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THE PROBLEM OF RECURRING CYSTITIS IN WOMEN

BY

H. P. WINSBURY-WHITE, F.R.C.S.

Urologist, Italian Hospital; Honorary Consulting Surgeon, St. Peter's, St. Paul's, and St. Philip's Hospitals for Genito-Urinary Diseases; Honorary Consultant Urologist, Queen Elizabeth Hospital for Children, London

The purpose of this paper is to draw attention to the fact that in many cases of cystitis the infection is of ascending rather than of descending origin. Below are presented 65 personal consecutive cases, compared in certain respects, in a series of charts, with the same number of cases of chronic frequency, which were also taken consecutively.

Clinical Types of Cystitis

Broadly, the following clinical types of cystitis in which recovery occurs can be identified: (1) a single attack, which clears completely and has no recurrence after many years; (2) one or more attacks of cystitis, followed by frequency and other residual symptoms; (3) several attacks of cystitis, with no intermediate frequency; (4) recurring cystitis after intercourse; (5) honeymoon cystitis; and (6) cystitis associated with pyelitis of pregnancy. Chronic increased frequency of micturition is a feature that is common to most recurrent cases.

In 1956 I published the results of an investigation of 274 consecutive personal cases of chronic frequency of micturition which occurred in my practice. The inquiry embraced all ages and both sexes. In many there had been incidents of cystitis. If we examine the features of the frequency in the cases of cystitis and simple chronic frequency we find certain similar characteristics in both, as already set out (Winsbury-White, 1956).

In the past there have been two practical obstacles to the recognition of the posterior urethra as a common site of chronic infection: (1) the presence of a clear and sterile urine, in spite of persisting disturbances of micturition; and (2) the conventional disregard of the possibility that the posterior urethra could harbour a cause of chronic symptoms. It is only by a routine examination of the urethra in all cases of disturbances of micturition that a proper consideration can be given to this potential source of recurring symptoms. Some surgeons are practised in urethroscopy and others are not; therefore the medical attendant may or may not get a full report on the condition of the lower urinary tract.

Urethroscopy

I have the impression that many surgeons employ urethroscopy from time to time without seeing anything very convincing. With the inexperienced, especially, this is likely

to result in a second urethroscopy being carried out several weeks later, the first instrumentation having caused the more flimsy inflammatory vegetations to disappear completely. Thus the observer begins to doubt whether he really did see anything positive on the first occasion.

I cannot emphasize too strongly the need to use the best type of instrument. My personal experience is that this is the Geiringer pattern—in common use to-day, in slightly modified form, as the Swift Joly—which gives direct vision through a circular orifice at the distal end. I find that the oblique opening of the panendoscope pattern gives an important difference in magnification, according to whether the mucosa at the near or distal part of the oblique opening is being inspected. This requires regular rotatory movements of the instrument in order to see clearly the small inflammatory lesions that are sometimes present. Neglect to carry out these movements can give an incomplete impression of what one is seeing. I have had no success with other types of urethroscope in identifying inflammatory processes.

For more than 25 years it has been my regular practice to urethroscopically all women, children, and young men with disturbances of micturition. This has given me an experience of several thousand urethroscopies in women.

I have already described the differences in inflammatory changes to be observed urethroscopically in cases of frequency (Winsbury-White, 1956); the same groups exist in cases of cystitis, and these are referred to under the various decades of life to show how they broadly follow the same patterns both in urethral conditions and in clinical types.

We have only to remind ourselves of the difficulty of completely eradicating infection from the prostate to be aware that the same kind of gland structure in the female urethra probably provides us with the same kind of problem; so that it is not surprising that polypi and lesser signs of chronic inflammation are often to be seen in the posterior urethra of women. It is the regular experience of us all that chronic inflammatory changes are encountered on cystoscopy on the front of the trigone, and sometimes all round the internal urinary meatus, often when inflammation is to be found nowhere else in the bladder. When the investigation includes urethroscopy, posterior urethral inflammatory changes are inevitably found as well. By this routine, urethro-trigonitis is established as a frequent and somewhat concealed infective lesion. The combined bladder and urethral lesion is commonly found in young adult women.

Analysis of Cases in Decades

I find it difficult to discuss cystitis in women without considering chronic frequency in female children, because of a common urethral pathology. The cases of frequency in children inevitably include some with enuresis.

It is clear (Fig. 1) that there is a real spate of cases of chronic frequency in early childhood, and that these tend to tail off as childhood advances. Indeed, all disturbances

FIG. 1.—Comparison of frequency with cystitis in females. —, Incidence of cystitis. ---, Incidence of frequency.

of micturition, including enuresis, tend to disappear as adolescence advances. This clinical fact corresponds with the prevalence of non-vegetative forms of urethral inflammation and the rareness of urethral polypi in female children. Of the 29 cases of frequency in females in the

first decade (0-10 years) 51% had non-vegetative urethritis and 10% had vegetative urethritis, hillocks only—that is, no actual polypi. Moreover, it is significant that, of the 34 children under 16 years of age with frequency, 79% had enuresis. Occasional cases without frequency or enuresis had such symptoms as terminal dysuria, holding the water for long periods, and even acute retention. Thus we see

Fig. 2.—Urethral contractions in relation to age groups in 65 cases of cystitis in women.

Fig. 3.—Residual urine in relation to age groups in 65 cases of cystitis in women.

Fig. 4.—Vegetative urethritis in relation to age groups in 65 cases of cystitis in women.

Fig. 5.—Incidence of hillocks and polypi in relation to age groups in 65 cases of cystitis in women.

(Winsbury-White, 1956), an increasing incidence of urethral contractions (Fig. 2) and residual urine (Fig. 3) in relation to age.

In the cystitis cases the incidence of vegetative forms of urethral inflammation is seen to be broadly more common in older patients (Fig. 4), the polypi being more in evidence than the hillocks (Fig. 5), although these often occur together in adult cases. They are both found in the posterior urethra; these two types of vegetations were

that the disappearance of frequency and that of enuresis in adolescence go hand in hand.

Another simple form of inflammation that is more prevalent in the younger than in the older children with frequency and is rarely seen in adolescence is vulvitis. This is always accompanied by non-vegetative urethritis. Vulvitis was present in 9 of the 13 (69%) children under 6 with frequency, whereas from 6 to 10 years it was present in only 2 out of 16 (12%). In these children mild degrees of inflammation varying in extent were almost without exception to be seen with the cystoscope in all urethral cases, the urine usually being free from pus and organisms.

Through the third decade of life both frequency and cystitis cases show a sharp rise; from then onwards they rise and fall roughly in parallel (Fig. 1).

A study of urethral infection as the years advance now becomes of increasing interest. If we take the separate items of urethral disorder in the cystitis cases in decades from 20 onwards we find, as in the frequency cases

(Winsbury-White,

described long ago (Winsbury-White, 1948). The urethral caruncle which arises in the anterior urethra is much less in evidence.

The non-vegetative forms of urethral inflammation in the older patients are usually apparent as fibrotic changes—producing rigidity of the internal urinary meatus and a raised and irregular posterior margin of this structure—or as the urethral contractions already referred to. A rare type shows pus oozing from numerous points in the urethral wall.

In 1956 I pointed out that 88% of 274 cases showed inflammatory urethral involvement. In the present 65 cases of cystitis there was an even greater incidence (94%); this is not surprising if we are to regard these cases as broadly representing a further stage of the same disease.

In considering the data I have presented it is difficult to believe that cystitis and frequency do not represent varying clinical states of the same pathological condition. Particularly is this conclusion justified when we see how, in a clinical sense, the two groups merge into each other.

Cervix Uteri.—The importance of a pathological condition of the cervix here should never be overlooked. Clinically, it is impossible to clear up the bladder neck if a cervical erosion is neglected. The experimental work which I carried out many years ago (Winsbury-White, 1933) emphasizes this point. An intact hymen must never be regarded as an assurance of a non-eroded cervix. Of my 65 patients aged 21-60, 7% had cervical erosion which needed attention. As urethral fulguration is often necessary in the same case, the urologist must be ready to deal with the cervix at the same time.

Gland Structures in the Posterior Urethra

According to Nelson *et al.* (1957), it appears that centuries before microscopy was available disease of the bladder neck in females causing obstruction was proclaimed by Ambroise Paré (1575) and De Groot (1672). Microscopical aid in due course brought pronouncements from Virchow (1853), Von Brunn (1883), Tournau (1881), and Albarran (1909) pointing to the theory that glandular hyperplasia, in some respects resembling prostatic hypertrophy, caused obstruction at the bladder neck in women. A particular point to be emphasized in relation to prostatic obstruction is the common incidence of inflammatory changes found in the removed prostate even when hypertrophy is the dominating feature (Franks, personal communication). The common incidence of inflammatory phenomena in the posterior urethra of women, as seen with the urethroscope, points to the same tendency in the female—namely, that the glandular tissue there encourages inflammation.

Felix (1912) stated that in the female urethra the glandular ducts may atrophy and disappear, or may be present. Other writers have described the glandular tissue in the urethra adjacent to the internal urinary meatus. Folsom and O'Brien (1945) reproduced a photomicrograph of glands in this situation in the female foetus. Huffman (1948) presented wax models of the gland ducts of the female urethra which show these structures in close proximity to the internal meatus on both the anterior and the posterior aspect of the channel. Folsom and O'Brien agree with me that it is in the posterior urethra, and not the anterior, where vegetative phenomena are common. Fig. 6 shows the gland structure in the tissue of a bladder neck, including the adjacent part of the posterior urethra, which I excised for a woman aged 58.

Even in female children with chronic disturbances of micturition, including enuresis, and involving persisting small amounts of residual urine, the excised bladder neck shows abundant evidence of chronic inflammation. I call to mind two such children, each with enuresis and frequency, with amounts of residual urine varying from 1 to 3 oz. (28 to 85 ml.); one aged 7 years was cured 18 months ago, and the other, aged 13, is a more recent case; both after suprapubic bladder-neck excision.

In noting that vegetative urethritis occurs in the posterior and not in the anterior urethra one recalls that this is what happens in the male in relation to urethritis generally.

In searching for aetiological factors, it is to be noted that posterior urethritis in the male either is accompanied by a non-vegetative anterior urethritis or there is evidence that inflammation has occurred in the anterior urethra in the past. In the female, signs of non-vegetative anterior urethritis always accompany the posterior urethral changes mentioned. Also there is the fact that, in the first five years of life, simple vulvitis is a very frequent incident in connexion with urethritis. These two separate pieces of evidence suggest that the posterior inflammation is secondary to an anterior one.

FIG. 6.—Section of bladder neck excised transvesically from a woman aged 58, showing a vertical cleft or pit, with a gland space on the left and a focal aggregation of chronic inflammatory cells on the right. There is some irregular hyperplasia of the surface epithelium. (H. and E. $\times 115$.)

General Survey of Cystoscopic Appearances in Cystitis

As chronic frequency is so commonly due to chronic inflammation in the lower urinary tract, in a general way, and as my purpose is to discuss inflammation in the bladder, these matters may wisely be considered together. Because it is unusual to carry out cystoscopy during an attack of acute cystitis, the appearances described below do not include this condition.

Speaking generally of the cases of chronic frequency, it can be said that cystoscopic evidence of cystitis is more common in the younger than in the older children. This is so in the first five years compared with the second five years. In adolescence, which embraces the period of relative inactivity of disturbances of micturition, of whatever origin, the signs of inflammation are nearly always confined to the posterior urethra. In the third decade, and before its commencement, a new era of micturitional disturbances unfolds. Sexual activity and reproduction cannot be excluded as dominating influences. A sudden onset of frequency, or an attack of cystitis which clears completely or resolves into chronic frequency, is a familiar event. It is in this period that urethro-trigonitis begins to be commonly seen, and continues in the later decades—sometimes with the general bladder cavity quite free of inflammatory changes, and sometimes with different degrees of inflammation in various parts of the bladder, particularly the base.

Unfortunately there is a widespread belief that in the absence of residual urine in the bladder the lower urinary tract can be absolved from causing symptoms in the upper

urinary tract, and this idea is often a sufficient reason for not making a complete investigation of the lower urinary tract. In certain cases of cystitis the infection seems to begin in the kidneys, and in a definite small proportion of cases full investigation shows that the primary cause of the bladder symptoms certainly lies in the kidneys. It is important to realize, however, that the renal symptoms of bladder-neck origin may completely overshadow vesical symptoms; thus treatment can be wrongly directed. Also minor renal symptoms, particularly in the nature of a recurring aching pain, can be made to disappear by finding and treating a posterior urethral lesion. I have often wondered whether the successes claimed for dilating strictures of the ureters were not due, at least in part, to the urethral dilatation which inevitably occurred at the same time. On the other hand, it cannot be expected that a prolonged renal attack from a long-continued urethral lesion will not produce permanent changes in the kidneys.

To put it in another way, when trying to influence renal symptoms by treatment of a bladder-neck urethral lesion it must not be forgotten that this may become all the more difficult to do according to the degree of change that has already taken place in the kidneys.

Intravenous urography, as most of us are aware, can give detailed information not only about striking renal changes but about minor ones as well when a series of films from an individual case are studied.

Treatment

The follow-up work done by Garrod *et al.* (1954) has shown that there has been too ready a tendency to claim a cure from internal antiseptics and antibiotics. For these workers have demonstrated that the more time that is allowed to pass before tests for relapse of infection are made the fewer are the cases found free of infection. Moreover, the fact that they proved that a clinical type that recurs is one that has a past history of urinary infection points to the likelihood of a latent urinary infective focus.

All persisting polypi of hillocks must be fulgurated. Urethroscopy must be carried out later if symptoms continue or return. Cases which react badly to treatment must be carefully tested for residual urine. Those with several ounces of residual urine require bladder-neck resection. Some cases without residual urine react badly to treatment, especially those that take sedatives regularly. Gentleness is the watchword for treatment of all cases.

The improvement which often follows the first examination draws attention to the benefit from simple urethral dilatation. This benefit is most likely due to the improved drainage which results from the dilating effect on glandular and adventitious orifices in the urethra. Doing this too often, and using coarsely graded dilators—all uterine dilators—are common faults in technique. Wyndham Powell dilators should always be used.

Uncertain Value of Urine Reports

I hesitate to put forward figures on urine reports in support of claims, because these can vary so much in relation to varying circumstances of the examination. But, for what they are worth, the single reports on urines taken in the 65 cases at the first visit are compared with single reports at varying times from 2 to 12 years after one form of instrumental treatment or another had been carried out; these show that 66% of urines were bacteriologically negative before treatment, compared with 77% after treatment.

The inconspicuous feature of the presence of pus cells noted in the urine reports is emphasized; only 7% of these merited one plus or more.

The value of urine reports, bacteriologically, may be summarized as follows: (1) In a high proportion of cases the urine reports are negative, although endoscopic and symptomatic evidence of an infective urinary tract focus exists.

(2) In spite of clinical improvement it is uncertain that evidence of complete cures from any form of treatment will be found.

Summary

The bladder neck, including the posterior urethra, is considered in some detail as a potential focus of chronic infection in recurring cystitis in women.

Some practical points in relation to urethroscopy are discussed.

There are common patterns of incidence and pathology in decades for cases of chronic frequency and cystitis.

The cervix uteri is considered.

Attention is called to the occurrence of gland structures resembling prostatic tissue in the posterior urethra of females.

A general survey of cystoscopic appearances in frequency and cystitis is made.

The efficacy of local treatment is based on the need to provide the best possible drainage from the infected focus. Residual urine which resists other forms of treatment sometimes calls for bladder-neck resection.

The uncertain value of urine reports is discussed.

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LYMPHOGRANULOMA VENEREUM

BY

H.-J. B. GALBRAITH, M.D., M.R.C.P.
Senior Medical Registrar

C. W. GRAHAM-STEWART, F.R.C.S.
Resident Assistant Surgeon

AND

C. S. NICOL, M.D., M.R.C.P.

*Physician in Charge of the Department of Venereal Diseases
St. Thomas's Hospital, London*

Lymphogranuloma venereum is a venereal disease, usually acquired in tropical or subtropical regions, caused by a filterable virus which is related morphologically and antigenically to the virus of psittacosis. There are even more descriptive synonyms for the condition than is usual, including lymphopathia venereum, lymphogranuloma inguinale, poradenitis venerea, climatic bubo, and Nicolas-Favre disease. It should be distinguished from granuloma inguinale (venereum), an infection by the Gram-negative pleomorphic organism *Donovania granulomatis*.

Although some of the classical studies of the disease were published in Britain (Stannus, 1933; Findlay, 1933; Hanschell, 1938), the number of cases diagnosed in this country is not high; thus new patients seen in special treatment centres in the five years 1951 to 1955 inclusive and enumerated in the annual reports of the chief medical officer of the Ministry of Health total only 363.

Stannus (1933), who suggested that John Hunter in 1786 and William Wallace, of Dublin, in 1833 may have

described cases of the bubonic form of lymphogranuloma venereum, thought that the scarcity of reports of infection in Great Britain was due to the lack of recognition of the disease by the medical profession. The experience of King *et al.* (1956) supports this view. Frei tests were performed on all patients attending the venereal diseases clinic of the London Hospital during a 13-months period. Active infection with lymphogranuloma venereum, as shown by a positive skin test and a complement-fixation test positive at a serum dilution of 1 in 32 or more, was found in 23 out of 1,119 patients (2%). Almost half of the patients with positive reactions had clinical evidence of infection. However, in spite of a more widespread appreciation of the clinical features of the disease, and in spite of the greater facility with which complement-fixation and skin tests for the disease can be carried out, there were, until the above-mentioned report, fewer than 20 instances in the literature of patients who have acquired the infection in this country and in whom the diagnosis is indubitable (see Subsidiary References).

Hanschell (1938), who had a considerable experience of the disease, reported that in 19 years of observation in a London dockside hospital he had seen no cases of indigenous infection. The disease is apparently transmitted in exudates from ulcerated lesions which in the male are usually present for only a short time. Males constitute the bulk of travellers from the tropical and subtropical areas where lymphogranuloma venereum is endemic, and the short incubation and infectious phases will often be completed during the journey to this country. It has been suggested that the infectious phase is for practical purposes further curtailed by the fact that the man is rendered *hors de combat* for much of this time by the concomitant painful buboes (Stannus, 1933). It is probable, therefore, that hitherto infectious cases have rarely reached this country and that "reservoirs" of infection have not developed here. With the increasing use of air travel and with the influx of immigrants from the West Indies, where lymphogranuloma venereum is extremely common, this situation may be altered.

In this paper the cases of two patients who acquired lymphogranuloma venereum in this country and who presented in the immediate post-primary stage are reported, together with details of four other cases which also attended this hospital during a recent period of four months and which illustrate other syndromes of the disease.

Case 1

A West Indian negro aged 39 while in his early teens had had swellings in the left groin which had discharged and healed, leaving some linear scars. He admitted several sex contacts before this. Since coming to this country three years ago he had been treated on two occasions for acute gonorrhoea. Three weeks before admission he had intercourse with a coloured West Indian woman whom he met casually. About ten days later he developed an itching blister on the glans penis. The blister was broken by scratching, but healed within a few days, at which time bilateral inguinal swellings developed; these increased in size and became painful. He came to hospital complaining of the painful groin swellings and of headache.

On admission he had an intermittent fever to 100.6° F. (38.1° C.) with a pulse rate of 70-84 a minute. There was no neck stiffness. On the dorsum of the glans penis adjacent to the corona there was a depigmented area indicating the site of the recent lesion. There were tender enlarged glands in both groins above and below the inguinal ligaments, with oedema and induration of the surrounding subcutaneous