men between the ages of 18 and 30. All the cases over 30 years of age were regular servicemen.

Rank Incidence.

Fourteen were officers, all of whom were aircrew; 38 were aircrew NCO's; 5 were non-aircrew senior NCO's; 63 were other ranks (corporals, leading aircraftsmen, and aircraft hands.)

Racial Incidence.

Ninety-four were British; 18 were Poles; 6 were West Indians; 1 was a Dutchman; and 1 was a German Prisoner of War.

History.

Every man had a history of sexual in-
tercourse prior to onset of the symptoms, and that was why he found his way to the Special Treatment Centre rather than to any other department of the hospital. In several instances, however, coitus took place so long beforehand as to cast doubt on its having anything to do with the discharge of which the patient complained; in some cases it is believed that there cannot have been any connection between the two, and the patient might well have attended a surgical or medical out-patient clinic, had not the discovery of a urethral discharge seemed significant to a mind that could not forget the exposure to the risk of catching venereal disease; such a discharge was often hopefully called a "strain."

Each case complained of a discharge (or, of course, they would not be included in this series), and an attempt was made to give a classification to the different types. Although it was often very difficult to place a particular discharge, it was found that two distinct groups existed into which each case could be fitted more or less readily.

There was first, a very big group, which had in the discharge, large numbers of pus cells, and micro-organisms, to which the name of Infective could justifiably be given. Second, there was a much smaller group, which had in the discharge no pus cells or micro-organisms - or at most only a very few - to which the name of Non-infective was applied. The few
organisms in this latter group were thought to be only those that inhabit these regions normally, (86) and that such pus cells as were present, were the result of an irritative, non-infective, inflammatory reaction. Non-Infective Group.

This group being the smaller, will be dealt with first. There were only 9 cases which could be considered to be primarily non-infective. Infection was added later in some of them, but when that had been cleared up, the non-infective discharge occasionally reappeared.

Of these 9, the most clear cut were those which were really an overflow of semen and not examples of urethritis at all; the discharge would probably have remained unnoticed if venereophobia had not lead to an unaccustomed, over-critical inspection of the meatus. There were 5 such cases, two of which first became aware of their condition when they started to train for athletic sports and consequently became sexually continent. Both of these later contracted an infective urethritis, in one case following intercourse, and the other following injury to the anterior urethra at football. Both had a seminal overflow discharge again when the infection of the urethra cleared up.

Of the other three, one developed a mucoid and seminal excess after a urethral infection had been cleared up, and this may have been the result of/
an unaccustomed continence, being unwilling to expose himself to re-infection. It is possible, too, that it had really been present before, but his attention had not been drawn to his urethra before he exposed himself to infection. Another had had such a discharge since puberty, and had a superadded infection following intercourse. The last merely had a very slight whitish discharge after defaecation, and had no infection at all.

In all these cases, the discharge appeared after micturition, especially if there had also been passed a large difficult stool at the same time. The discharge was not associated with any other symptoms such as pain or tingling. It was especially marked in the morning, and was white and sticky; sometimes a gelatine-like blob appeared at the meatus. Microscopically, it consisted of mucus, some lecithin crystals, and an occasional spermatozoon; no pus or micro-organisms were seen. The patients themselves noticed that the discharge was absent for a few days after intercourse or a nocturnal emission.

Two of the remaining 4 cases were the result of alcoholic excesses. The interval between the onset of symptoms and the intercourse was 14 and 16 days respectively. Alcohol was consumed to excess not only on the occasion of the coitus, but also one night, in one case, and two nights in the other, before the discharge appeared. In both cases, only an occasional/
occasional pus cell was found and in one a few micro-
organisms which were not identified. Both cleared
up spontaneously in two days and did not recur.

The remaining two cases of the nine
were both preceded by heavy colds 4 days before. One
was a senior officer who had only had marital inter-
course, (6 days before the cold) using Volpar gels as
contraceptive. The discharge was at first watery, with
only a very few pus cells and micro-organisms, becoming
thicker 2 days later when presumably secondary infec-
tion from skin contaminants had taken place. The other
was a Dutchman who had had no intercourse for 5 months
previously, but had been steadily drinking alcohol, and
developed a cold with diarrhea. At first there were
only a few pus cells, but after a week, pus increased
and micro-organisms appeared.

Those cases just mentioned which be-
came secondarily infected are included in the figures
for that group too. It is possible that many of
the Infective group started after alcoholic excesses
but did not remember the occasion when this occurred.

**Infective Group.**

By far the majority of cases (111) fall
into this category. But while the infective element
was undoubtedly present, as was evidenced by the large
numbers of pus cells in the discharge, there were other
factors which played their part; this will be discuss-
ed later.
History.

In 32 cases coitus took place very shortly after the end of a menstrual period; and in 2 cases it took place the night before, and in 1, two nights before it started.

Alcohol was imbibed in 53 cases, in 16 resulting in drunkenness. Twelve cases relapsed after having a "night on the beer."

A history of gross trauma was only obtained thrice: two cases were of injury to the anterior urethra during a football game, and the third was a kick on the penis which lead to the formation of a stricture. One of these flared up a second time after cycling on a hard saddle for 16 miles. In a great many more cases there was probably the minor trauma of a difficult penetration into a dry vagina, a possibility which will be discussed later.

Prophylactic measures, it may be mentioned conveniently at this point, were undertaken by only 25 men; 13 used a sheath alone; 8 only the official Early Treatment packet (British or Canadian); and 3 used both. One contented himself with merely swabbing the external genitalia with TCP, which may either have not been strong enough to kill any microorganisms or too strong for his sensitive urethra.

Contraceptive chemicals may also damage the urethral mucosa. Only 5 men used such, and they used them without condoms, during marital coitus.
The preparations used were: Rendells (2); Volpar gels (1); Gynimon (1); Lebresseur jelly (1).

A history of previous gonorrhea was obtained in 13 cases; but in only 6 of these was the attack within 3 months; of these 6, 2 started a non-specific discharge within 3 weeks of a gonorrhea being cleared up with penicillin. Two others were relapses after alcoholic excesses and in the remaining two, one started spontaneously after 2 months, and the other spontaneously after 3 months, associated with symptoms and signs of an acute pyelitis.

Previous non-specific urethritis was found in 6 cases, one of whom had had it twice, and one thrice before; possibly these were really continuations of the original infections. Two were in the middle of their month's rest during the arsenical treatment for syphilis when they exposed themselves to the risk, and they cleared up as soon as the arsenic recommenced.

Sixteen of the men had marital intercourse only, and two more admitted having extra-marital relationships as well; all the others were extra-marital. Five of the wives also had discharges.

Two cases which were very persistent had histories of headache; on examination they were both found to have chronically infected maxillary antra, and one had a few septic teeth. They did not respond to treatment till these areas of abscess were removed.
Symptoms.

1. Dysuria.

The most common symptom was dysuria. The term dysuria, from the Greek 'dys' meaning bad, hard, or ill, and 'ouron,' meaning urine, is an unsatisfactory one, as it is used meaning difficulty in passing water as well as the painful passing of water. But for want of a better and equally short term it is used here to mean the passing of water associated with pain, or tingling in the urethra.

Forty-eight cases had no dysuria, but 72 had. The symptom varied in its intensity, its location in the urethra, and its time relationship to micturition. Most of the 72 patients described the feeling as a tingling or at most a slight burning; but a few actually felt it as an ache. Thirty-one of them felt the sensation in the urethra about ¼-½ an inch from the meatus; 10 felt it all along the anterior urethra; and 30 were unable to localise it accurately, but said it was "somewhere in the pipe;" 1 said it was at the root of the penis.

Frequently it was noticed that massage of the prostate produced a similar pain, but felt more nearly at the frenum on the external surface, or at that level inside, rather than at ¼-½ an inch from the tip. A few who had dysuria towards the end and after micturition, described a feeling of warmth and well-being in the urethra as the sensation wore off.
In 27 cases the dysuria came before the discharge, usually 2-4 days before, although in two cases it was as long as 10 days before. In 8 cases the discharge came first. In 37 cases the men were not sure or thought they came together.

Twelve cases felt pain at the start of micturition; 22 all during; 25 towards the end; and 5 immediately after; 2 felt it at the beginning and at the end; 1 at the beginning, during, and after; and 1 before. Four had dysuria apparently unrelated to the act at all. In order to find out if there was any significance in this variation of pain sensation, the incubation period, the forms and results of treatment were analysed in each of these groups. An additional group was also analysed consisting of the dysurias before, at the start, towards the end, after, and those which were combinations of these, as it was thought that there might be some connection between these groups. Only the Incubation period will be considered at this point.

As frequently intercourse took place on two or more consecutive nights, and sometimes, too, the date could only be given approximately, it was found convenient to localise the coitus in a particular week, rather than on one particular day; the incubation periods are therefore referred to as so many weeks. A big difficulty was to decide where to fit in those who had regular intercourse, and it was finally decided to leave them out, but stating in
passing how many were concerned.

A. No Dysuria.

48 cases (44%).

5 had regular intercourse and 4 had no intercourse for over 3 months. The others were as follows:

<table>
<thead>
<tr>
<th>weeks</th>
<th>cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
</tr>
</tbody>
</table>

Average: 3.15 weeks. (Obtained by multiplying the week number by the number of cases in each, and dividing by the total number of cases.)

B. Dysuria During.

22 cases (20%).

1 had regular intercourse. The others were:

<table>
<thead>
<tr>
<th>weeks</th>
<th>cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

Average: 3.6 weeks.

C. Dysuria at the Beginning.

12 cases (11%).

3 had regular intercourse. 1 had none for 5 months. The others were:

<table>
<thead>
<tr>
<th>weeks</th>
<th>cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

Average: 3.25 weeks.

D. Dysuria at the End.

25 cases (23%).

3 had regular intercourse. 1 had none for 5 months. The others were:
weeks: 1 2 3 4 5 6 7 8
cases: 1 5 6 5 3 0 0 1
Average: 3.4 weeks.

E. Dysuria After.
5 cases (5%).
1 had regular intercourse. 1 was in the 2nd week, and 3 were in the 4th.
Average: 3.5 weeks.

F. Dysuria Before.
1 case (1%), in the 4th week.

G. Dysuria Before and After.
2 cases (2%).
1 in the 2nd week, and 1 in the 8th.

H. Dysuria Before, During and After.
1 case (1%), in the 3rd week.

I. Unrelated to Micturition.
4 cases. (4%).
weeks: 1 2 3 4 5 6 7 8
cases: 1 1 1 1 0 0 0 0
Average: 2.5 weeks.

J. Combination of C D E F G H I.
46 cases (41%).
7 had regular intercourse. 2 had intercourse 5 months previously. The others were:
weeks: 1 2 3 4 5 6 7 8
cases: 1 11 8 11 0 3 1 2
Average: 3.56 weeks.
Total number of cases with an incubation period of less than 14 days is 36 = 30%. 
2. Frequency.

This symptom was only present in 33 cases (27%). In 2 cases only could it be said to be very great (12 times daily) while in the others it was only moderate (up to 6 times daily.) Six cases, one being of the former group, had to get up during the night as well. The distribution in the various dysuria groups is as follows:

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dysuria</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>Beginning dysuria</td>
<td>3</td>
<td>12-25%</td>
</tr>
<tr>
<td>During dysuria</td>
<td>10</td>
<td>22-45%</td>
</tr>
<tr>
<td>Terminal dysuria</td>
<td>7</td>
<td>25-26%</td>
</tr>
<tr>
<td>After dysuria</td>
<td>1</td>
<td>5-20%</td>
</tr>
<tr>
<td>Before dysuria</td>
<td>0</td>
<td>1-0%</td>
</tr>
<tr>
<td>Before &amp; After dysuria</td>
<td>1</td>
<td>2-50%</td>
</tr>
<tr>
<td>Before, during and After dysuria</td>
<td>0</td>
<td>1-0%</td>
</tr>
<tr>
<td>Unrelated dysuria</td>
<td>2</td>
<td>4-50%</td>
</tr>
<tr>
<td>Combined Group</td>
<td>14</td>
<td>50-23%</td>
</tr>
</tbody>
</table>

3. Haematuria.

This occurred only twice, both times being at the end of micturition. One case had dysuria at the beginning of micturition, and the other at the end. In neither cases did it consist of more than a drop or two.


There were two instances of this. One had no dysuria, but had terminal dribbling. In his
Examination.

The external genitalia were normal in nearly every case, there being two instances of pin-hole meatus, and several of rather tight preputces. Four cases of epididymitis were found.

The discharge was nearly always first noticed in the morning when urination was attempted. Either a small blob of pus appeared, sometimes white, sometimes greenish, just as the urine appeared; or the meatus was sealed over and the urine dribbled out at first in several streams, until, with greater force, it burst its way out in its usual flow. During the day, the discharge disappeared, leaving at most a dampness of the meatus. A very few patients stated that there was more than just this dampness; but then, others stated that they were not even aware of a dampness. Sometimes the underclothing, especially the pyjamas were slightly stained.

No case ever had a profuse discharge or one that lasted all day.

Examination of the urine for threads was carried out in every case, and the usual interpretations of their presence in the first and second glass were made; this was found useful in estimating the progress made towards cure. Midstream urines were examined microscopically and cultured; the results of these examinations are detailed below. One case was found in an uncentrifuged specimen on two separate occasions to have a profuse oxaluria.
Laboratory Investigation.

A search was made in smears from the discharge for various organisms known to be associated with infection of the urethra.

First of all, the gonococcus was excluded by repeated gram-stained slides from the urethral discharge and prostatic fluid. All new cases and old ones which still had a discharge had, in addition, a culture taken on a Chocolate Agar plate. By this method 7 cases, previously thought to be non-specific were shown to be due to the gonococcus; 4 were after the organism had been seen on a slide - 2 of which were confirmed by culture - and the other 3 were after repeated urethral smears. Of these latter 3, one had a flare up of his discharge following excessive alcohol, and the other two were believed to be re-infections. None of them are included in this series.

Trichomonas vaginalis was next sought for in a wet film, examined immediately on a warm stage. The film was made either from a urethral discharge or the prostatic fluid and sometimes both. No such organisms were ever found. Ultra-centrifuging of the urine as recommended by Cabot and Crabtree (20) was not done, as it was considered that if centrifuging was necessary to disclose the protozoa in sufficient numbers to be seen, they could hardly have been present in sufficient numbers to have caused the discharge.
discharge; in women so infested, the trichomonas are present in great numbers.

The results of examining the slides and cultures were not altogether satisfactory as it was sometimes very difficult to determine whether an organism was a saprophyte, a pathogen or a contaminant from faulty technique; for example some organisms, e.g. the staphylococcus, could be all three. However, if one organism was present in great numbers, and its disappearance coincided with cure of the condition, it was thought reasonable to conclude that it was the causative organism.

One case had a very profuse growth of staphylococcus albus, verified on two occasions. This was in a man who had been confined to bed with a fractured tibia and fibula; he had an outbreak of boils on his legs a few weeks prior to his reporting with a urethral discharge. He stated that the boils had come first, but that the discharge appeared only a few days later. On examination he was found to have a congenital stricture of the anterior urethra. It was concluded that the urethral discharge was the result of a blood borne infection from the boils, which had settled in the urethra because of the stricture. It is regretted that he was not seen when his boils were active so that a comparison could be made between the causative organisms.

Eighteen cases had numerous Gram +ve cocci; 1 had Gram -ve cocci; 4 had Gram-ve diphther-
oids; 3 had Gram positive diplococci.

Twenty-three had mixed organisms including Gram positive and negative cocci and bacilli.

In 11 cases no micro-organisms were found at all.

The remaining 59 cases had very few micro-organisms, usually mixed and more often than not, they were mostly Gram positive cocci.

Urethral scrapings were made after urination in 33 of the 50 new cases seen. Doctors Meenan and Henderson Begg reported that no virus inclusion bodies or L organisms were seen in any of them.

No tubercle bacilli were seen on examining the deposit of the centrifuged 24 hour specimens; nor did culture on Loewenstein's medium reveal any either.

Instrumentation.

Anterior Urethroscopy was not done as a routine while a urethral discharge was present except in those cases where the discharge was so persistent that folliculitis or stricture was suspected.

In cases where the instrument was passed, the following appearances were to be seen:

the mucous membrane is normal in most of its length, but here and there, are patches of congestion and oedema which give it a blotchy appearance. The epithelial cells sometimes proliferate giving rise to little eminences which can be clearly seen and even
heard exploding when touched with the cautery. (30). Discharge can be seen in the mouths of the glands of Littré when these are infected. Strictures can be seen when they are present as small bands, not entirely surrounding the urethra, but only part of the way round; they are relatively soft compared with those encountered in gonorrhea, and dilate easily without much bleeding.

Cystoscopy was performed on 4 cases, two of whom had terminal haematuria. Of these two, one showed an exceedingly diffuse cystitis, while the other showed only a mild one. Of the remaining two, one showed a trigonitis and the other was not well seen as the light failed in the cystoscope which took longer than the patient did to get better.

X Rays.

Intravenous Pyelograms were taken in 6 selected cases, which were admitted to hospital for this part of the investigation. Four of these were done within 7 days of the onset of the discharge, and 2 within a month. Five of them had terminal dysuria, and the sixth felt pain at the start of micturition. Two of them had a slight terminal haematuria.

The results of the pyelograms were: 4 were completely normal; one had a very long, bent left ureter; and one had a "wooliness" of the left renal pelvis suggesting there was an infective process going on there. Two
of those in which the kidneys and ureters were normal showed a marked reduction of the bladder capacity, with a "wooliness" of its wall suggesting a very marked infection there.

Treatment.

Several forms of treatment were tried. Most of the cases which came for continuation and observation had had their treatments started with some form of sulphonamide preparation, usually sulphathiazole. Cases which did not respond to this, either had another similar preparation such as sulphadiazine or sulphamezathine, or had one of the following: intravenous neoarsphenamine, penicillin, or pyreto-therapy with TAB vaccine. The methods of administering these therapies will now be described.

A. Sulphonamide.

Eight gm. of the drug were given during the first 24 hours, and 6 gm during the next. This was sometimes enough, but more often than not, a further 6 gm was needed on the third day, making a total of 20 gm. It was found usually that the discharge showed signs of improvement at this point, and the sulphonamide was discontinued; but if the discharge was still as much as ever, then the drug was continued until there were signs of improvement. With this technique it was found that those discharges associated with no dysuria, dysuria at the beginning, and after required on an average 20 gm sulphonamide; those with terminal dysuria required 22 gms, and those with dysuria during 23 gm. The significance of this will
be commented on later.

B. Neoarsphenamine.

The arsenic was given in 3 injections at first consisting of .3gm, .45gm and .6gm at 5-7 day intervals; later, this was reduced to 3 smaller injections of .3gm each as perusal of the literature revealed that this smaller dosage was just as effective as the larger and less likely to produce toxic effects.

C. Penicillin.

This was given intramuscularly in doses of 20,000 or 30,000 units till a total of 150,000 or 200,000 units had been given. It was never given orally as has been recently done in the treatment of gonorrhea.

D. TAB Vaccine.

Fifty million units were given intravenously, and if no reaction resulted in 4 hours, 75 million units were given. Usually one good rigor was produced after the single injection, giving rise to a rigor, with a temperature of 104 deg. F. for 6 - 12 hours. This was sufficient to produce a cure.

E. Irrigations.

Irrigation of the anterior urethra was performed in 30 of the cases treated with sulphonamide. The solutions used were either 1:8000 mercury oxycyanide, or 1:10,000 potassium permanganate. The results in these cases were as follows:

7 cleared up in 4 days.
12 " " 7 days.
3 " " 14 days.
8 did not clear up at all with sulphonamides.

F. Prostatic Massage.

In a few cases, where it was believed that the cause of the persistent urethritis was a chronically infected prostate, massage of that gland was carried out on alternate days for a week, sometimes being followed by irrigation of the posterior urethra. The rationale and dangers of such massage will be considered in the discussion.

G. Passing of Sounds.

Where a discharge persisted in spite of repeated investigation and treatment, sounds were passed to see whether folliculitis or stricture were responsible. If the former, then the follicles were palpated against the sound to try and break them down; if the latter, increasing sizes of sounds were passed to dilate it and usually one such dilatation was sufficient.

H. Hyperthermia.

None of the cases in this series was so treated; but mention of the results obtained elsewhere with this form of therapy will be made in the discussion.

Relapse after any of the above-mentioned therapies was treated in various ways, depending at which Special Treatment Centre the man happened to be. Every possible combination of treatments seems to have been tried in one or other order, in some of these.
The results of treatment in the various dysuria groups are stated below; they have been subdivided thus to see whether there is any significant relationship between the form of therapy and the type of dysuria. Later, a summary in tabloid form will be given comparing the various therapies with each other.

A. No Dysuria.

Sulphonamide: 31 cases with 13 relapses. (Details of the subsequent treatment of all the relapses are given later.)

NAB: 7 cases. All cleared up within 14 days except one which did not clear up until a second course had been given.

Penicillin: 2 cases, 1 of which relapsed.

Other Treatment: 1 case of stricture cleared up after dilatation with sounds.

1 cleared up after prostatic massage.

1 mild case cleared up spontaneously in 2 days.

2 cases of alcoholic urethritis cleared up in 2 days. 1 case of seminal overflow needed no treatment at all. 2 cases were really balano-posthitis and they cleared up with saline soaks.

B. Beginning Dysuria.

Sulphonamide: 8 cases of which 4 relapsed.

NAB: 2 cases of which 1 was repatriated to Barbadoes before treatment had been completed.

Penicillin: 2 cases, both relapsed.
### Table 1

Comparison of the various dysuria groups.

<table>
<thead>
<tr>
<th>Type of Dysuria</th>
<th>Sulphonamide Relapses NAB</th>
<th>Penicillin Relapses</th>
<th>Prostatic Massage</th>
<th>Dilatation</th>
<th>Spontaneous Soaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Dysuria</td>
<td>31</td>
<td>13</td>
<td>7</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Beginning dysuria</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>(e)</td>
<td>2</td>
</tr>
<tr>
<td>During</td>
<td>17</td>
<td>8</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Terminal</td>
<td>15</td>
<td>9</td>
<td>7</td>
<td>(k)</td>
<td>0</td>
</tr>
<tr>
<td>After</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before and After</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before, During &amp; After</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrelated dysuria</td>
<td>3</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>40</td>
<td>21</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

(a) One case repatriated before treatment finished.

(b) Two case demobilised before treatment finished.
### Table 2
Comparison of Principle Forms of Initial Treatment

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>82</td>
<td>21</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cleared in 4 days</td>
<td>5</td>
<td>11</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleared in 7 days</td>
<td></td>
<td>23</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleared in 14 days</td>
<td></td>
<td>4</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleared in 18 days</td>
<td></td>
<td>4</td>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never cleared or relapsed</td>
<td>0</td>
<td>40=49%</td>
<td>0</td>
<td>4=80%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Posted during treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

The relapse column refers to those that did not clear up after having been given the routine amount of that particular drug as mentioned on page. The subsequent treatment of these relapses is detailed below:

**A. Sulphonamide Relapses. (40 cases.)**

Required more Sulph. up to 20gm (ie a repeated = 5 course)

- " " " 38gm 2
- " 150,000 units penicillin (av) 3
- " " + 26gm sulph. as well 3
- " " + 2 inj. TAB vaccine 1
- " NAB (3 inj.) 16
- " " + the passing of sounds 1
- " " + prostatic massage 1
- " " + antral washouts, teeth extractions, 3 more NAB and irrigations 1
Required TAB (2 inj.) + NAB (1 inj.) + 20gm Sulph.  1
Posted before cleared up  1

**B. NAB Relapses (1 case.)**

Requiring a repeated course of 3 injections there was 1 case. It should be noted however, that 3 others were posted before the success or otherwise of this therapy could be ascertained.

**C. Penicillin Relapses (4 cases.)**

Required NAB (3 injections)  1
Required NAB (2 injections)  1
Required up to 32gm sulphonamide  2

Since NAB therapy will be discussed in some detail later, it is proposed to set out in tabloid form the results of all the cases so treated.

**Table 3**

<table>
<thead>
<tr>
<th>Cases treated with NAB</th>
<th>New Cases</th>
<th>Sulph relapses</th>
<th>Pen relapses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number treated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleared in 4 days</td>
<td>21</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>&quot; 7 &quot;</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>&quot; 14 &quot;</td>
<td>4</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>&quot; 18 &quot;</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Required more treatment</td>
<td>0</td>
<td>4*</td>
<td></td>
</tr>
<tr>
<td>Posted during treatment</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* These cases were as follows:

1 had folliculitis which cleared up with the passing...
of sounds.

1 had chronic prostatitis which cleared up with pro-
static massage.

1 had septic foci elsewhere and when these had been
eradicated, the discharge stopped.

1 case had been given 2 injections of TAB after
sulphonamide had failed to clear it up; later, it was
given 1 injection of NAB and then 20gm more of sulph-
onamide before it finally cleared up. This case occ-
urred overseas, and the unusually concentrated acid
urine which was passed then may have contributed to
keeping the urethritis going.

Complications.

A. Prostatitis.

In 20 cases in which a dischar-
ge persisted as a morning drop or a dampness during the
day, pus was found in the prostatic fluid; micro-organ-
isms of various kinds (cf those in the urethral dis-
charge) were often found but not always. This was
interpreted as evidence of chronic prostatitis, and was
treated by giving three prostatic massage to the gland
on alternate days and the patient was instructed to
drink copious bland fluids following each. Sometimes
irrigation of the bladder and posterior urethra was
carried out after each massage to ensure that infect-
ous material was washed away. In all but two of
these cases, the prostatic fluid became pus-free by the
end of 7 days.
Of these two cases, one had a soft stricture which was dilated by passing sounds of increasing calibre and the discharge then stopped in 4 days. The other had also infected maxillary antra and when these were washed out weekly for 5 weeks, the discharge gradually lessened and finally disappeared.

No cases of acute prostatitis or of prostatic abscess occurred.

B. Folliculitis. (Littritis.)

Three cases which did not clear up after treatment, and in which there was no evidence of prostatic involvement, had sounds passed. The glands of Littré were massaged over the sound, and in each case there was a slight flare up of the discharge for the following two days, and thereafter it cleared up altogether.

C. Cystitis.

Four cases occurred, all being confirmed by cystoscopy. Three of them had pain at the end of micturition, and one at the beginning. This latter case and two of the others had terminal haematuria. None of them showed any micro-organisms in the discharge, nor could any be grown on culturing the centrifuged deposit of a mid-stream specimen. Many pus cells were seen both in the discharge and the mid-stream deposit. They all responded quickly to NAB and cleared up in 7 days.

D. Epididymitis.
Four cases occurred. One, in a German Prisoner of War, first appeared two years before, after a previous attack of non-specific urethritis; recently he had started to feel pain again in his left groin and in the lower pole of his left testicle where there was a small, tender, indurated nodule. This pain stopped after a course of NAB.

Another case was very acute and followed the injudicious massage of his prostate by a medical officer who was over-anxious to obtain prostatic fluid. The next day both epididymes were greatly enlarged and acutely tender. He had a history of a slight discharge 3 weeks previously which had cleared up by itself in a few days. No gonococci were found, and the GCFT was negative. The pain stopped dramatically the day following the first injection of NAB and the swelling got steadily less.

The remaining two cases occurred for no apparent reason 2 months and 5 months respectively after non-specific urethritis. Both denied any further intercourse or excessive intakes of alcohol. Both cleared up with sulphonamide and a suspensory bandage was applied.

E. Other urinary Tract complications.

No other complications occurred in this series, but such as have been reported in the literature will be discussed later.
F. Sexual Disorders.

One case complained of impotence some weeks after he had been treated. But with re-assurance his confidence returned and no further complaints came from him.

No cases of premature or painful ejaculations were encountered.

Test of Cure.

At the last visit, after the treatment had been completed, the patient was told to report again for Test of Cure in 3 months; when penicillin had been given, a final blood Wassermann, Kahn and GCFT test was done to make certain that no syphilis had been overlooked, after 6 months.

The patient was considered cured if:

(1) he had not noticed any discharge since the end of his treatment.

(2) no discharge was found at this examination.

(3) the Two Glass Test did not show any threads.

(4) the prostatic fluid, if obtainable, did not contain any pus or organisms.

(5) blood Wassermann, Kahn and GCFT tests were negative.

(6) Sometimes sounds were passed.
DISCUSSION.

Before discussing the nature of non-gonococcal urethritis, it is proposed to make some comment on the salient findings described above.

The low incidence is the result of conscription, most of the men in the Royal Air Force at the time this series was collected being in the 18 - 30 age group. The incidence of the condition outside the Services would be expected to be parallel to the years of sexual activity, and Sanders (150) found that this was so; his cases occurred most often between the ages of 18 and 45, with a maximum between 30 and 35.

The racial incidence reflects simply the Royal Air Force population round the hospital where the cases reported. It would be interesting to know the total percentage affected of each nationality, as it might be expected that those who had been home longest from and security e.g. the Poles, might have the highest rate of infection.

As far as rank is concerned, the explanation of the fact that all the officers and most of the senior NCO's affected are aircrew is that most of the officers and senior NCO's in the Royal Air Force are aircrew. They live an unsettled, dangerous life and are more like to have sexual adventures than others who have safer duties on the ground; ways of/
living, enjoyed during the short and therefore-let-it-be-sweet life of the war are hard to stop, and habits acquired then are difficult to break in peacetime, until demobilisation and settling down to a career and a family make a clean cut. Accordingly, the percentage of aircrew infected is still high in these immediate years after the war.

One of the most striking features of this series is the high ratio, 51.9%, of non-gonococcal urethritis to gonorrhea. During the war of 1914–18 the incidence was low, being only 4.4% of all cases of urethritis (180); since then it has got increasingly higher. In South Africa in 1938, Behr (9) found it to be 15%; in this country in 1940, Burke (19a) gave the figure as about 30% and this was confirmed by Salaman (149), and in America by Hull (80) who found it to be 32%, and by Leberman (96) who, in a series of 500 cases, found it to be 30%. Even higher figures are given by Gibsch (52) who found in Australia that 45% of his cases of urethritis were non-gonococcal, while Willis (180) found the rate was 62% and 64% in two areas of the same continent. Lees (97) found that 35% of all his admissions to hospital of venereal cases amongst servicemen were non-specific urethritis.

Now, it may be that cases in doubt in the past have been loosely labelled gonococcal even
although no gonococci were seen; but this is a very unlikely explanation, as there is no evidence whatsoever to suggest that venereologists were any less careful in hunting for gonococci in the years gone by than they are now.

A more likely explanation has to do with the modern methods of treating gonorrhea with chemotherapy; possibly the incidence of non-gonorrheal urethritis was fairly high before but the non-specific discharge was obscured by the gonorrheal discharge which persisted because of ineffective treatment. Nowadays, since most cases of gonorrhea clear up in a matter of days, more non-specific discharges are noticed, as they usually develop later. Another point, which will be discussed below under the heading of aetiology, is whether some non-specific urethritis cases are really atypical forms of gonorrhea resulting from either partial treatment with penicillin and sulphonamides, or from atypical gonococci which have become so as a result of these forms of treatment; that is to say, that the increase in the numbers of cases of non-gonorrheal urethritis is not really so high as some of them are really cases of gonorrhea. However, this will be discussed later.

Another explanation is that the propaganda put forth by various public health bodies has made the populace increasingly "VD" conscious, so that the very slight discharge of non-gonorrheal urethritis which hitherto, if noticed at all, was not considered to be of any significance, is now observed at once and
brought for inspection immediately.

The modern contraceptive technique of douching the vagina is also more widely known; and a woman, be she a wife or a prostitute, may regularly douche her vagina for this purpose - and also in the hope of preventing infection - with solutions of such strength as to irritate the more sensitive mucosa of the male coming into contact with the residuum later. Such solutions may be also too strong for the woman herself, and lead to a secondary non-specific infection of the vagina or cervix which she can then pass on to her partner. It is probable too, that many women have become aware of the efficacy of sulphonamide tablets and take them as a prophylaxis before or after intercourse; thus they may pass on a discharge from which the gonococci have been removed, but which is still capable of causing a urethritis in the male.

In this particular thesis, there is also the effect of war and its aftermath to take into consideration: firstly, a trivial discharge which may not concern a contented civilian who is happily occupied with not much spare time to come to a clinic, may cause a great deal of worry to a serviceman who is neither so happy or so busily occupied, in mind at any rate; consequently, the serviceman is more likely to report to his medical officer than the civilian to his doctor. Secondly, there is the upsetting of normal marital relationships and the transferring of men over-
seas, where, away from home and its restraints, more sexual adventures are sought; these extra-marital relationships encourage the amateur prostitute, so that more women may harbour infection than in peacetime. Thirdly, inadequate automedication may have taken place in some cases, since many servicemen, particularly aircrew, jungle and paratroops carry first aid kits which contain sulphonamide tablets. Fourthly, in VD lectures, great emphasis has been laid on the efficacy and importance of the so-called "early treatment" given in the prophylactic rooms. This early treatment may have suppressed a gonorrhea, but left a slight non-specific discharge; or, alternatively, the preparation may have irritated the urethral mucosa, allowing secondary infection to establish itself.

Grenley (56) gives it as his opinion that the Protargol used for this purpose in the United States Army was too strong, and that a certain proportion of cases of urethritis have been due to it.

Most of these possible causes of increased incidence will be referred to again later when the aetiology of the condition is considered.

The Effect of Irritation.

The role of irritation in producing a urethritis will now be discussed.

It was noticed, both in this series and in the literature that the history of most cases contained/
contained incidents which suggested that irritation of the urethra predisposed to the development later of infection. These irritants, broadly speaking, were either chemical or mechanical, and can best be discussed here by first considering those which are associated with the female partner, and then those which are purely of male origin. These will now be enumerated before proceeding to the discussion of the infective aetiology, although, in passing, some mention will inevitably be made of the latter.

A. Female.

Mention has already been made of various irritating solutions that many women use as hygienic and contraceptive measures; such solutions include: mercury perchloride, lysol, alum, quinine, vinegar, and even strong soap, all of which may remain in the vagina in such strength as to effect the male. No estimate can be made of how often this takes place, but it is probably of frequent occurrence.

In 32 cases in this series (approx 25%) intercourse took place just after a menstrual period. This is a considerable percentage and suggests that coitus at this time is potentially dangerous; this opinion is shared by Luys (cited by Harrison (69)), and indeed it was laid down long ago by Moses et al (118) that Jewish women should be considered unclean for seven days from the start of a period, and that intercourse was to be prohibited at this time; penalties were even prescribed for infringers of this law. Harrison (69)
in 1859 recognised that "morbid secretions of the female parts" may produce inflammation of the male urethra, and it is not unreasonable in the light of modern knowledge to expect that the mixture of hormones, blood and products of tissue breakdown should be foreign and therefore injurious to the male urethra. Pelouze states (130a) "An acute discharge, recurring from time to time, and showing a varied bacterial flora in the absence of stricture and redundant prepuce is generally caused by irritating vaginal secretion." It is further known, that any infection that the woman has in her genital tract is likely to flare up at the time of menstruation, so that the man is more likely to contract whatever infection is present. An infection, therefore, borne by a leucorrhrea from, say, a chronic cervicitis, may more readily establish itself in a male urethra which has been irritated and damaged by the menstrual discharge.

One case in this series illustrates this very well: it is of a man, only able to return home at the weekends, whose wife had a leucorrhrea. One weekend, when she was having a period, coitus took place on its second day, and the husband developed a non-gonoccal urethritis two days later. This happened to him on two occasions.

Intercourse, then during or too soon after a period is dangerous, partly from irritation caused by the flow, and partly because of the increase/
increased chances of contracting any infection present in the woman.

Doble (34) quotes an unusual case where a foreign body in the vagina lead to a cervicitis. The foreign body, strangely enough was a small bust of Napoleon which the woman had inserted some months previously to keep her prolapsed uterus in position; the cervicitis caused a urethritis in her partner which cleared up as soon as she removed the bust!

This leads to the thought that the various rings retained, sometimes for months, for the same reason may lead to a urethritis in the husband if the irritation is sufficient to cause a cervicitis in the woman. Even contraceptive occlusive caps, if retained carelessly, could cause cervicitis and urethritis in the same way.

B. Male.

(i) Chemical.

Chemical contraceptives have been blamed for causing urethritis. Dietal (cited by Harkness (67)) reported 3 such cases, Hull (80) a further 3, and Nicol (124a) several. In this series, they were used by only 5 men, all of whom had only marital intercourse; it is impossible to say whether they had anything to do with the production of the discharge. If the chemicals had been responsible, then a repetition of the symptoms would be expected on each occasion the preparation was used; in fact, none of
of the men reported that this happened. However, in two cases the men themselves decided to change the preparation they had been using, in case it had been a contributory factor.

Prophylactic measures were not undertaken in any shape or form in 95 cases (86%), and only 16 (14.5%) used sheaths. There is the possibility that some men may be unduly sensitive to the rubber or rubber-substitute used in the manufacture of the sheath. But it is far more likely that the technique of putting it on was faulty, or that the sheath ruptured.

Early treatment was carried out in 9 cases, although one can hardly merit the name, as it consisted only of swabbing the external genitalia with TCP. The others used the various types of official packets, which contained usually calomel and argyrol, or both; in some cases the treatment was not used quickly enough and in others, was probably inefficiently applied. It may be, however, that the preparation was too strong for some or that others were allergic to the mercury. For the former reason Grenley (56) condemned the use of 2% Protargol in the United States Army as being too strong.

Harkness (67) gives instances of German soldiers in the 1914-18 war introducing corrosive sublimate into the urethra to produce a urethritis in order to get admitted to hospital and so avoid duty in the front line trenches. Behr (9) describes
similar cases occurring amongst troops in Siberia who used vodka to achieve their ends; Lees (97) reported that Cypriots made use of various irritants for the same purpose.

(ii) Mechanical.

Prolonged friction in a dry vagina such as frequently exists in the non-sexually-aroused prostitute, may lead to bruising of the urethral mucosa and make subsequent secondary infection easy.

The repeated anxious milking of the anterior urethra to see whether infection has taken place can lead per se to the production of a discharge. So can excessive masturbation, the incidence of which may be much higher than generally believed. Young (135a) and Harkness (67) give instances of this.

Coitus Interruptus (Winfield Pugh cited by Behr (9)) and prolonged sexual excitement and frustration (Ricard cited by Behr (9)) have also been blamed for causing a discharge, the urethra becoming damaged through repeated congestion.

The careless use of instruments, or even using too hot instruments in the urethra, or leaving in too long an in-dwelling catheter (Harkness (67) and Behr (9)) can be held responsible for trauma predisposing to infection. Radon seeds left too long in the urethra, or excessive diathermy has lead to a discharge according to King (93a).

Various foreign bodies have been found/
found in the urethra associated with discharge, e.g. matches, pins, pieces of catheter, slate pencils, pipe stems, clinical thermometers, cordite from a rifle cartridge etc. (51) and (138). Apart from the catheter remains, the others are usually found in the mentally deficient or the sexually perverted.

(iii) **Systemic.**

Underlying systemic irritants may exist but yet be overlooked by both patient and physician whose minds are pre-occupied with the fact of venereal contact; such a cause may not be looked for until it is realised, after some time, that the discharge is persisting in spite of treatment. Such irritants can be further subdivided:

(a) **Constitutional.**

Discharges have been described occurring in Gout; the explanation here is probably that the urethra is irritated by uric acid (67). Rheumatism has also been supposed to cause a discharge by Harrison (69). Harrison (69) and Harkness (67) also describe cases of Diabetes associated with urethritis, and it is probable that the concentration of sugar in the urine acts as an irritant in the urethra; it is less likely to occur nowadays with modern treatment of diabetes.

Calculi in the kidney pelvis, bladder or prostate may be associated with a discharge as they can give rise to a descending infection. X ray may be
the only way to exclude these; in this series, no calculi were seen.

A growth, benign or malignant, anywhere in the genito-urinary tract may first declare its presence through a discharge from a secondary infection taking place at that point. Diagnosis is made by X ray or cystoscope. No such growths were found in this series.

(b) Ingestants.

Probably the most common irritant of the urethra is alcohol, predisposing both to infection and relapse of an apparently cured urethritis. Fifty-four cases (48%) partook of it on the occasion of the coitus, and 16 (14.5%) admitted to being drunk. This of itself might not be considered significant, but in a further 12 cases (10.9%) relapse occurred within 48 hours of an alcoholic bout. It is well-known that alcohol has an irritant effect on the urethra since it is excreted by the kidney in a concentration approximately that of the blood at any given time; but Farrell (44) in experiments in dogs showed that it is also excreted by the prostate and testes. Confirmation of this has not been found in the literature, but if it is so, then it would explain how relapse can occur in cases apparently cured: the irritation of the prostate leads to damage of its mucosa, and a quiescent infection, which may have been lurking in a few follicles in the posterior urethra or even in
in some of the prostatic acini, can easily re-establish itself.

Whitney (cited by Arknness (67)) describes discharges in men who had definitely no sexual relationship with anyone, which he believed were entirely due to alcoholic excess. As these were described during the period of Prohibition in America, probably the inferior alcohol sometimes imbibed at that time was very irritating to the urethra. Some of his cases, he admits however, had an underlying chronic prostatitis.

A case was encountered in this series of a man who had a severe oxaluria which resulted in a discharge. Phosphaturia has also been believed (67) and (9) to be responsible for one kind of discharge. Another case in the series was that of a man who had a discharge following the eating of an unusually large amount of cucumbers; Davies (28a) described a similar case. Other foodstuffs said to be responsible for a urethral discharge are: Cress (67), Asparagus (67, 69), Strawberries (67) and Dandelions.

Various drugs, if taken to excess, can also lead to a discharge: Cantharides, capsicum, copaiba, cubebs, arsenic, iodides, turpentine (9),(67) guiacum cayenne pepper (69) mustard (129). These substances are broken up into chemicals which irritate the urethral mucosa as they are excreted in the urine, so that secondary infection is easily superimposed.

Thus it can be seen that irritation
of one sort or another is associated with discharge; sexual contact may or may not be the act that provides the organisms which set up the infection. It is concluded that the irritation either produces a true a-bacterial urethritis or else lowers the resistance of the urethra enabling the easy establishment of infection.

Consideration will now be given to the role of infection in the production of non-gonococcal urethritis.

**Manner and Nature of the Infection.**

As a result of the various methods of investigation (smears, cultures etc.) numerous organisms were found in 49 cases in this series, there being in each case one organism judged to be predominant; in 59 cases, there was no one predominant type, but a mixed infection of various organisms; and in 11 cases, no organisms could be found at all.

This would suggest that there are three types of infection: (1) where there is one predominant infecting organism; (2) where there is a mixed infection; (3) where there are no demonstrable organisms at all.

Each of these groups will be examined in turn, and the role of the various organisms concerned will be discussed. A digression will be made to include Reiter's Disease and Abacterial Pyuria as this is/
a convenient point to discuss their place in the differential diagnosis of non-gonococcal urethritis.

1. One Predominant Organism.

This group includes all those organisms which it is believed can produce a urethritis by themselves or with, maybe, favourable predisposing conditions of trauma and irritation. Not all of them were encountered in this present investigation, and it should be remembered, too, that the gonococcus is omitted as it does not directly cause a non-specific urethritis.

Many of the organisms (Staphylococcus, streptococcus, diphtheroids etc) form the normal flora of the glans penis, prepuce and fossa navicularis, as described by Jungano (86). It is therefore sometimes difficult to decide whether the presence of any particular one in the discharge is indicative of its pathogenicity or not. The only way to settle this would be to culture the organism found, and inoculate another urethra from a subculture, and see whether a similar urethritis developed. No record of this having been done can be found in the literature, so that it cannot be definitely established that any of them can cause a direct urethritis. What is significant however, is that, in such cases, the particular organism found is present in large numbers at the height of the infection and disappears as the
infection clears up; this strongly suggests that it has a part to play in the production of the urethritis.

A. Staphylococcus.

Many cases of staphylococcal urethritis are mentioned in the literature, and most authorities are of the opinion that it is the commonest causative organism. (67). More recent discoveries concerning L organisms and viruses may modify this opinion in the future, but this will be discussed below.

Direct infection following sexual contact is the usual way of contracting a staphylococcal urethritis, and cases have been described by, amongst others, Harkness & King (63), and Herrold (74). Usually, staphylococcus albus is the type concerned, but staphylococcus aureus has also been found (63).

Blood borne infection can also occur. One such case occurred in this series: a man who had been bed-ridden for some months had an attack of boils followed in a few days by a urethritis, the predisposing factor being a congenital stricture. Two similar cases of boils and urethritis are recorded by Harkness (67), who also noted that stricture, postgonococcal, traumatic or congenital can be a predisposing factor. One other case is described by Hull (80).

B. Coliform Organisms.

Opinions vary as to the frequency with
which these organisms are met with in urethral infections. In this series it was never identified, though it was probably one of the Gram negative bacilli occasionally seen on a slide from a smear. Romanis & Mitchiner (139) placed Bacillus Coli at the head of the list of infecting organisms; they record the case of a medical student who gave himself a coliform urethritis by taking his temperature first in the rectum and then in the urethra without washing the thermometer in between. Kretschmer et al. (92) also thought the organisms of this group were the most common, but they were discussing chronic prostatitis, some of which were associated with a urethral discharge. Gibson & Wiley (53) stated that in their opinion it was the second most commonly met organism. Other workers only found it occasionally present such as Walker (173) and Harkness (67) found that such a urethritis took a longer time to clear up than other types and was very likely to become complicated by spread to the upper urinary tract giving rise to cystitis and pyelitis. Another case is described by Fieldsend (48).

C. Other relatively common organisms.

Many other organisms have been reported as being present in urethritis, and they usually occur as mixed infections. They are too numerous to have a paragraph each and will be described under the heading of mixed infections. Bacillus Proteus, however, may occur by itself (140) sometimes after rectal coitus.
Like the coliform infections, it is liable to
give rise to a protracted infection which may spread
to the upper urinary tract.

D. Treponema Pallidum.

This organism is not found very of-
ten, but it is mentioned now, because it is so impor-
tant that it be remembered and excluded in every case.
An intra-mental chancre may give rise to a slight pur-
ulent discharge which may be thought insignificant
unless the meatus is examined. Hull (80) had one
case, and Behr (9) mentions others.

The meatus should be palpated for
hardness, and the lips opened for inspection. Blood
Wassermann and Kahn tests, which should in every case
be taken at the first visit and at the last, will safe-
guard against missing such a chancre.

E. Bacillus Ducrey.

A soft chancre may exist in the me-
atus and give rise to a discharge. But the presence
of others on the external genitalia, and the demonstra-
ton of the bacillus microscopically should make the dia-
gnosis clear.

F. Tubercle Bacillus.

This organism should be suspected
and searched for when the discharge persists and other
causes for this e.g. chronic prostatitis, folliculitis
and stricture, have been excluded. In this series,
only 2 cases came under suspicion; three 24 hour specimens of urine were centrifuged and the sediment examined for organisms. Guinea pig inoculation was not done on the advice of the bacteriologist, and the cases in question cleared up later. X ray of the kidney may reveal a focus of infection there, and examination of the prostate and epididymes may reveal spread of the disease to these glands. It is rare to have a tuberculous urethritis without a lesion higher up the urinary tract and in the prostate or epididymes.

G. Trichomonas Vaginalis.

This protozoon was first described by Donne in 1836 (35). In women, it is commonly met with in association with a profuse foul-smelling discharge, which usually clears up after one or more courses of acetarsol tablets inserted into the vagina. The tendency to relapse is great. Stuhler (163) gave it as his opinion that 40 - 60% of adult women harboured the organism in the vagina. In view of this high incidence, a similar finding would be expected in man; but this is not so. Up till 1941 only 145 cases had been collected in the literature (7); since then, probably as a result of the increasing interest taken in non-gonococcal urethritis, more cases have been recorded; but even so, the incidence is nothing like so great as in women. Liston & Lees (170) found it in only 16 out of 400 consecutive cases at a VD clinic. Hogue (170) found it only once in the examination of 633 urinary/
sediments.

The reason for this is probably that the male urethra is regularly flushed with urine so that any incipient infestation is thereby washed away; whereas, in the vagina, there is no such washing, and the organism has time to establish itself in its crypts and folds. If trichomonas vaginalis is a pleomorphic form of trichomonas hominis, as is believed by Nit-schke (121), which frequently inhabits the large intestine, then contamination by it of the vagina would be an easy matter; further, owing to the proximity of the two organs in the female, such contamination is more likely than in the male where the two organs are separated. But this pleomorphism is disputed, although as Lydon points out (183) it might explain the occurrence of the infestation in virgins.

The first case of male infestation was described in 1893 by Miura (113).

In such cases, the discharge is slight and the other complaint usually is frequency. Sometimes there is an itching of the glans. The diagnosis can only be made if the organism is seen either in the urethral discharge, prostatic fluid or urinary sediment. Skin tests and complement fixation reactions have been tried in cattle (in whom the disease causes great havoc with much economic loss,) but the results to date have not been very reliable.

Infestation of the male or female
can take place during coitus either from the infected vaginal discharge or the prostatic secretion. Nitschke (120) describes an example of the latter taking place when a wife was re-infested by her husband whose prostatic fluid was later proved to harbour the organism. Drummond (37) in a small series of cases found 80% of the husbands of infested wives to be infested, although they did not always have a discharge. Kar- naky (89), on the other hand, found that only 25% of such husbands were so affected.

Although a discharge does not always take place, it can do so as rapidly as 24 hours after infestation (182). Nitschke (120) considers that when there is a discharge, it is not due to the trichomonas but to the accompanying bacteria, and this is now generally believed. It is in keeping with the common observation that sometimes the organism is present without any discharge, and when there is a profuse discharge, gonococci, staphylococci, or other mixed organisms are also present in large numbers; this would appear to indicate that some form of symbiosis is necessary before the trichomonas becomes pathogenic (cf Vinvent's infection of the mouth.) It may also be, however, that the presence of the trichomonas is quite incidental, merely taking advantage of the other infections to multiply.

Lydon (103) describes what he thinks is a resting, "encysted" phase which he claims to have
watched, and he postulates that alteration to this form may explain the difficulty in recognising it. He also suggests that the flagella are for feeding rather than for movement.

Various complications have been described, including pyelitis in the male (103), and pyelitis and cystitis in the female (112) (123). Although this infestation causes abortion in cows and sterility in bulls, no such effects have been described amongst humans. Stricture is often associated with it (170), but this is considered to be the result of some other previous or concomitant infection. 65% of Riba & Harrison's cases (133) had previously had gonorrhea.

In this series, in spite of intensive search, no such protozoa were found. It is probable, however, that the two cases who developed a discharge from their wives - their discharges being very foul-smelling and clearing up with insertion of tablets into the vagina - were cases of infestation with trichomonas. Unfortunately neither of these or their wives were seen during the course of the disease.

Treatment in the female is usually successful with pentavalent arsenical in tablet form inserted into the vagina; other methods have been tried in the male. Lydon (103) reported that penicillin, sulphonamide and mepacrine have not produced any dramatic results; others (170) recommend various
solutions (protargol, potassium permanganate, silver nitrate, silver picrate, mercurochrome, acriflavine, metaphen, mercury oxycyanide, hydrogen peroxide, and zephiran.) The very number of these preparations shows that it is the mechanical washing effect rather than any specific virtue in any of the solutions that clears the condition up.

It is more difficult to eradicate it from the prostate; daily diathermy and prostatic massage every second day, followed by bladder lavage, would seem to be the most successful method of treatment.

H. Virus Infection.

A urethral discharge may be an early sign of Lymphogranuloma Inguinale (3) (162a). The intra-cutaneous Frei-Hoffman Test is needed to diagnose the condition with absolute certainty, but usually, the inguinal buboes make the nature of the infection clear.

The suggestion that there may be other viruses which can give rise to urethritis has been made by several writers, and the long incubation period of 3 or more weeks in some of the cases in this series is in keeping with a virus infection, (cf. mumps.)

Several clinicians claim to have seen inclusion bodies in urethral smears: Johnston
& McEwin (85) found them in 2 cases, and Williams (179) working with Australian troops, found them in 8 out of 34 cases in North Queensland, and 10 out of 19 cases in Borneo.

The inclusion bodies were always in the large epithelial cells, and never in the smaller polymorphonuclears; they were very small being from .3m to .5m and quite different from those causing marine and scrub typhus, psittacosis and lymphogranuloma inguinale. (179).

On the other hand, expert bacteriologists, as opposed to these clinicians, who after all are not necessarily first class microscopists, have failed to find any viruses. Henderson & egg (73) found no evidence of inclusion bodies in a series of 52 cases nor did Rhodes (73) in over 300 cases, nor did either of them, along with Meenan, find any in the cases they examined for this series.

The matter must therefore rest sub judice for the moment, with possibly a slight bias in favour of their being a virus yet to be discovered. More will be said on this subject later.

I. Pleuro-pneumonia-like Group of Organisms.

Pleuro-pneumonia bacilli were first cultured in a cell-free medium in 1898 (124b) by
by Nocard and derive their name from the disease they cause in cattle. Other similar organisms are found in decaying leaves, soil and manure (156) and are capable of causing disease in certain animals.

Some cause agalactia in sheep and goats, which is a mammary gland infection associated with joint and eye manifestations; others cause lymphocytic choriomeningitis in mice (145) and a form of ankylosing arthritis (146); they also occur in the normal conjunctival and nasal secretions of mice (147). In rats, they cause bronchopneumonia, bronchiectasis, and one form of rat-bit fever in association with streptobacillus moniliformis (144).

This latter disease is of particular interest here, since it was while investigating it that Kleineberger first used the name L organisms for the sake of brevity when describing the pleuro-pneumonia-like organisms; this contraction is now in general use.

In humans, L organisms have not been found in the faeces (93), nor in the throat (144) nor in the conjunctiva (147a). It is therefore a reasonable assumption to suppose that they are not human commensals, and that when they occur they are pathogenic. They have also been looked for and not found in the joints of persons suffering from Rheumatic Fever (51a) (147) (164).

They were first described in genito-
urinary infections by Dienes (32) who found them in
the genitalia of 5 out of 15 women. Two years later,
in 1942, in collaboration with Smith (33) a series of
129 unselected cases of urethritis and cervicitis had
been examined, from which 24 out of 85 females, and 4
out of 44 males had yielded L organisms from their
genito-urinary tracts. All of the males had chronic
prostatitis, and 2 of them had in addition arthritic
symptoms. In another series of 100, they found L
organisms in smears taken from cases of cervicitis,
Bartholin Gland abscesses, and salpingitis. They
also described a case of a man which chronic prostat-
itis who developed a wrist synovitis from which L org-
anisms were isolated; the wrist cleared up, but shortly
afterwards, his wife came to hospital with swelling of
both knees which had started 2 weeks after her mar-
riage; L organisms were isolated from her cervix, but
not from her joints. In all the male cases of
Dienes and Smith, there was always a chronic prostat-
itis, chiefly of gonococcal origin. Salaman, however
(149) did not confirm this relationship with prostat-
itis.

Beveridge (11) with a careful tec-
nique to prevent contamination, isolated L organisms
from 4 out of 24 cases of male non-specific urethritis,
and concluded that this figure would probably have
been higher if he had been able to examine the cases
when they were fresh and had not been treated with
irrigations as some of them had. Johnston and McEwin (35) found them in 2 cases which also had inclusion bodies; (this will be remarked on later during the discussion on Reiter's Disease.) Beveridge et al (12) found them in 20% of their cases of non-specific urethritis and 3 out of 11 cervical smears taken from the female partners, none of whom complained of a discharge. These workers also found them in the apparently normal female cervix, but they were absent from the urethroae of 67 male students.

Salaman (149) isolated them from 34% of his cases of male gonorrhea, only 7% of his cases of non-gonococcal urethritis, and 6% of his post-gonococcal urethritis. In a control group of 24 cases from the skin department, none of which had any obvious urethritis, 4 had L organisms in the urethra or urine. In a further communication, (148) Salaman described a very interesting association between these organisms and gonococci; when penicillin was placed on the chocolate agar medium in which there were growing colonies of gonococci and L organisms, the former disappeared leaving vesicles indistinguishable from L colonies. This raises the question of the nature of these organisms.

They are in size and culture habits intermediate between bacteria and viruses, being filterable through bacteria-proof filters, and yet able to grow on/
on non-living media; their granula-containing vesicles resemble very much the intra-cellular inclusion bodies found in certain viruses (148). Their ability to survive penicillin as described above and their apparent increase coincident with the disappearance of gonococci, suggest that they may be pleomorphic, involutionary forms of gonococci. It is not without significance in this connection that Salaman was able to isolate them in all the 83 cases he had tried to so far where he grew gonococci in the presence of penicillin. (The gonococci were, of course, obtained from genital discharges.) It is possible, of course, that these two organisms live in obligate symbiosis, or that the L organisms are just frequent contaminants.

Subculturing of the organisms on to another chocolate agar plate has not yet been achieved but it has been done on other media, notably that described by Henderson Begg as "Sloppy Agar" (73). This worker has also worked out a rough life cycle of the L organisms, details of which will appear shortly in the literature; he also does not consider that they are the cause of urethritis, and has considerable evidence to suggest that they are not.

In this series, it is very much regretted that it was not possible to isolate these organisms for reasons which have already been stated during the description of the investigation. Consideration was given to the possibility of sending speci-
mens to Henderson Begg in London, and a few of the slides taken for virus search were so examined; but it was decided that the time taken for them to reach London was too long to permit of the useful examining of fresh, undried-up specimens.

Dienes and Smith (33) devised a serum complement fixation test which, however, only gave positive results in 2/3 of the sera tested. Further, 44 out of 158 sera which were WR positive also gave a positive reaction to their reaction, and the sera of 17 out of 24 cases of atypical pneumonia were also positive. It was therefore realised that the test was unreliable, for even if it reacted to show the presence of the L organisms in the body, there was no means of showing whether it was reacting to their presence in the urethra or perhaps in the lungs.

To sum up: Pleuro-pneumonia-like organisms have been found in the genital discharges of many cases of gonococcal and less frequently non-gonococcal urethritis and cervicitis. It has been shown that they can be passed from one to another by sexual intercourse. Joint manifestations, both in animals and humans have been mentioned in association with their presence elsewhere in the body, and conjunctivitis has also occurred. In spite of all this circumstantial evidence there is so far nothing to show that the organism definitely causes a urethritis but the possibility of this should be borne in mind for the present.
It is convenient at this point, to make a small digression from the discussion of the micro-organism predominant in the discharge to consider this question of associated joint and eye affections.

**Joint and Eye Manifestations.**

It is generally held that there are three main types of the syndrome where there are a urethritis, conjunctivitis and an arthritis. The fundamental difference between them being that the first and second are associated with definite infections, i.e. gonorrhea and dysentery respectively, and the arthritis is usually monarticular, while the third, known as Reiter's Disease, has no connection with either of these infections and the arthritis is usually polyarticular. Sargent (151) has suggested that until the true nature of this last is known, it should be called Idiopathic Blennorrheal Arthritis. It is not considered, however, that this is a good term to adopt since, often, the keratodermia blennorrhagica is absent.

It should also be mentioned that conjunctivitis and arthritis have been reported occurring in cases of Syphilis (105), Staphylococcal septicaemia (37) and Amoebic Dysentery (46). These cases were reported many years ago, and it may be that in the first, a non-gonococcal urethritis was also present, in the second a staphylococcal urethritis, and in the third a bacillary dysentery. But this is rather begging the question, and more/
Altogether nearly 100 cases, purporting to be Reiter's Disease, can be found in the literature, although in not all of them was the symptomatology completely developed, nor were gonorrhea and dysentery for certain excluded; more modern serum agglutination tests, had they been available and made use of, might have disclosed some more dysenteries.

The first true case was described in 1899, before Reiter, by Launois (104). Lever & Crawford (104a) collected 45, one of which was in a woman up to 1944, and Miller & McIntyre brought the total up to 65 in 1945. Since then, more cases have been reported by others, among them Gerah & Reich (57a) Baxter (6a) and Jackson (83a). The correspondence started by the last-named ran for some time and several writers wrote of the confusion between this disease and dysentery. The fact remains that such a syndrome does exist in the absence of both gonorrhea and dysentery.

Reiter's Disease may start either with the urethritis - most commonly - or with a conjunctivitis, the arthritis occurring some days, weeks, or even months later. (6a) (45) (67a). Very occasionally the arthritis has been the first to be noticed (71a) (67a). The arthritis usually affects the larger joints more than the smaller, such as the interphalangeal ones; the X ray appearances of the joints suggest that the changes are akin to the "rheumatoid"
type of arthritides (45). The aspirated fluid, however, resembles the specific infectious types containing, as it does, polymorphonuclear cells and an excess of protein (13).

The urethral discharge has considerable numbers of pus cells, but no organisms. The urine contains albumen. There is frequency with dysuria, usually terminal, and sometimes meatal itching is felt. Prostatic massage often reveals pus cells, and, if the condition progresses to cystitis, the frequency and dysuria become more marked and there is a terminal haematuria. Upper renal tract complications have been described by Colby (23) - 2 cases of hydronephrosis - and by Feiring (45) 1 case of pyelonephritis and by Harkness (67a) dilatation of the renal pelvis.

The conjunctivitis may progress to an episcleritis, an irido-cyclitis and a keratitis. Superficial ulcers may appear on the buccal membrane, the lips, tongue, glans penis and scrotum. Keratoderma blennorrhagica often occurs on the soles of the feet and palms of the hands (66).

A moderate pyrexia accompanies the symptoms; the WBC count is raised maybe to 10 - 20,000; there is often an eosinophilia; the BSR is raised; the GCFT is, of course, negative as are all agglutination tests for bacillary dysentery. Sometimes there is splenomegaly. Feiring (45) described two
cases in which there was delay in the Auriculo-ventricular conduction while the condition lasted.

The disease usually gets worse for 1 - 4 weeks after its onset, clearing up spontaneously in 1 - 7 months. Physiotherapy, and pyrotherapy are of value (15) (151) but sulphonamides and penicillin are in most cases useless (67a). In those cases where chemotherapy has been of value e.g. Jackson's cases (83a), the possibility of dysentery had not been ruled out, and it is further known that some types of dysentery react very favourably to chemotherapy. (Such treatment might form the basis for a therapeutic diagnostic test, in so far that if the condition did not respond to penicillin or sulphonamides, then it was more likely to be a true Reiter's Disease, than a manifestation of gonorrhea or dysentery.)

There are other cases too, where ocular symptoms have been described in association with genito-urinary infection, but in which no arthritis has developed; these might be considered as examples of incompletely developed Reiter's Disease, although there are points of difference which will be mentioned below. Various eye inflammations, iritis, irido-cyclitis, uveitis etc, have occurred in persons suffering from chronic prostatitis of non-gonococcal origin, which did not yield to treatment until the latter was cleared up. Dernehl (31) in 1914 was the first
to describe this, citing 5 cases. He was followed by Zentmeyer (188) who had 4 cases, Schweinitz (155) with 3, Thomasson (165) with 5, and Irons and Brown (33) who had 3, 1 of which relapsed when the prostatitis flared up again through riding in a car over a very bumpy road.

The consensus of opinion amongst these writers was that various organisms, lurking in the prostate, were for some reason (e.g. passage of a hard constipated stool, coitus) forced into the bloodstream and came finally to rest in the eye because of some unknown tissue affinity there. It was pointed out that bacteria present in the prostate were nearly always extra-cellular, thus indicating the poor response of the body's defence mechanisms, so that when they arrived in the bloodstream they were able to survive and reach the eye. None of these workers however, demonstrated that the organism in the prostate and in the eye were of one and the same strain; in fact, the only relationship definitely between them was that they cleared up together when treatment for the chronic prostatitis was commenced. Thomasson (165) claimed that a similar process of metastasis occurred in some cases of gonorrheal ophthalmia.

If this hypothesis is correct, it could also be expected to explain arthritis complicating similar infections; the joint fluids on such occasions, however, are almost invariably sterile.
A similarity, at any rate, can be seen in outward appearances between these ocular manifestations subsequent to chronic prostatitis and those occurring in Reiter's disease, and it may be that the former are but incompletely developed forms of the latter. If that were actually the case, it would be expected to occur more often when chronically infected prostates are massaged, whereas, what usually happens then, if anything, is that an epididymitis develops, and no cases of epididymitis have been described occurring in Reiter's Disease. Another point of difference is that the discharge in Reiter's disease is sterile, while in most cases of chronic prostatitis, microorganisms can be demonstrated.

The aetiology of Reiter's Disease is still unknown. Reiter thought he had found the cause in a spirochaete, which he called Spirochaeta Arthritis (143a), but this has not been confirmed. Sargent considered the possibility of the syndrome being due to a vitamin deficiency, but concluded that if it were, it would be found more often than it is amongst large bodies of men, amongst whom, in fact, there had occurred only one or two cases.

Bauer & Engleman (19b), in a very thorough search failed to find either bacteria or virus inclusion bodies. Recently Harkness (66) claimed to have isolated the latter from the discharges of the urethra and conjunctiva in 5 cases; he also claimed to/
to have produced a urethritis in a volunteer who had synovial fluid from an affected joint from a case of Reiter's Disease injected into his urethra; the urethritis took 17 days to develop.

Other clinicians too, have found inclusion bodies in the epithelial cells of cases of urethritis and conjunctivitis; but none, however, have been found in the joints, which is not surprising considering the difficulties of obtaining synovial epithelial cells. Braley (15) demonstrated that a virus he found was limited to living in the transitional zone of epithelium of the cervix which resembled that of the conjunctiva.

The first to describe inclusion bodies occurring in conjunctivitis were Halberstaedter & Prowazek (60) in 1907, and though at first some thought that the bodies found were only the cellular reaction to typical or atypical gonococci (75), it was finally agreed that they were true inclusion bodies. The same two workers in 1909 further demonstrated the presence of morphologically similar inclusion bodies in the cervix uteri of mothers whose babies developed inclusion conjunctivitis shortly after birth, and this was confirmed by Hamburger in 1934 (62) and Thygeson & Mengert (167) in 1936; the latter also mentioned a case where a gynaecologist received a spurt of blood in his eye while performing a Dilatation and Curettage.
and he developed an inclusion cervicitis 6 days later.

Fritsch et al (cited by van Rooyen and Rhodes (141)) found that they could produce an inclusion conjunctivitis in baboons using scrapings from an infected male urethra; this conjunctivitis could then be passed from animal to animal. Huntemuller & Paderstein (cited by Thygeson and Stone (169a)) described a form of inclusion conjunctivitis occurring as an epidemic amongst swimmers, and thought that the cause was a virus liberated in the water of the swimming pool through urination.

Van Rooyen and Rhodes gave it as their opinion that in inclusion conjunctivitis, the genital tract was sometimes infected as well, being a cervicitis in the female and a urethritis in the male (141).

When viruses were discussed as a possible cause of non-gonococcal urethritis, it was shown that some workers had found them in a few cases, but that others, in larger series, had found none. In connection with this form of urethritis in Reiter's Disease, many authorities have shown that viruses found in the urethra can produce a conjunctivitis. It must be accepted therefore, that there is a virus which can produce urethritis (and/or cervicitis) and conjunctivitis; but whether it can also lead to arthritis is another very debatable matter. So far no inclusion bodies have been found in the epithelial cells of the joint membrane. But that there is some infective re-
relationship is shown by Harkness's case, quoted above where a urethritis was produced by washing the urethra with fluid from the affected joint.

L organisms have also been isolated from the discharges of a few cases of Reiter's Disease. Dienes and Smith (33), quoted above, isolated them from the discharges of 2 men who had joint symptoms, 1 who had a synovitis, and 1 woman who had joint symptoms; but they did not have any conjunctivitis. Recently, Henderson Begg, cited by Harkness (67a) found them in the discharge of a typical case. It has been already remarked, however, that they have also been found in normal urethrae and cervices, so that their pathogenicity is in doubt.

Another explanation, not yet discussed, is that the arthritis is an allergic manifestation, the body having been rendered hypersensitive by the urethral and/or conjunctival infection (cf the supposedly allergic arthritic phenomena of streptococcal tonsillitis.) This explanation was favoured by Biegibock (13), especially as there is often an eosinophilia present. Further, there is usually an interval of 14 days or more before the arthritis succeeds the urethritis and conjunctivitis.

It is not impossible that the body becomes hypersensitive to more than one organism e.g. the gonococcus, the bacillus of dysentery or a virus, which would then explain why the same symptom triad.
is found in association with such differing diseases as dysentery, gonorrhea and non-gonococcal urethritis.

It is our belief that some explanation of this nature is the correct one.

After this discussion on Reiter's Disease, a summary of the whole of this first section on infection will not be out of place.

The various organisms which have been found predominant in the urethral discharges have been enumerated and their pathogenic role as causative agents has been discussed. It has been concluded that all of those mentioned, with the exceptions of Trichomonas Vaginalis and the L organisms, can cause a urethritis. These exceptions were considered to be organisms which were taking advantage of the inflammatory reaction to multiply, and were not by themselves capable of causing a urethritis; in the case of the trichomonas, it may be that some process of symbiosis is present, and in the case of the L organisms, they may be involutionary forms of some other micro-organism.

Consideration will now be given to the organisms which are present as a mixed infection, no one of which can be considered as being predominant.


So many organisms are sometimes found that
it is impossible to incriminate any one of them as the primary infective agent. Their very mixture suggests that they are all secondary to some other primary cause. This primary cause may be

(a) severe trauma.

(b) some other infective agent which has been cleared up or has died out e.g. the gonococcus, or some of the organisms in the first section.

(c) some other organism has been missed through faulty laboratory technique.

(d) some other organism, present but has not yet been discovered e.g. a virus or a spirochaete. This possibility will be discussed under the next heading.

Since the L organisms and inclusion bodies have only fairly recently had attention drawn to themselves, they are not generally sought after as a routine at every VD out-patient clinic; and it may be that when easier methods of isolating and identifying them are known, some cases of urethritis will be found directly due to them, although other organisms may be present as well to obscure the picture.

The organisms which have been found occurring in mixed infections, apart from those mentioned in section 1 are: streptococcus, and diplococcus pneumoniae (114); micrococcus catarrhalis (154) (74) (26) (105); micrococcus faix and caeruleus (181); diplobacilli (67); enterococcus protoformis (109); bacillus influenzae (150)/
bacillus acidophilus (150); various spirilla from the mouth, which in Abeshouse's opinion (1) arrived in the urethra either from using saliva as a precoital lubricant, or from buccal coitus. Frequently, diphtheroids are found and Ritter & Lipow (134) quoted the work of Heckel et al. who thought that these were dissociating forms of streptococci; they claimed to have produced such diphtheroids from a pure single cell culture of streptococci in broth.

It is considered that it is extremely unlikely that all of these can individually produce a urethritis, and so it is concluded that each takes advantage of some previous infection already present to multiply to such numbers that they can be seen microscopically as a mixed infection.

Some authorities (148) (67) talk of a post-gonococcal urethritis; by this they mean that there has been a gonorrheal discharge, which cleared up, but was followed by another discharge sometime later. As an explanation of this, it can be possible for a double infection to have taken place at the time of risk viz. a gonococcal and a non-specific, so that when the former is cleared up, the latter, commonly resistant to chemotherapy, remains, or appears for the first time. It is believed that 2 cases in this series were of this type, as they both developed a non-gonococcal urethritis 5 weeks after the date of risk, and 21 days after the complete clear
up of the gonorrhea with penicillin.

Another possible explanation is that gonorrhea leaves a damaged urethra with lowered powers of resistance. So that later, in circumstances not normally favouring infection e.g. moderate alcohol intake, urethritis develops, with any of the above named organisms which happen to be around on the skin multiplying in the discharge. Four cases of this nature occurred in the series, where the gonorrhea had been within 3 months; in the 12 other cases where the gonorrhea had occurred more than 3 months before, it was considered that there was no connection of this nature between them.

There is still another possibility to be considered, and that is that the gonorrhea had left eventually a chronic prostatitis in which the gonococci had either died out or existed in an altered form; then with suitable stimulus to the prostate, i.e. excessive intercourse or chronic constipation, the gland had discharge some irritative fluid into the urethra and set up a non-specific urethritis.

To sum up: when a mixed infection is found in the urethral discharge, then, most likely, there has been some previous irritation of the urethra; this irritation may have been due to any of the irritants mentioned when these were discussed, or it may have been some previous infection of the urethra such as gonorrhea. The resistance of the urethra is thus
lowered and any of the above-mentioned organisms which are about take advantage of this to multiply and produce the mixed infection urethritis. Such a urethritis is primarily an irritative rather than a specifically infective one.

A typical example of this type of urethritis is as follows: a man, more or less under the influence of alcohol, has intercourse, and during the next few weeks anxiously milks his urethra to see if he has picked up any infection. The urethral damage that all this causes, facilitates the entry and establishment of whatever skin, clothing, or oral microorganisms are available so that a urethritis is inevitable.

3. No demonstrable organisms.

In 11 cases in the series, no microorganisms were demonstrated, and many other such cases are on record in the literature. It is likely, that with wider knowledge and a better technique, organisms already known about will be discovered more frequently; but that does not exclude the possibility of there being as yet undiagnosed organisms responsible for the condition.

It is convenient at this point, to include in the discussion the question of the so-called Abacterial Pyurias. It was, indeed, this condition which originally stimulated the collection of this series of cases, since it was thought, that in some cases, the amount of pus in the urine might amount to a dis-
charge, so that the condition might present as a non-gonococcal urethritis.

It is believed that the term Abacterial Pyuria embraces a number of conditions, (cf non-specific urethritis,) but that amongst them there is one which has such very similar clinical manifestations to one type of non-gonococcal urethritis that it is concluded that they are different stages of the same infection. This type of Abacterial Pyuria has its pathology centred in the bladder, and it will henceforth be referred to as Abacterial Cystitis to distinguish it from other forms; it is this form which has aroused so much interest in the journals recently.

This Abacterial Pyuria is thought to start in most cases, as an anterior urethritis which spreads upwards to involve the posterior urethra, the trigone and finally the whole of the bladder. (36) (48). On the other hand, quite often, no discharge is noticed, and this may be because the infection did not start in this fashion but attacked the bladder directly; but more likely, it is thought, the discharge, like all non-specific discharges, was so trivial as to escape attention.

Nearly all the cases admit to sexual intercourse beforehand, and a very large percentage of cases are respectably married people. Handley (65) in a series of 433 women, found that 80% of them
first complained of symptoms within 3 months of marriage, and in 10%, the symptoms were so soon after marriage as to be called "honeymoon cystitis." In 310 of his patients, there was evidence of urethritis, and he described areas of hyperplasia of the urethra which he termed "hillocks", which correspond, doubtless to the eminences described by Deakin (30) which have already been mentioned when dealing with the urethroscope appearances of the infected male urethra.

The manifestations of the condition are well described by Wildbolz (178) (177) who first treated it with NAB, and by Cook (25). The symptoms are; frequency, dysuria, usually terminal and severe, and sometimes terminal haematuria. The urine is nearly always sterile, or it wouldn't justify the name, although in some of the acute cases, some bacteria, such as Bacillus Coli are occasionally found at the very onset and they disappear in a day or two. Pus is always present, and usually red blood cells and albumen. On cystoscopic examination, the bladder capacity is found to be very markedly reduced; there is sooner or later, a very severe inflammation of the bladder mucosa, and there may even be ulceration; but in other cases, the inflammation is patchy, being most marked in the trigone area. The posterior urethra is usually also inflamed.
or retrograde pyelograms occasionally show dilatation of the pelves of the kidneys, amounting in some cases to hydronephrosis (28a). Whether this is only a congenital defect, found by accident during the course of investigation, or whether it is a result of the toxicity of the infecting organism is difficult to say. Probably both can occur. Evidence in favour of the second possibility is supplied by Colby who described such happening during the course of two cases of Reiter's disease: in one, a bilateral dilatation of the renal pelves occurred, and in the other, the dilatation first appeared on one side and developed into a hydronephrosis which was removed, and after this had been done a similar dilatation appeared on the other side which had hitherto been normal. These dilatations disappeared as the condition cleared up. These cases are put forward as evidence that toxic dilatation of the renal pelvis can take place, and not to try and prove that Reiter's disease and Abacterial Cystitis are the same condition, although that is quite possible.

Whether there is pelvic or ureteric dilatation or not, catheterisation of the ureters will very often reveal the presence of pus. This has led to the belief that in some cases, at any rate, the infection is a descending one. While this is probably so, it does not exclude the supposition that there is a form of abacterial cystitis which appears as just
described and which is definitely an ascending infection resulting from sexual intercourse, the pus in the upper urinary tract being evidence that the infection is widespread in that system.

The course of this ascending type is very chronic and may resist the usual forms of therapy for months and even years. It clears up, however, very dramatically after a few intravenous injections of arsenic. Indeed, so dramatic is this cure, that Schaffhäuser (153) uses it as a diagnostic test: if a cystitis with an abacterial pyuria of longstanding clears up within a few days with NAB, then it is assumed to be non-tubercular and no further investigation for tuberculosis is undertaken.

The aetiology of the condition is not fully understood. In some of the acute cases, bacteria have been found, and it may be that these persist in small numbers sufficient to maintain the infection, but insufficient to be seen or cultured (171) (49). It is thought that this is an unlikely explanation as centrifuging the urine and culture of the deposit would surely produce a colony if there were any organisms there at all. The conclusion to be drawn from this is that there must be some organism or organisms, as yet undiscovered, which are responsible for the condition.

Several workers, among them Ewert and Hoffman (42) Moore (115) /
Donovan (36) and Briggs (16) have thought that a virus might be responsible, but none of them have actually demonstrated the presence of one. It would almost seem that they had finally come to blame a virus, faute de mieux, because the usual methods of isolating and identifying bacteria have failed.

The fact that the condition clears up so dramatically with arsenic suggested to Peters (130) that some spirochaete might be responsible since some other spirochaetal infections also cleared up with arsenic e.g Syphilis, Relapsing Fever, Chicken Spiroillosis, Yaws (39), Vincent's Angina (136), Pulmonary Spirochetosis (124) and Weil's Disease (132). The fallacy of this argument is, of course, obvious, but spirochaetes have been reported as having been seen by Bisquertt-Torres (13a) and more recently by Coutts and Vargas-Zalazar (28a). These latter workers found spirilla under dark-ground illumination, which were of diverse morphology and they thought they belonged to the buccal or intestinal mucosa; they did not say how, in their opinion, the organisms arrived there, whether it was by pre-coital lubrication with saliva, buccal coitus, blood borne, or direct spread from the anus.

While there is no reason to doubt that these spirilla were present - and spirochaetes have been found in the urine of cases of nephritis, trench fever, relapsing fever, and Weil's disease (28a) - it
is questionable whether they are responsible for the infection or not; certainly their disappearance coincided with the exhibition of arsenic and was followed by cure of the condition, but the smegma spirochaetes were probably eliminated by the arsenic too, and they are believed to be non-pathogenic.

Nevertheless, it does seem likely, principally because of the well-known effect of NAB on spirochaetal infections, that this form of Abacterial Cystitis is due to a spirochaete.

Attention will now be turned to the other forms of abacterial pyuria, including those that are the result of descending infection, some of which can present as a urethritis. When the pyuria is so marked as to amount to a discharge, it is obviously a pathogenic entity; but, sometimes, when it is much less marked, there is difficulty in deciding whether the pus cells seen microscopically are indicative of urinary infection or are quite normal.

Helmholtz (71) believed that to find 2 - 3 leucocytes in a low power field of centrifuged urinary deposit in the male was quite normal; in a high power field, Eisendrath and Rolnick (40) stated that 5 - 7, Helper (72) up to 8 and Dukes (33) up to 10 were still normal. Anything over these figures is generally agreed to be abnormal and to constitute a pyuria.

In the lower urinary tract, a chronic
prostatitis may cause a persistent abacterial pyuria, without any other signs or symptoms being present, although, usually, perineal or low-back pain will draw attention to the condition. In this series, there were several cases in which the only sign of a chronic prostatitis was this mild pyuria with an occasional flare up into a discharge. Faltin (43) gave instances of similar happenings in cases of gonococcal prostatitis.

Aseptic calculi, anywhere in the urinary tract may irritate the mucous membrane leading to the production of pus cells which appear in the urine; in most cases, a few red blood cells will also find their way into the urine; Moore (115) and Peters (129) both give examples of this. Other symptoms and signs which draw attention to the calculus usually appear before long, such as pain locally or referred to the very tip of the penis, or lower pole of the testicle, and frequency with the passing of more red blood cells in the urine.

Moore also had 2 cases of carcinoma of the bladder which had sterile pus in the urine (116). Adjacent inflammation e.g. chronic salpingitis, appendicitis, or an abscess near a ureter, may cause a pyuria in which no bacteria can be found (8). Lindajo (100) removed what he thought was a tuberculous kidney, and later found, when the pyuria continued, that there was a small ureteric fistula connected with a focus of
chronic bone sepsis.

Briggs believes that a hydronephrosis per se may cause a sterile pyuria (16).

At one time, it was thought that pus coming from the kidney was always tuberculous (131) (142) and many nephrectomies were performed on this evidence alone. This belief was challenged by Runeberg in 1920 (143) since he found at necropsy on kidneys he had removed as tubercular, that only 33% of them actually were so, whereas 12.5% had aseptic calculi, and in 55.5% (30 cases) no evidence of tuberculosis could be found. Bumpus and Thompson (18) said that in nearly every case (80% in their experience) of tuberculosis of the upper urinary tract there is spread to the genitalia which can be discovered clinically; Moore (116) claimed that in 90% of cases of renal tuberculosis, tubercle bacilli could be seen in the microscopic examination of the centrifuged urinary deposit. This is tantamount to saying that if there are no tubercle bacilli to be seen in the urine, and no signs of tuberculosis in the prostate and epididymes, consideration should be given to the possibility of the condition being an abacterial pyuria before nephrectomy is performed to remove what is taken to be a tuberculous kidney.

What, then, is the nature of this condition if it is non-tubercular? In some of Runeberg's cases staphyloccoci were found in the renal cortex,
and he thought that the pyuria was a result of a blood-borne staphylococcal glomerular nephritis, during which bacterial waste-products were eliminated by the kidney causing what he called an "elimination pyelitis."

In this connection, it may be mentioned, Moore (116) had 9 cases of nephritis in which there was a sterile pyuria. Troell (169) had 1 case of chronic nephritis.

Peters (129) also found non-tubercular inflammatory changes in 5 out of 15 nephrectomies which he had performed for suspected tuberculosis. Soderland (158a) described a case in which he performed a unilateral nephrectomy, whereupon the remaining kidney began to produce more pus than formerly.

Schaffhauser (153) had 19 cases, and in the kidneys of some of these he found an unusual strain of streptococci; this strain only grew, and very slowly at that, on special media; when injected into dogs, these organisms produced a subacute pyelitis. This finding, however, has not been confirmed by others. Moore (116) found a facultative anaerobe and streptococcus viridans in the urine of one of his cases. Other cases have been reported by Oudard (127) Bonanome (14) and Houtappel (79).

The consensus of opinion concerning this type of abacterial pyuria seems to be that it is due to kidney infection; the result of the infection i.e. the pus, is eliminated and excreted in the urine, while the cause, i.e. the organism, is retained.
Soderland (158a) thought that the original infection might die out, but leave sterile pus behind which was slowly excreted, and quoted as an analogy to this the sterile pus left in the gall bladder after acute infections had died out as noted by Gray (55). Peters (129) recalled that various chemicals could irritate the kidney and thought that this irritation could lead to the production of sterile pus.

It could be concluded that in cases where the pyuria clears up with the usual therapies, that the infection is probably caused by one of the common organisms, and where it is resistant to these but clears up with NAB, then it may be that the spirochaetal infection mentioned above, has spread upwards from the lower urinary tract.

Cook (24) and Coutts and Zalazar (28a) made some interesting observations on the relationship between some cases and septic foci elsewhere. It appears that chronic sinusitis, cervicitis (65) dental decay (28a) etc have some connection with pyuria and discharge, if not actually causing them, at least preventing their cure. Two cases occurred in this series where cure was delayed until the maxillary antra were washed out, and a tooth extracted. It may be that because of these septic foci, a mild bacteraemia exists which leads to a mild infection of the kidney parenchyma with the production of pus which is then eliminated in the urine.
To sum up: various conditions can cause pus in the urine; when pus originates in the upper urinary tract it may be from adjacent sepsis, calculus, or neoplasm, or may be the result of a blood-borne kidney infection; when it originates in the bladder or lower urinary tract, it is usually the result of an ascending infection, and in some cases the pyuria may be so gross as to amount to a discharge; the etiology of some of these lower types is straightforward e.g. gonococcal prostatitis, but in other cases no organism can be found and they may be due to a spirochaete or a virus.


A urethral discharge has been recorded during the course of several systemic infections, and this possibility must be borne in mind when there is doubt as to the origin of any particular discharge. Usually, however, the diagnosis is not in doubt as the main infection is well established before the discharge appears; then the doubt may arise as to whether this is a venereal infection which is only then showing itself.

The presence of a discharge during Dysentery has already been mentioned in the discussion on Reiter's Disease.

Sreenivasan (159) described a case occurring in typhoid fever in a Chinese patient. The dis-
charge showed itself on the 41st day of the disease, and there was no previous history of venereal disease. Bacillus Typhosus and Staphylococcus Albus were cultured from the discharge, and he suggested that the staphylococci were secondary contaminants of the discharge which he considered to have been caused by the typhoid bacilli. It may, of course, have been the other way round, and he makes no mention of whether the man had any staphylococcal skin conditions at that time. He quotes Fraser as referring to other cases occurring during typhoid.

Berry (10) records a case where a discharge appeared due to Bacillus Diphtheriae, and one man in this series said that his discharge became much worse while he was suffering from Diphtheria. Discharges have also been recorded during Mumps, "measles, Influenza (163) and Intermittent Fever (181), Typhus, and Malta Fever (67). It is possible that some of these were non-gonococcal urethritis of the virus type with the long incubation period so that they were missed, not being generally known about.

In this series, one urethritis was preceded by diarrhoea a few days before; but this was considered to be only a mild gastro-enteritis, and anyway, it cleared up by itself in a few days.

There would appear to be a relationship between the production and maintenance of a urethral discharge and the upper respiratory tract. In this series, 2 cases suffered from colds prior to the
onset of their urinary symptoms. Another two, referred to in the previous section, did not clear up until the maxillary antra had been thoroughly washed out, and in one of them a tooth also extracted. This is in keeping with the findings of Cook (24) and Coutts and Vargas-Zalazar (28a). It may be that infection of the respiratory tract with L organisms could lead to, or at any rate maintain a urethritis, since the serum reactions of Beveridge et al (12) were positive in 17 out of 24 cases of atypical pneumonia. However, it has already been decided that these organisms have little if anything to do with these conditions.

5. Skin Affections.

Cases of urethritis have been reported as being due to a spread of various skin affections into the urethra. The skin conditions concerned are: herpes genitalis (Harkness (67)) and it is usually easily recognised by its vesicles elsewhere on the glans and shaft; psoriasis (Behr (9)) which is present usually elsewhere on the body; and various forms of dermatitis, which again are usually present on the rest of the body as well. Intra-meatal warts have also been known to become infected and give rise to a discharge (67).

6 Neoplasms.

Cases are on record where the first
sign of a new growth in the bladder, prostate or urethra was a persistent discharge, (9). Instrumentation is necessary to make this diagnosis, and treatment is, of course, in the hands of the surgeons.

7. Preputial Infections.

Discharges from a Balanitis or a Balanoposthitis may lead a patient to think he has a urethral discharge. When the area is thoroughly examined, however, the true nature of the condition will be seen, and can be treated accordingly.

Two such cases occurred in this series, and they cleared up rapidly with repeated washings and the application of saline soaks. In spite of the simple nature of this infection, blood tests should be taken monthly for three months to exclude syphilis and gonorrhea.

Symptomatology.

All the cases in this series had a discharge, and this has already been described in the section dealing with the results of the investigation.

The most conspicuous thing about this type of discharge is that it is very slight and not at all resembles the profuse one of gonorrhea. In some cases, all that can be seen is a stickiness of the meatus in the morning/
with perhaps a slight staining of the underclothes; in others there is a definite "morning drop" but it clears up during the day after micturition and there is only a slight meatal dampness till next morning again. The discharge itself is painless.

When pain is felt, it is nearly always in association with the passing of water - hence its name, dysuria - although in a few cases it is apparently unrelated to it. Often, too, the sensation is more of a tingling or a burning sensation than a pain. In three times as many cases, it came before the discharge, suggesting thereby that the inflammation at first was only slight and later as it got worse pus was formed so that a discharge appeared - possibly indicating secondary infection.

At one time it was considered that it might be possible to tell from the type of dysuria which part of the urinary tract was infected and how severely; it was even wondered whether the particular infecting organism could be identified from the type of dysuria it caused. (This was the original reason for analysing the dysuria groups in such detail.)

It has been realised that this latter view is untenable since it has been found that the same organism can give rise to different types of dysuria as the infection spreads up the urinary tract. The former view, however, has a certain amount of truth in it, but it is not always easy to interpret any particular dysuria with certainty.
It is believed that when there is no dysuria, the infection is a mild one and confined to the anterior urethra. This is confirmed, it is thought by the fact that, in this series, the infection associated with this type of dysuria clears up more rapidly than the other types with a lower percentage of relapses on only 20gm of sulphonamide.

More difficulty is encountered in interpreting the other forms of dysuria. Dysuria before, at the start of, towards the end of, and after micturition, it is believed, indicate infection of the bladder, and probably of the posterior urethra, and prostate as well. This type of pain is usually referred to the anterior urethra about $\frac{1}{4} - \frac{1}{2}$ an inch from the tip. These three areas are often all infected together; this is almost inevitably so, because of their proximity, but maybe also because two are developed from the same mesodermal structure (4) (5) (175a), so that spread between them should be easy.

(It should be mentioned that others, notably Frazer (50) think that the trigone is entodermal in origin. But if they are all mesodermal, it may explain the similarity of their referred pain (cf the results of bladder sympathectomy and parasympathectomy (95)).

The severity of the infection determines how acutely the dysuria is felt, and also, it is thought, whether it is felt at the end of micturition only or at the beginning as well. In the
severest infections, the pain is felt at the start, because the bladder muscle commences to contract on the very sensitive congested mucous membrane; this pain may continue all through the act, but in less severe cases it stops, but starts again towards the end and may persist for a few moments after until the new tension is developed and the membrane adjusts itself. The time at which the pain is felt does vary to some extent with the region of the bladder, posterior urethra or prostate that is affected, but no anatomical studies to demonstrate this could be found and the matter must be left as a hypothesis.

The nervous pathways of this reflex is presumed to be through the parasympathetic fibres supplying the bladder (183) to the hypogastric ganglia and thereafter back through the 3rd and 4th sacral nerves (70) (95).

Dysuria during the act is also difficult to interpret. It may arise from the bladder in the manner just described if the infection is very severe; but more often it is due to some of the following causes. The acidity of the urine may irritate the inflamed surfaces of the urethra, and certainly the taking of alkaline mixtures often relieves the pain which starts again if these are stopped. Such pain is usually felt all the way along the anterior urethra, though it may be felt most as one particular point where there is a chronic folliculitis or a
stricture. Chemical substances in the urine e.g. oxalate crystals, may also cause dysuria during the act. The very volume of the urine may cause much pain by stretching the oedematous mucous membrane.

Another type of dysuria associated with the prostate has a slightly different mechanism, it is thought. It has been noticed (and this has been confirmed by some colleagues on themselves) that suitably delicate stimulation of the frenum will produce a tingling which is described as somewhere in the perineum. It is suspected that "prostatic" dysuria is this sensation in reverse; that is to say, irritation of the prostate will reproduce a sensation in that area of the penis, namely the frenum, which normally when stimulated itself, will cause the prostate and vesicles to react and so induce an ejaculation. Such an irritation of the prostate may be produced by the lower pelvic organs re-adjusting themselves to a new mutual tension after emptying of the bladder or rectum. A few cases in this series remarked during prostatic massage that they felt a tingling at their frenum. It is probable that it is this reflex working in reverse that cause the painful erections associated with chronic prostatitis.

Pain unrelated to micturition obviously cannot be caused by happenings in the anterior or posterior urethrae, as these structures are at rest when no urine is being passed. This sensation must there-
Before come from the prostate or the bladder or maybe both. This pain may be caused either by rise in tension in the bladder as it fills up with urine, or by increasing and decreasing tension in the prostate as it produces its own secretions.

The symptoms of frequency occurred in only 27% of these cases. This is not a startlingly large figure, but the distribution of cases amongst the dysuria groups is rather surprising. Nineteen per cent of those who had no dysuria, 45% of those who had dysuria during, and 23% of those who had dysuria before, and after etc., complained of the symptom.

It had been previously thought that frequency was mainly a symptom of cystitis, since the bladder capacity was then reduced and had to empty more often, and the mucosa was more irritable so that it sent distress signals at the least feelings of tension. These figures now suggest that frequency can also occur in anterior urethritis. It is believed that the explanation of some of these is psychological; many of them were aware that all was not well with their urinary system, and as they worried about this, their mind was drawn to the realisation that their bladder was filling and needed emptying, which gave an excuse to see if the discharge had cleared up. It is further significant, that all the cases in this group complained of a very mild frequency of not more than 6 times.
during the day and in only 5 cases, once during the night as well. In the cases where the frequency was more severe - up to 12 times daily and more than once during the night - it was believed that there was bladder infection present, the pain during the act of micturition being due to the bladder muscle squeezing the congested mucosa the whole time.

Haematuria occurring in association with a urethral discharge may appear at the start of or the end of micturition; it rarely appears during it as then it is due to a sharp urethral calculus, neoplasm or injury. If it is present at the start it is probably due to an injury to the anterior urethra as from a kick. If it is terminal, which is the commonest kind, then it is due to the final contraction of the bladder muscle squeezing a few drops of blood from the congested mucosa, and is accompanied by pain.

Both the cases of haematuria in this series were due to severe cystitis which was confirmed by cystoscopy.

The symptoms of backache and other referred pains from the prostate and seminal vesicles will be discussed later in the section on complications. The sexual disorders described in cases of urethritis are nearly all psychological.
Incubation Period.

One of the chief values of knowing the incubation period of a disease is that that knowledge helps towards the diagnosis of the condition.

The most significant fact about the incubation period of most cases of non-specific urethritis is that, in the majority of cases (in this series 70%), it is much longer than that of gonorrhea which Young (134) stated was 2 - 14 days with an average of 5 days. In only 30% of the cases of this series was it less than 14 days. This is in keeping with the findings of others such as Harkness (67), Beveridge et al (12), McRea (109) and Williams (179). But others consider the period to be shorter, such as Walker (173) 4 - 9 days, Grenley (56) 1-16 days, and Wolbarst (131) who gave no specific number of days.

A difficulty was encountered when analysing the dysuria groups to know where to place those that had intercourse regularly, and it was finally decided that there was no alternative to omitting them; there were not very many anyhow, and it is unlikely that they would alter the other figures to any great extent. The analysis only included those whose incubation period was from 1 - 8 weeks; when the period was longer than that, it is doubtful if there was any relation between the intercourse and the symptoms. But there may be an answer, however, to this doubt: either the condition is caused by a virus/
with a very long incubation period (cf virus jaundice) or the urethritis was at first so mild as to escape notice entirely, and as it was consequently neglected, it gradually became worse till finally, with much super-added infection it produced a macroscopic discharge with a slight dysuria which was then observed.

In other cases where intercourse took place much longer ago than 8 weeks ago, there is the suspicion that the whole truth has not been told in the subconscious hope that if the doctor has no grounds for saying that the disease was contracted during intercourse he will tell the patient: "yes, this is not a venereal disease, and must be due to some other cause." Possibly too, some of these cases are due to masturbation, and the trauma so produced enables the skin organisms or maybe some organisms collected during coitus, to start an infection.

The shortest incubation period was that of the group which did not have any dysuria, the average being 3.15 weeks. It should be noted, however, that in 27% of the cases in this group, the incubation period was 4 weeks. As this was also the group in which there was the smallest number of relapses after sulphonamide therapy, the view that it is the mildest form of non-gonococcal urethritis is confirmed. In the group where there was dysuria during micturition, the average incubation period was 3.6 weeks. One
conclusion that could be drawn from this is that the body's resistance was less in this group than in the preceding one, so that a more severe urethritis can take place, although the infecting organisms may be the same in similar cases.

In the other groups, taken as a whole, to indicate bladder, prostate or posterior urethral infection, the average incubation period was 3.56 weeks. As this is slightly shorter than the second group, it is concluded that even though the organism has a longer distance to spread, it must have a partiality for the upper regions of the lower urinary tract, and the disease starts there without giving any signs of its presence in the anterior urethra beforehand.

Division of the cases into the smaller dysuria groups did not yield any significant finding.

Complications.

There is always the danger in an untreated or inadequately treated anterior urethritis, that the infection will spread up the urinary tract; or for infection starting in the upper urinary tract to spread downwards. This spread of infection to cause complications elsewhere will now be considered.

A. Folliculitis.

The glands of Littré often become chronically infected and as they then do not drain properly,
they prevent the complete clearing up of the urethritis. In some cases (3 in this series), these enlarged glands can be felt like hard peas when palpated against a urethral sound, and if they are then burst open by digital pressure, they drain and the urethritis is given a chance to heal. In other cases, where the infection is not so marked as this, the mouths of the infected glands can be seen through the anterior urethroscope; in such cases, some authorities (30) recommend their being treated with the cautery under direct vision.

E. Stricture.

If a urethritis is left untreated for a long time, a stricture is liable to be formed. Two such cases took place in this series. The stricture is soft compared with the type found in gonorrhea, probably because the infection in non-gonococcal urethritis is less severe in the anterior urethra so that less fibrous tissue is formed. Deakin (30) describes areas of hyperplasia in the epithelium of the urethra which he called "Tabs" and possibly several of these coming together would cause a stricture; the stricture is usually not present all the way round, but only one half or three quarters of the way.

The first symptom of stricture is simply that the discharge persists, and then pain may be felt at its site. Later, the flow of urine may be gradually reduced and terminal dribbling may occur.
is either made by a sound meeting obstruction or by seeing it through the urethroscope. The treatment is not difficult and consists in passing sounds of increasing calibre until the urethra is the normal size; sometimes meatotomy has to be done to let the larger sounds in.

Congenital and Traumatic strictures also exist and greatly dispose to the development of urethritis later if suitable circumstances arise.

C. "Cowperitis."

Retention cysts of this gland were first described by Fenwick (47) in 1896; in his cases, the principle symptom was a chronic urethral discharge, some, if not all, of them being due to the gonococcus. The glands can become chronically infected in nongonococcal infection too.

The symptoms and signs are: a dull heavy feeling on one or other side of the urethra in the perineum near the anus, which is exacerbated by cold and may spread down the leg; a sense of tickling or formication in the posterior urethra; a distinct, though slight obstruction to the flow of urine, probably due to spasm of the compressor urethrae, which Fenwick demonstrated by pumping air into the urethra; finally, the enlarged glands can be palpated with one finger in the rectum and the thumb on the perineum.

No such cases were encountered in this series. The treatment consists in cauterising the glands, usually after incising them to permit /
D. Posterior Urethritis.

If the infection spreads up the urinary tract, the posterior urethra is inevitably infected. It is rather surprising that this does not happen more often than it does, since there is no mechanical bar to prevent it; an explanation of this may be that there are possibly differences in the epithelium composing the anterior and posterior urethrae since the former is developed from the ectoderm, and most of the latter from the mesoderm (4), so that infection will not normally spread from one to the other without some stimulus to do so e.g milking of the urethra or prolonged coitus.

The symptoms of posterior urethritis are sometimes difficult to distinguish from those of prostatitis and cystitis; and it is probably true to say that it is best diagnosed by the absence of the other signs and symptoms of these other areas. There is a discharge in no way different from that of anterior urethritis and the dysuria is usually terminal; there may also be a mild frequency. Haematuria is rare unless the infection is one which has been superimposed on an impacted calculus or bleeding neoplasm. This form of urethritis takes a longer time to heal up than the anterior form and is very prone to relapse.

E. Prostatitis.
The anatomical relationship of the posterior urethra to the prostate is so close — the latter being derived from the former — that it is almost inevitable for infection to spread into the prostate, giving rise usually to a chronic prostatitis, although sometimes an acute prostatitis or even a prostatic abscess will occur.

In this series 20 cases (17%) were found to have a chronic prostatitis. Very few of them had any other signs or symptoms of prostatitis than pus in the prostatic fluid, and it was concluded that the infections were mild and, indeed, they all cleared up with massage of the gland within 7 days (except 2 that had septic foci elsewhere.)

In the pre-chemotherapeutic era post-gonococcal prostatitis was much more common than it is today; but even in those cases, it was sometimes impossible to find the gonococcus, and it had to be assumed that the original infection had died out. Nowadays when a prostatitis comes on some time after the gonorrhea has been cured, it is realised that a double infection can take place in which the gonorrhea is cleared up by the penicillin or sulphonamide while the non-gonococcal urethritis is incubating and then spreading to involve the gland. But even in the old days, some authorities (92) recognized that non-specific prostatitis was relatively common, in the opinion of Kretschmer et al. even being as high
as 33% of all cases of prostatitis.

Chronic prostatitis should be suspected and looked for when a discharge does not respond to the usual forms of treatment, especially when sounds have shown that no folliculitis or stricture are present. There may, also, be other signs and symptoms to draw attention to the gland as the seat of the infection, such as pain in the perineum. This pain is most likely to be felt when something upsets the pelvic equilibrium or presses directly on the gland e.g. the passing of a hard, constipated stool, or there is sexual or emotional stimulus to the gland. This latter effect was so common an experience in the longshoremen of San Francisco, a large number of whom were sufferers in the pre-chemotherapeutic era, from chronic prostatitis that Wesson (175) states that there used to be a common expression amongst them: "You give me a pain in the perineum!"

Prostatic pain may be referred to other regions of the body, notably the lumbar area; Young et al (186) give an interesting table showing the areas of the body so affected in 358 cases. A peculiar sensation which is sometimes felt, and which is thought to be pathognomonic of the condition is a floating feeling felt in the perineum when coming to a sudden stop after running upstairs, or going over a switchback in a road in a car.

The diagnosis is confirmed by find-
ing on palpation that the gland has either soft, boggy or hard, indurated areas in it. Curiously, in most of the cases in this series, the induration was in the left-hand lobe. It must be remembered that the infection may be confined to the anterior parts of the gland and therefore not palpable rectally. Pus in the secretion expressed by massage, after urination so that any infection in the anterior urethra is washed away, makes the diagnosis certain. Very frequently, there are organisms in this fluid, but unless the very elaborate technique outlined by Ritter and Lipow (134) is followed, it cannot be said for certain that they come from the gland or not; but this technique is too elaborate for every day use in a clinic, and it has therefore to be assumed that any pus and organisms that are found after prostatic massage are from the gland. Butchel and Cook (19) state that there are normally cocci in the gland but that is not believed to be true, as many prostatic secretions have been examined in which there were neither pus nor organisms; it is believed, therefore, that the presence of pus, with or without organisms is always indicative of infection in the gland.

F. Vesiculitis.

Wesson (175) considers that prostatitis and vesiculitis are one and the same disease, since infection of one inevitably involves the other.
It is doubted whether this is quite true of every case, but if it is, the infection of the vesicles must be a very low grade one as few cases are recorded of acute symptoms being complained of, (aching in the perineum, and pain referred to the iliac fossae, on the right side simulating appendicitis.) No such cases were encountered in the present series, although in other series, one or two have been seen.

G. Epididymitis.

Non-gonococcal epididymitis has attracted a lot of attention during the recent war as so many cases occurred as sequelae of non-specific urethritis. In one series of 680 cases, 582 followed non-specific urethritis, 19 were tubercular, and only 79 gonococcal (6).

Tubercular epididymitis is not usually difficult to diagnose since it rarely occurs as a primary manifestation of tuberculosis, but nearly always is the result of spread downwards from upper urinary tract infection. Often tuberculous nodes can be palpated in the prostate, and ureteric catheters produce pus with demonstrable organisms in it.

Many conditions have been associated with epididymitis: Mumps (103) Smallpox (6), Meningococcal septicaemia (64), Undulant Fever (32), Typhoid Fever (63) (174) /
Influenza (27) and non-gonococcal urethritis (99), (135) (2) (108). It is only those that are a complication of non-gonococcal urethritis that will be considered here, but the others should be borne in mind in difficult cases, especially the tuberculous kind.

The non-gonococcal type is most likely to occur when an acutely inflamed prostate is examined per rectum, no matter how gently. This happened in two cases in this series; but other cases occur without this interference. There is the possibility then that there has been some strain, such as lifting a heavy weight, passing a constipated stool, which has resulted in the backflow of urine down the vas deferens (160) (2) (107); Handley (64) casts doubt on this conception, since he considers it unlikely that a fluid which excited no inflammation in the bladder should be responsible for an inflammation in the epididymes. This objection does not seem to be a very good one, as first of all, the bladder is designed to deal with urine and the vas and epididymes are not; and second, the urine on its way from the bladder may pick up infection from the posterior urethra and prostate and carry it down to produce epididymitis.

Another way in which infection could spread is after prolonged sexual excitement such as in coitus interruptus or erotic thinking, so that the whole genital tract becomes very congested and infection is encouraged to spread (135) (6).
It has also been suggested that it is more likely to occur in men who are dirty and careless about washing these areas; but in that event, troops under field conditions would be more liable to develop it, whereas, the reverse is the case: it is in comfortably home-based troops that the condition appears.

It may also be caused by chill and trauma (6) (107). This is likely to be the explanation of those cases who deny ever having had sexual intercourse; if there is any septic focus in the body with a resultant bacteraemia, the lowering of the resistance following chill or injury, is sufficient to allow an infection to establish itself there.

Treatment will be discussed later.

H. Cystitis.

In this series, there were 4 cases of cystitis which occurred as a complication of non-gonococcal urethritis. Other cases can be the result of a descending infection from the kidneys, or the result of a blood borne infection, or the result of direct spread from an adjacent abscess. Sometimes a definite organism can be incriminated, but more often none can be found, and this abacterial type has already been discussed.

The symptoms and signs are:

(1) Frequency because of the decrease in capacity of the bladder wall, and increase in the
wall; this irritability is most marked during the day when it is aggravated by movement, so that the frequency is mainly diurnal.

(2) Dysuria is usually towards the end, after or in severe cases before or even all during the act of micturition. This has already been discussed, but one further point is that patients will often say that the last drop is the most painful to pass, being followed by a stabbing pain as the external sphincter closes; they will, therefore stand for as long as possible passing an occasional drop of urine, trying to postpone the final closure, and if they wait long enough, sometimes the two inflamed surfaces come together relatively painlessly. Sometimes the pain is referred through the hypogastric plexus to the supra-pubic region or the groin, or through the sacral nerves to the scrotum, perineum or inner surfaces of the thigh (133).

(3) Haematuria and its mechanism has already been described.

(4) Intravenous pyelograms should always be done to exclude calculus and also upper urinary tract lesions which may have lead to the infection. In such films, the bladder can often be seen to be smaller than normal and with a very "wooly" outline indicating gross infection.

(5) Cystoscopy should also always be done to exclude calculus, neoplasm and tuberculosis. It will
also give an approximate idea of the extent and severity of the inflammation, though it must be remembered that the reddening of the mucosa seen inside can be greatly modified by altering the pressure in the bladder caused by the irrigating fluid.

In the 4 cases cystoscoped in this series, 2 were very severe infections, and 1 was mainly a trigonitis. This latter finding is of particular interest since Handley (65) is of the opinion that nearly all the cases of non-specific urethritis in women are really cases of urethro-trigonitis; in men, that would be analogous to the belief that when infection spreads from the anterior urethra, the posterior urethra and trigone are simultaneously infected. This is quite possible since it is known that these two structures are probably developed from the same embryological tissue (4).

I. Pyelitis and Pyelonephritis.

These complications from an ascending infection are rather rare. One case however did occur in this series, where the pyelitis and the urethritis started simultaneously. There was shivering rise of temperature and pain in the loins; toxic signs of headache, malaise and anorexia were also present. The causative organism was not found and the condition subsided on sulphonamide.

Before the treatment of gonorrhoea by chemotherapeutic means, more cases occurred;
these were either directly due to the gonococcus itself or to the associated secondary infection. But now with better methods of treatment fewer cases occur; such as have been recorded will be discussed in the section concerning treatment.

**Treatment.**

Several forms of treatment have been tried at one time or another to clear up non-gonococcal urethritis, and considering the number of different causes of these conditions, it is not surprising that they do not react in the same way, some clearing up quicker than others. Sometimes, in very protracted infections, after many forms of therapy have been tried, the discharge gradually disappears; it is then suspected that the particular therapy being given at that time gets the credit for the cure, whereas, in point of fact, the condition has actually died out. It should be understood that in addition to the treatments mentioned below, every encouragement was given to healthy habits of living, eating and drinking.

1. **Simple, Non-infective Discharges.**

   (a) **Seminal Excess.**

   The only treatment, if treatment it can be called, is normal, regular sexual intercourse. Most cases occur in virile men, who, for one reason or another are continent, although exposed to sexually
arousing stimuli. When regular ejaculation can occur there is no overflow, and the symptom disappears. Often a patient will volunteer the information that he has noticed this happening after a nocturnal emission. Reassurance of the patient should be all that is necessary.

(b) Alcoholic Excess.

Provided there has not been any secondary infection, which so frequently, however, does occur, this form of urethritis will clear up spontaneously in a short time. The taking of mild alkaline diuretic mixtures and copious bland fluids accelerates its disappearance. If there is infection it should be treated as an infective condition (see below.)

2. Systemic Infections.

These forms all clear up with the disease they are associated with, unless secondary infection is allowed to set in. A mild alkaline diuretic mixture and copious bland fluids should prevent the irritating, concentrated urine of pyrexia from doing any damage.

3. Skin Affections.

(a) Herpes Genitalis.

A dry dressing with dusting or sulphathiazole powder is usually all that is required. The area should be washed daily before the clean dressing is applied.
(b) Psoriasis.

The nature of this skin complaint is unknown. The usual tar preparations that are customarily applied to the skin are too strong for the sensitive urethral mucosa, and it is best left alone; or at most, a mild ointment such as Boracic can be applied daily. The condition will disappear in its own time, but may come back again later.

(c) Dermatitis.

Various forms of Dermatitis can spread to the glans and meatus, and the diagnosis depends on recognizing the condition elsewhere; the same treatment that is applied elsewhere on the body can be applied here too, bearing in mind the sensitivity of the urethra.

4. Infected Urethritis, Anterior and Posterior.

It has been shown that many different organisms can cause a urethritis; but in spite of this, it is customary to treat non-gonococcal urethritis as though it were one disease. In the pre-sulphonamide era, chief reliance was placed on urethral irrigations and the taking of copious bland fluids by mouth. There is no doubt that in many mild cases this is all that is necessary, and even where more intensive therapy is employed, irrigation forms a useful adjunct as it ensures the washing away of any discharge which might otherwise accumulate and tend
to spread the infection farther up the urinary tract.

With the discovery of the efficacy of sulphonamides in the treatment of gonococcal urethritis, it was a natural conclusion to expect similar good results in the non-specific type as well; and in many cases the giving of 20gm sulphathiazole is adequate to ensure cure. But it is also true that a very large proportion of cases so treated either never clear up or relapse very quickly. This is either because the drug was not given in adequate doses, or more likely, because the infection was due to sulphonamide resistant organisms.

Accordingly, the rational way to treat a case of non-gonococcal urethritis would be to identify the causative organism - if that be possible - and find whether it is sensitive to chemotherapy. If it is, then the appropriate drug will clear it up, and if not, then pyretotherapy should be instituted at once as it is the most consistently successful method of treatment available today.

To illustrate, however, the general attitude towards non-gonococcal urethritis at the present day, a series of 98 cases reviewed by King and Williams (90) will be considered. They treated their cases in bed with 23 - 25gm of sulphapyridine given in 3 days. Their results, less 1 who died and another who became seriously ill (presumably because of the side-effects of the drug), are given in Table 4.
Table 4

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number cured</th>
<th>Av. number hosp. days</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 - 25gm needing more treatment</td>
<td>28%</td>
<td>13</td>
</tr>
<tr>
<td>&quot; considerably &quot; &quot;</td>
<td>7%</td>
<td>23</td>
</tr>
<tr>
<td>&quot; considerably &quot; &quot;</td>
<td>65%</td>
<td>48</td>
</tr>
</tbody>
</table>

In addition to having the sulphapyridine, they all had a citrate mixture by mouth.

Comparing this method of administering sulphapyridine with a series in which the drug was given over 14 days (4gm for 3 days, 3gm for 11 days), the results are as follows:

Table 5

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number cured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requiring no additional treatment</td>
<td>35%</td>
</tr>
<tr>
<td>Requiring a little additional &quot;</td>
<td>6%</td>
</tr>
<tr>
<td>Requiring considerably more &quot;</td>
<td>59%</td>
</tr>
</tbody>
</table>

It is unfortunate that in neither of these two series was the additional dosage of sulphapyridine given.

In this series, the routine treatment laid down by the Special Treatment Centre at Halton was to give 20gm sulphthiazole at first, but giving more if the discharge showed no signs of abating when this had been given. Occasionally, sulphadiazine or sulphamezathine were given instead. The maximum amount
given of any of the sulphonamides at one time was 38gm.

Of the 82 cases treated with sulphonamides 51% only cleared up; the other 49% required further treatment in some other way. That is to say that 49% of the cases were caused by sulphonamide-resistant organisms. (It is possible that if the drug had been continued, eventual cure might have resulted; but there are two reasons why this was not done: firstly, because sulphathiazole can cause skin hypersensitivity reactions if given for too long, and secondly, because it was considered that these resistant cases would probably clear up quicker with a different therapy, and to save the patient's time, this was tried at once.)

The subsequent form of therapy varied, depending at which Centre the patient was being treated. At Ely, injections of NAB were given. This was done because of the believed connection between some types of non-gonococcal urethritis and the type of abacterial pyuria which clears up so dramatically with arsenic.

Arsenic was first used in the treatment of urinary infections by Gross (57) who successfully treated pyelitis and pyelocystitis of gonococcal origin with neosalvarsan; he also noticed that coliform infections were unaffected by it. It has also been used as a urethral irrigation by Heslin and Wilner (77) in cases of acute gonorrhea; but as their results appeared just at the time the sulphonamides began to be-
come known about, and were not so good, no more was heard of this method. In passing, they stated that they had "startlingly good results" in so-treating cases of staphylococcal urethritis.

Kall (88) also showed that injections of neosalvarsan had a beneficial effect on some cases of non-gonococcal pyelitis. Young (136) cleared up 1 case of staphylococcal pyelitis and elsewhere (135) stated that it had no effect on pyelitis caused by streptococci or bacilli.

Butchel and Cook (19) tried NAB (.15gm, .2gm or .3gm being the usual dosage) against various types of urinary infection caused by different organisms. They found that in 189 patients (male and female) whose infections were caused by cocci (staphylococci, streptococci and micrococci,) 48% did not improve; and in 57 patients where bacilli were responsible (Bacillus Coli, and other Gram negative bacilli) 93% did not improve. Nine per cent of their cases had toxic reactions, mostly of the skin.

The dramatic cure of both upper and lower urinary tract infections effected by NAB has already been referred to. The first to use arsenic in this connection was Wildbolz (178) in 1933, and his favourable results were confirmed by Schaffhauser and de Minicis (152) in 1935. Since then others have reported successes with it: Briggs (16), Moore (116), Ewert and Hoffman (42), Cook (25), Donovan (36), Lydon
In this series, 21 new cases, 20 sulphonamide resistant, and 2 penicillin resistant cases were treated with NAB (see Tables 2 and 3). It will be seen from Table 1 that none of the 21 fresh cases required any subsequent treatment apart from 1 who had a repeated course, although 3 were posted before treatment could be completed; it is possible that these three would have relapsed.

It would appear, nevertheless, that NAB therapy is very successful in treating non-gonococcal urethritis. But it may well be, as this is a small series, that it was just good fortune that these particular cases were chosen, and they might just as well have cleared up with sulphonamide therapy; a reason for thinking that this may be so, is that 4 of the sulphonamide resistant cases were resistant to NAB too, and that is to say that if they had by chance been treated with NAB alone they would have been counted as failures. (Three of these four cases were kept going by a focus of chronic sepsis, which shows that neither sulphonamide nor arsenic can penetrate sufficiently deeply to eradicate such a focus, and mechanical interference is necessary to promote drainage.)

As the other 16 sulphonamide resistant and the 2 penicillin resistant cases did well with NAB, it must be concluded that NAB is a better treatment that either of them. But/
it must be remembered that NAB has very unpleasant toxic effects, and while none were encountered in this series, one of another series developed a severe rash after his second injection, and several writers make mention of this and other toxic phenomena (25) (153) (177). Of course sulphonamides can cause toxic effects too, and King and Williams (90) record one death and one serious illness amongst their cases; but such severe effects are rare nowadays, and the skin sensitivity can be treated by desensitisation.

Another limitation to arsenic therapy is that it is difficult to give, and if by any chance the vein is missed, an abscess may result. Nothing however could be simpler than the swallowing of a sulphonamide tablet.

The mode of action of the arsenic is not understood. The early German writers (57) believed that it was broken down with the liberation of formaldehyde which was then excreted in the urine killing any susceptible organisms there. But as so very little formaldehyde is liberated per dose of arsenic this explanation is not generally accepted (185).

Pace (123) believed that the arsenic is itself concentrated and then excreted by the kidney. Butchel and Cook (19) quote a personal communication from Gaudin who stated that he was unable to confirm this and believed that there was something more than just
a concentration of arsenic. However, if the cause of some of the cases is a spirochaete then the arsenic will kill it wherever it is met with, in the blood or in the urine.

In other cases, where the organism is not a spirochaete and not directly susceptible to the arsenic, it may be that the drug stimulates the body's defence mechanisms to react more vigourously against the infection. However, the matter is not yet clear.

Several cases in this series were treated with penicillin when they had been shown to be sulphonamide resistant; but only a relatively few cases were treated initially with the drug. This is because it had been decided to treat all the fresh cases which came to Ely with NAB, and it was expected that more cases would be treated with penicillin at other Special Treatment Centres than actually were. In fact only 3 came from other centres, and with 2 who were treated at Ely made a total of 5 cases. Of these 5, only 1 was treated successfully, the other 4 failing completely to clear up. Conversation and correspondence with the venereologists at other Royal Air Force Treatment Centres confirmed this view that penicillin was not a good method of treating non-gonococcal urethritis, but no actual figures were available. Why this should be so, is not clear as it is thought that penicillin should be able to clear up the same number of cases as sulphonamides.
In the literature Campbell (21) reports that he was able to clear up only 24 out of 150 fresh cases of non-gonococcal urethritis giving 3 injections of penicillin. It must be admitted, however, that he succeeded in clearing 86 sulphonamide resistant cases in the same series with the same dosage; while on the other hand, again, 40 did not clear up with either, possible because some of them were being kept going by septic foci, as 4 had littritis, 14 epididymitis and 1 chronic prostatitis, and the others were probably due to penicillin resistant organisms.

Another form of therapy which has been tried with spectacular success is pyretotherapy, artificially induced with TAB vaccine. It is recommended that the injection be made intravenously (98). Johnston and McEwin (35) favour the use of Dmelcos vaccine rather than TAB.

The two cases in this series which were treated in this fashion, had their TAB injections at the Special Treatment Centre at Cranwell. There Levinson (98) treated a series of 180 sulphonamide-resistant cases with only 1 relapse, and it responded to re-inducement of the pyrexia 2 days later.

This would appear to be the most successful therapy of all, but it is not without its limitations. Firstly, an artificial pyrexia cannot be induced without danger of death from hyperpyrexia, and such have been recorded during treatment (98).
Secondly the selection of cases is limited to those whose physical condition is good enough to withstand a fever of 104 - 105 deg. F. for 6 - 12 hours; this admits of only the young and fit being so treated.

Another drawback is that it involves the admission of the patient to hospital for 24 - 43 hours (maybe longer if there are complications) thus entailing the provision of a large number of beds, and the services of skilled nurses. Further, in civilian life, it is not always convenient or desirable for a patient to have to leave home for a while, thereby drawing attention to a complaint he or she wishes to keep private.

A similar form of therapy, not used for any of this series is pyrexia induced by means of the hyperthermia cabinet. A series of 76 cases so-treated is described in the literature (81). The conclusion reached there was that this was a reliable form of therapy, although the results are not so good with non-gonococcal urethritis as with gonorrhea. The technique is to induce a temperature of 140 deg. F. in the cabinet which results in a body fever of 110 deg. F. Six to eight hours of this is sufficient in most cases to effect cure. The results of a series is as follows:
Table 6

Results of Hyperthermia Treatment.

<table>
<thead>
<tr>
<th>No other treatment</th>
<th>Previous Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SulphaTh. 7 cases</td>
</tr>
<tr>
<td></td>
<td>SulphaPy. 5</td>
</tr>
<tr>
<td></td>
<td>SulphAn. 5</td>
</tr>
<tr>
<td>Hours of fever</td>
<td>8</td>
</tr>
<tr>
<td>Immed. cure</td>
<td>6</td>
</tr>
<tr>
<td>Partial cure</td>
<td>7</td>
</tr>
<tr>
<td>Failure</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
</tr>
</tbody>
</table>

These results compare favourably with the other forms of treatment, though perhaps not quite so good as the pyrexia induced with TAB vaccine. The same limitations apply to it as with that form of therapy, with an additional one viz. that the apparatus is expensive, cumbersome, and needs constant skilled attention for upkeep and usage.

The 5 failures in the sulphonamide column may have been due, as in other cases of failure to the presence of chronic ltitritis or prostatitis, which would have to be broken down by mechanical interference.

To sum up: probably the safest way to approach treatment of a non-specific urethritis of doubtful aetiology is to start with sulphonamide, and if the case is resistant then it should be followed by pyretotherapy. If however, the age or physical condition of the patient precludes this, then NAB
should be exhibited. It is assumed of course, that chronic focal sepsis has been eliminated.

5. Infections of the Prostate.

In acute prostatitis, no examples of which occurred in this series, the patient should be put to bed given sulphonamides, and left alone as far as prostatic investigation is concerned till the acute stage is past. Heat in the form of sitz baths may be very soothing. Any attempt at mechanical interference will inevitably lead to an acute, probably bilateral epididymitis.

If an abscess develops, which is not very common, heat should be applied in whatever form it is most soothing (see below) until it subsides. Incision may be made if the abscess points, but usually it will subside spontaneously.

When the condition becomes chronic, the patient need not be in bed, and there are several ways which are recommended to clear it up. These are:

(1) The application of heat to the gland by sitz baths, diathermy and rectal irrigations (22). It is hoped thereby to increase the blood supply to the gland and thereby bring more leucocytes and antibodies to combat the infection.

(2) Direct irrigation of the gland itself per urethram, per rectum or through the perineum. This latter route was preferred by Grant (54) who used ei-
ther phenol, serum or 1% mercurochrome for the purpose. It was expected that this would wash out the debris from the blocked prostatic acini and so promote drainage; or if it failed to do this, it would stimulate fibrosis and so seal off the infection.

(3) Autogenous vaccination was recommended by Cumming and Chittenden (28) although they admitted that severe reactions might follow since the body was already trying its best to produce antibodies.

(4) Elimination of other foci of infection such as septic teeth, tonsils, appendix, gallbladder and gastritis. Some workers regard a chronically infected prostate as just one manifestation of a general state of body sepsis which has to be treated as a whole (28).

(5) Pyretotherapy was recommended by Clark (22) especially in cases originally caused by the gonococcus.

(6) Prostatic massage is probably the best method of treatment and it has been left to the last so that it can be discussed at length. It must be performed carefully and properly. O'Connor and Ladd (126) carried out experiments on dogs which had been subjected to prostatic massage of varying severity and frequency. They found that gentle stripping produced areas of hyperaemia and later a round cell infiltration. After daily stripping for 3 days, the alveoli were denuded of their epithelial cells and a
marked inflammation was present. After daily stripping for 7 days, there was a marked destruction of tissue. They concluded that gentle stripping of a chronically infected prostate would not only promote the blood supply of the gland and promote drainage, but would also stimulate reaction in the body to the infection by a process of auto-vaccination.

The danger of too often repeated massage was illustrated by a case of a man who was examined rectally at a clinic by 5 people within 36 hours; the first examiner found the prostatic fluid to be normal, while the last found it to be teeming with pus cells, and it took 14 days for it to return to normal.

Another and bigger danger of too firm massage is that the infection may spread to the epididymes. One case occurred in this series when an over-enthusiastic medical officer was determined to produce fluid from the gland.

Accordingly it should be the rule never to massage a prostate if there is an acute urethritis present or if the gland is enlarged or tender. Massage should wait until the infection becomes chronic (if it does not clear up) and it is suspected that the gland is harbouring the causative organism. Then firm, but gentle massage should be carried out, by stroking from each side to the midline and then from the proximal to the distal part in that line; in all
about 6 strokes in each area should be sufficient to cause a drop of fluid to appear at the meatus. The massage should not be repeated more often than every second day; the discharge probably will get less on each occasion and finally after 3 or 4 massages none will be produced at all. Some authorities believe that massage should be followed each time by irrigation of the posterior urethra to wash away any infectious material before it has time to attack the urethra. Any mild solution, such as potassium permanganate is ideal for this purpose.

6. "Cowperitis".

Fenwick originally treated his 9 cases by touching the glands per urethram with a silver nitrate stick and obtained very good results. A modern method of doing this is with the electric cautery under direct vision; once the gland has been opened up and allowed to drain, the infection clears up.

7. Epididymitis.

Most cases of non-specific epididymitis, apart from tubercular and syphilitic types that is, clear up in about 14 days with rest in bed, heat and a suspensory bandage applied to the part. The heat may be given in the form of a kaolin poultice, or it may be given as diathermy once daily.

Laird (99)
was of the opinion that sulphonamide accelerated abatement, at any rate it did in all but a few of his cases. Handley (64) found that 100,000 units of penicillin given daily for 5 - 10 days relieved the pain, even after only 24 hours, but did not affect the swelling.

One of the cases in this series cleared up with sulphonamide, and another with just a suspensory bandage. The remaining 2 received NAB: and one of them whose condition was the result of injudicious prostatic massage cleared up dramatically the pain ceasing and the swelling starting to subside within 24 hours of the first injection. The other cleared up too, but not so dramatically. Seminerio (157) also treated his cases successfully with NAB.

The end-result is usually a small thickened nodule about the size of a pea, at the lower pole of the testis. In 3 of Handley's cases (64), complete resolution without any thickening was obtained.

8. Cystitis.

The treatment of cystitis is often very difficult and protracted. But if it is of the abacterial type, then cure is magical after 3 or 4 injections of NAB. Improvement is usually noticeable after the first injection, and if it is not, then other septic foci should be sought for and dealt with (25). If there is still no improvement, a thorough search for tuberculosis should be instituted.
When cystitis is due to other organisms e.g. B. Coli, B. Proteus, or Streptococci, the usual methods of therapy should be tried, that is to say, sulphonamides or penicillin depending on the sensitivity of the organism; mandelix in an acidified urine can be tried in the resistant cases. It is often very beneficial to combine these therapies with diathermy and bladder lavage.

Successful treatment of staphylococcal cystitis with NAB has been reported by Young (136).


Gross (57) first demonstrated the efficacy of neosalvarsan in non-gonococcal pyelitis in 1917, and he was followed by Kall (88) in 1920. Young (136) cured 7 out of 11 cases of pyelitis caused by the staphylococcus, but found that it was useless in cases caused by the streptococcus or Bacillus Coli. Butchel and Cook (19) found that NAB combined with mandelic acid was the most effective method of dealing with infections of the upper urinary tract.

Nevertheless, arsenic is a toxic substance, and it is safer to make use of the safer methods of chemotherapy, reserving arsenic with possibly mandelic acid for cases where they fail.
SUMMARY AND CONCLUSIONS.

1. Methods of investigating, diagnosing and treating non-gonococcal types of urethritis and their complications have been described. It has been shown that there are several such conditions, and that therefore the term non-gonococcal or non-specific is only justifiable when the nature of the discharge is in doubt, and it is desired to reassure the patient that he has not got gonorrhea. When the correct cause has been discovered, if that is possible, the urethritis should be properly labelled: e.g. Staphylococcal, Alcoholic, Tuberculous etc.

2. Non-gonococcal forms of urethritis have been shown to have become more common in recent years, the incidence relative to gonorrhea being 4.4% during the 1914-18 war, 30% in 1940, and 50-60% in 1946.

3. It was found possible to divide the types of urethritis very broadly into non-infective or irritant, and infective. A list of the irritants and infecting micro-organisms is given in appendix B.

4. The non-infective types are relatively simple conditions to clear up once the causative irritant is removed e.g. alcohol, asparagus, or some drug, unless, of course, secondary infection has taken place meanwhile.
5. The infective types are more numerous and much more difficult to treat. Often they are complicated by spread of the infection to farther up the urinary tract where it is more difficult to treat.

6. A search was made for all the organisms mentioned in Appendix B, para B, but special attention was paid to four of them: Trichomonas Vaginalis, the L organisms, a possible virus, and a possible spirochaete.

No Trichomonas were found, and it is concluded, taking into consideration the cases recorded in the literature, that its occasional presence in the male urinary tract is no evidence of any pathogenicity. Anatomical reasons were given to explain its infrequent presence in the male as compared with the female.

Although no virus was found in this series, several instances of one being found in cases of urethritis have been reported in the literature; it is concluded that there is at least one type of urethritis that is due to a virus.

L organisms were also not found in this series, and the opinion of the bacteriologists rather than that of the clinicians was accepted, namely that their presence is incidental to urethritis, and
indeed, it was shown that they occur more often in gonococcal urethritis than in non-gonococcal.

No spirochaetes were found, but it was mentioned that some had recently been seen in the urine of some cases of abacterial pyuria; and the fact that some cases reacted so well to arsenic rather supported the possibility that some forms of urethritis are due to a spirochaete yet to be identified.

7. An attempt was made to show that amongst the various types of urethritis, there is one syndrome, the causative organism of which has not so far been identified, but whose clinical features are recognisable. This infection is contracted through sexual intercourse, has a long incubation of 3 – 8 weeks, produces only a slight discharge, and has usually a terminal dysuria; if untreated it may persist for a very long time, but as few as three injections of arsenic produces dramatic cure.

It is believed that the condition may at first show itself as only an abacterial pyuria, but that nearly always a urethral discharge develops; in a few cases where there is a conjunctivitis as well, there may be additional allergic manifestations of arthritis and keratodermia blennorrhagica.

It is thought that the causative organism is either a spirochaete or a virus. The
points for and against both of these have been discussed, and the conclusion reached that while neither has been proved to be responsible, there is a slight bias in favour of the spirochaete.

8. The present method of treating all non-specific cases with only 20gm. of Sulphathiazole was found to be inadequate in 49% of cases. Nevertheless, it is believed that unless a definite organism can be identified and its appropriate therapy be given, sulphathiazole or some other sulphonamide preparation remains the first choice for treatment. The reasons for this are: it at least will cure 50% of cases, it is very simple to give, and has few dangers.

It has been shown that the best subsequent treatment for those cases which relapse is the induction of artificial pyrexia, although unfortunately this is not unassociated with danger and can therefore only be done in the physically fit. In other cases, NAB therapy may be tried since in this series at any rate, it has been shown to effect cure in nearly every case.

Other cases have failed to clear up until various septic foci e.g. chronic prostatitis, chronic folliculitis, chronic sinusitis have been eradicated.

9. Discharges in association with systemic disease have also been described (see Appendix B.)
10. Some conditions, often mistaken for urethral discharges have been described. (See also in Appendix B.)

11. The symptom-complex known as Abacterial Pyuria has been discussed at length. It has been shown that pus can arise either from the upper or the lower urinary tract. An example of the latter occurring, it is believed, is the type of urinary infection mentioned in para. 7. Another is chronic non-specific prostatitis. In the upper urinary tract, there may be sterile pus in connection with aseptic calculi, areas of sepsis adjacent to the ureters, or from septic foci in the kidney parenchyma which themselves may be the result of septic foci elsewhere in the body.

12. Reiter's Disease has also been discussed in detail. Amongst the various theories mentioned which have been advanced to account for this phenomenon, it was thought that the disease was an allergic one, since such similar if not identical symptoms arise in such dissimilar conditions as gonorrhea, dysentery and non-gonococcal urethritis. Mention has been made of this type of urethritis in para. 7.

13. It is finally concluded that non-gonococcal types of urethritis are likely to be as common in the future as they are at present, since
the populace has become VD conscious, since more people are using chemical contraceptives and vaginal douches, and since chemotherapeutic treatment for gonorrhea unmasks any latent non-specific infection.

Further, if the hypothesis of para. 7 is correct, that a new type of urinary infection is spreading, then it is to be hoped that its cause will be soon ascertained so that its own particular therapy can be devised.
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Appendix  A.

Copy of the proforma which was sent to 11 cases who were demobilised before the 3 months observation was completed. Eight men completed it and returned it.

Since I saw you last, have you had any discharge_____. If you have, was it just a stickiness____ dampness____ slight actual discharge____ or profuse_____. How often____ In the mornings only____ during the day_____. Was it after taking any alcohol____ a lot of alcohol____ or after intercourse____. If so, after how long an interval____ or is it only immediately after your bowels have moved_____

Have you had any tingling or burning sensation connected with passing water____ if so, at the beginning____ during____ towards the end of____ after urination____ or unrelated to it____. Was the pain felt at the tip of your penis____ all along the pipe____ at the root of the penis____. Have you had any pain over your bladder____ in your abdomen____ in your back passage_____

Have you had to pass water more often____ if so, how often during the day____ night____

Have you passed any blood____ if so, at the beginning____ during____ after____ passing water. If you are married, has your wife noticed she has any discharge____

If you have had any of the above symptoms
did you have any treatment for them since I saw you

Have you had any pain in your joints or any eye inflammation

Any other remarks you would like to make

APPENDIX B.

Summary of the Caustive Irritants and Organisms

A. Irritants.

In the Female:

1. Menstrual Discharges.
2. Irritating vaginal solutions.
3. Foreign bodies in the vagina (e.g. pessaries, contraceptive caps.)

In the Male:

A. Chemical

1. Contraceptives, both rubber and chemical.
2. VD Prophylaxis (overstrong solutions etc.)
3. Urethral solutions in malingering.

B. Mechanical.

1. Prolonged friction as from a dry urethra, masturbation, milking of the urethra.
2. Urethral congestion as from coitus interruptus, or prolonged sexual frustration.
3. Careless instrumentation.
4. Urethral Foreign Bodies as in sexual perverts and in the mentally deficient, but also remnants of in-dwelling catheters.

C. Constitutional.
1. Gout.
2. Rheumatism.
3. Diabetes Mellitus.
4. Calculi.
5. Neoplasms.

D. Ingestants.
1. Urinary Tract Irritants such as Asparagus, cress, cucumbers, dandelions and strawberries. Effects maybe are produced by oxaluria.
2. Drugs such as alcohol, arsenic, cantharides, capsicum, cayenne pepper, copaiba, cubebs, iodides mustard, and turpentine.

B. Micro-organisms.

Primary Infectors:
1. Staphylococcus.
2. Coliform bacilli.
3. Bacillus Proteus.
5. Bacillus of Ducrey.
6. Tubercle Bacillus.
7. Treponema Pallidum
8. ? Unknown Virus.

Secondary Infectors:
1. Any of the above.
2. Various other cocci (streptococci, micrococci catarrhalis, falx, and caeruleus, pneumococci enterococci protoformis.)
3. Various Diphtheroids.
4. Various Bacilli (acidophilus, influenzae, diplobacilli.)
5. Various sarcinae, spirilla and spirochaetes.

Organisms in Doubt.
1. Trichomonas Vaginalis.
3. Inclusion bodies of Harkness.

C. Systemic Diseases.

1. Bacillary Dysentery.
2. Enteric Fever.
3. Diphtheria.
5. Mumps.
6. Intermittent Fever.
7. Typhus.
8. Malta Fever.

D. Skin Affections.

1. Herpes Genitalis.
2. Psoriasis.
3. Dermatitis.
4. Warts.