

Nonspecific Urethritis in the Male*

CHARLES H. GARVIN, M.D., *Cleveland, Ohio*

Clinical Instructor in Genito-Urinary Surgery, Western Reserve University School Medicine

“NEVER diagnose gonococcal urethritis without substantiating proof of a positive stained spread or a positive culture.” This has been an unalterable rule in my private and clinical practice. Urethral discharges involving male patients often pose a baffling diagnostic problem to the urologist. Although *Neisseria gonorrhoeae* is the most frequent cause of infection in the urethra, other pus forming organisms or non-bacterial irritants may cause a urethritis. Pelouse¹ frequently called attention to the fact that 30 per cent of urethral discharges are non-gonococcal. When urethral discharges are proven to be gonococcal there is no problem, but when the cause of nonspecific, that is, non-gonococcal, there is need of careful observation. Every discharge from the urethra must be considered gonococcal until proven otherwise.

Dr. Blanche, your executive secretary, in assigning this subject to me for the Andrew W. Cheatham Memorial Lecture, believed that a review of this subject might be of interest to those of you who are specialists as well as to the general practitioners. Do we not all claim to be specialists in gonorrhea in this antibiotic era, when it is believed that a handful of sulphonamide tablets or a shot of penicillin will cure all cases? Far too many of us diagnose every urethral discharge as gonococcal in origin and often institute therapy without investigation. We are well aware that a diagnosis of nonspecific or non-gonococcal urethritis has a tendency to cause disbelief and even ridicule.

First impressed many years ago with the fact that many cases in my practice with a urethral discharge could not be absolutely labeled as gonococcal, I noted that there is an abundant accumulating literature sustaining this viewpoint. There are numerous articles pointing out the frequency of nonspecific urethral discharge in the armed services of ours as well as other nations. We had ob-

served this as a medical officer in World War I and it was a major medical problem in World War II and today it is a civilian problem. Baier² in a study of nonspecific urethritis in the V Air Force in Japan in 1947-48 studied 475 cases and found an average incidence of 23.9 cases per thousand troops per year. When one considers a large group of young men undergoing severe physical training, fatigue under various emotional and physical strains, the lack of proper sexual hygiene, unsatiated sexual desires, imbibing alcoholics; it is not difficult to understand why a nonspecific urethritis may occur. The same factors in civilian life will produce the same entity. We see it occasionally in students who indulge in “petting” causing sexual excitement, without sexual gratification or in those who practice withdrawal. These practices induce a hyperemia of the prostate which is followed by chronic nonspecific prostatitis. Remember, however, that if gonococcal urethritis is proven it cannot be caused by any “strain,” except the “strain” on the urethra and prostate during the sexual act.

ETIOLOGY

Infections of the urethra may result from the introduction of pathogens from without, from infections in the upper urinary tract or may develop on a traumatized mucosa by the development of pathogenicity by the normal urethral flora. The trauma may be either chemical or physical. Many cases occur in males who have had frequent attacks of gonococcal urethritis and now have untreated chronic prostatitis. They usually give a history of heavy lifting and excessive alcoholic imbibing. These factors lower the resistance of the urethra. Baier² states that 46 per cent of his series of 475 cases had a history of previous gonorrhea. We have records of cases that have had from three to four attacks of acute gonococcal urethritis within one year.

Nonspecific urethritis may follow an apparently cured attack of gonorrhea. It is a well known

* The Andrew W. Cheatham Memorial Lecture of the Mound City Medical Forum, read at the Fifth Annual Convention of the Homer G. Phillips Hospital Internes Alumni Association, St. Louis, Mo., April 19, 1950.

clinical fact that gonococcal infections of long standing rarely remain pure infections and that secondary invaders are common. Keelsal³ states that 3 to 5 per cent of gonococcal infections may resist the usual brief courses of sulfonamides and antibiotics and a discharge may persist. Parkhurst, Harb and Cannefax⁴ in studying 2821 cases labeled as penicillin-resistant gonorrhea found that many of these cases were found to be nonspecific infections. They state that they have never observed strains of gonococci refractory to intensive penicillin therapy. Those who were found to harbor the gonococci were cured with penicillin. Reinfection must be considered. In the clinic we are often consulted on so-called penicillin-resistant cases of gonococcal infections and we have yet to see a case that has not responded when complicating pathology is corrected. Many patients receiving repeated injections of penicillin may persist with a mucoid and often purulent discharge. We have not been able to demonstrate gonococci by spread or culture in these penicillin treated cases. We now use penicillin SR. in 4000 unit doses.

In the consideration of a persistent urethral discharge it is always necessary to exclude the following lesions of the urogenital tract:— 1.) Stricture of urethra. 2) Contracted or small meatus resulting from chronic inflammation and fibrosis resulting from intra-meatal chancre. 3) Bizarre hypospadias openings. 4) Urethral polyps—rare—we have seen only one such case. 5) Tight prepuce with chronic balanitis. We have one such case under treatment at present. 6) Diverticulae. 7) Prostate-urethral fistula. 8) Intrameatal chancre. 9) Littritis. 10) Infections of upper urinary tract. 11) Chronic prostatitis and seminal vesiculitis.

Other factors that must be considered. A) Inadequate treatment of previous gonococcal infections. B) Old latent gonococcal infections associated with low grade secondary invaders. C) Excessive use of chemical prophylactics. D) Cases of persistent discharge due to over zealous or injudicious treatment with irritating chemicals. E) Many cases are caused by the apprehensive patient who habitually squeezes his penis too hard and too often in an attempt to express a discharge. This habit should of course be prohibited. F) Post-menstrual irritating discharges in the female mate.

BACTERIOLOGY

There are normally numerous bacteria found in urethral exudates:

1) Streptococci, 2) Staphylococci, 3) Micrococci, 4) Diplococci, 5) Diplobacilli, 6) Diphtheroids. Specifically, the *E.col.*, *Aerobacter aerogenes*, *Enterococcus (Streptococcus-Fecalis)*, *Proteus vulgaris*, *Staphylococcus albus*, *Pseudomonas aeruginosa*, *Trichomonas vaginalis* and tubercle bacilli have been found to be the cause of nonspecific prostatitis with accompanying urethritis. Fedder⁵ reports two cases due to tubercle bacilli. We have recently seen a case of nonspecific urethritis in a young boy, age 16, who on investigation showed upper urinary tract infection due to *Pseudomonas aeruginosa*. Willcox and Findlay⁶ state that a "pleuropneumonia-like organism is present in the distressing and by no means uncommon complaint of nonspecific urethritis." Rivelloni and Spannedà⁷ reported 48 men with nongonococcal urethritis due to the enterococcus (*Streptococcus fecalis*).

TRICHOMONAS VAGINALIS URETHRITIS

Trichomonas vaginalis infection of the urinary tract is by no means a recently recognized entity. It was known as early as 1868.¹⁹ Its frequency in the female is well known. In the male, infestation is not as common. The incidence varies from 1 to 10 per cent. Allison⁸ found an incidence of 15 per cent of trichomonads in the male, and Riba⁹ and Liston and Lees¹⁰ found 10 per cent. It is stated that 80 per cent of the mates of female have the infection. Symptoms may be urethral itching, dysuria, diuria, frequency, often nocturia and urgency. There is a milky or watery discharge from the male urethra. The anterior urethra is irritated and the meatus is slightly inflamed and pouting. These symptoms should call for a careful search for this organism especially in the absence of the gonococcus. The discharge usually begins a day or two after sexual exposure. These organisms are often associated with the gonococcus and with other bacteria, especially the streptococci, staphylococci and with bacilli of varying types. It is well known that the particular organisms present are rarely the sole etiologic factor.

In about 1 per cent of the cases the trichomonas may be found in the secretions of the prostate and seminal vesicles. It is generally agreed that the

organisms gain entrance to male urinary tract following sexual contact with infected females. Numerous reports in the literature reveal that acute non-gonococcal urethritis follow such exposure. Reinfection in the female can thus be inferred in cases where male harbors the organism. Sexual mates should always be examined in resistant female infections.

Young¹¹ found in a study of 2500 urinary sediments from male patients admitted to his clinic, 53 adults males (2.12 per cent) infected with the trichomonas. He found 26 positive smears in 171 prostatic secretions, an incidence of 15.2 per cent. Many patients who have trichomonas vaginalis in urine, discharge, or prostatic secretions have urologic symptoms. When the trichomonads are eliminated there is a disappearance of the symptoms; this is especially true in those whose complaints are chronic urethral discharge. While the pathogenicity of trichomonads in the urine is frequently doubted, laboratory examinations of the prostatic smear certainly suggest that the organism is pathogenic. There may be associated staphylococcus albus and the question arises whether the trichomas are secondary invaders. We know that the disappearance of the trichomonas causes the complaints to be relieved. In urine the trichomas lose their motility in a relative short time, but they can readily be found in the expressed prostatic smear. The association of trichomonal infections in strictures of the urethra and in meatal contraction is well recognized.

CHRONIC PROSTATITIS AND VESICULITIS

It is a feeling of many that most cases of non-gonococcal urethritis have or have had nonspecific chronic prostatitis or vesiculitis, or both, and that this infection produces the urethritis and the "morning drop." Many cases of chronic prostatitis are caused by direct extension of an acute gonococcal urethritis by way of the prostatic ducts, especially in cases delaying the start of treatment. We are firm in our convictions that the institution of early and proper treatment in these cases will lessen the frequency of this type of infection. We are equally convinced that no case should ever be discharged as cured without provocative prostatic massage as well as using it as a method of determining cure. Residual subacute and chronic prostatitis after, penicillin and sulfonamide

therapy for acute gonococcal urethritis is always to be considered and is of wide-spread occurrence; giving rise to a chronic discharge. In all cases of chronic prostatitis the urethra should be examined for obstruction.

If gonococcal urethritis were a surface infection it could be easily eradicated, but since it is a disease of tissue penetration, penetrating between the epithelial cells and into the intracellular spaces and into the peri-urethral glands; difficulty of eradication and secondary infection is expected. Chronic anterior folliculitis and littritis is found in many cases of nonspecific urethral discharge. Smears will often show myriads of secondary organisms, usually small gram negative bacilli and pus cells. Folliculitis is common in many untreated cases of acute gonococcal urethritis, especially if delay in seeking treatment is at least three weeks. Also, it is often seen in cases inadequately treated with the sulfonamides or penicillin. This is often revealed in observation of the shreds in the two glass test. It can also be detected by palpation of the urethra over a sound.

STRICTURE OF URETHRA

The importance of stricture of the urethra in trichomonal infections has already been alluded to. Stricture of the urethra is very common in cases of nonspecific urethritis. In every case of urethral discharge or in any urinary infection, urethral lesions should always be considered as a possible cause. While a clinical stricture might not be demonstrated, patients are often benefitted by dilatation. Keesal³ believes that the most probable cause of the "morning drop" is a urethral stricture at the bulbo membranous urethra. It must be pointed out that a dormant infection in the urethra may be provoked by dilatation and symptoms intensified. This again substantiates my argument that no case of acute gonococcal urethritis should ever be discharged until provocative dilatation is carried out.

SYMPTOMS

Persistence of itching in the urethra, vague perineal or inguinal discomfort, frequency of urination, often slight dysuria, a scant watery, mucoid or viscous opalescent discharge which may only be manifest on arising or may occasionally come on during the day and only slightly

staining the underclothes; may be the only symptoms. The "morning drop" may be only a tear or a bead or a gluing of the meatus. There may be a one to three year history of intermittency with an exacerbation following a night of imbibing alcoholics or after a sex orgy. We are quite certain that some patients will have a urethral discharge as an allergic manifestation to alcohol.

DIAGNOSIS

It is well to recall that the incubation period in acute gonococcal urethritis is from three to five, to seven and often ten days. It takes a minimum of 36 hours for the gonococci to penetrate and seventy-two hours for the asymptomatic cycle of penetration, sensitization and the production of pus cells. The incubation period of nonspecific urethritis may be much shorter and is often much longer after exposure. The symptoms are usually milder with only a history of urethral discharge. A complete genital examination and a laboratory test of the urine and discharge should be done at once. If unable to obtain a spread at time of the first visit the patient should be given slides and instructed in making a spread from the "morning drop." The stained spread examined microscopically may show mucous, small squamous epithelial cells, just a few pus cells and often no organisms or perhaps a few gram positive cocci or bacilli. If the discharge is mucopurulent we may find staphylococcus aureas, diptheroids and pleuropneumonia like organisms.

Of course, if the study of the stained spread reveals the gonococcus the question is solved. But, it must be recalled that a spread may often fail to reveal evidence of specific infection and yet patient may harbor the organisms, so a culture is necessary. It is well recognized that in chronic cases the culture is far superior to the spread. If a urethral spread, prepared from material removed from within the meatus and stained by gram method fails to reveal the gonococci a culture of both the urethral discharge and the expressed prostatic fluid or a stained spread of the sediment of the centrifuged urine passed after massage. Nonspecific urethritis should not be diagnosed until the above tests are negative. We have found that a stained spread of the sediment of the urine voided after prostatic massage very practical and beneficial in evaluating urethral and prostatic discharges especially if there is a history of urethral

discharge. It is often revealed that many of the lesions are not in the urethra but in the prostate and seminal vesicles and diagnosis and treatment depends upon a proper evaluation.

A study of the urine by the two glass test following the making of spread and culture is most valuable. In a study of the urine there will often be seen a persistence of a hazy urine with epithelial debris in suspension and often there will be sinking debris and mucous and comma shreds coming from the prostatic ducts. The second glass is often cloudy revealing posterior urethral involvement. A serological test of the blood should be done the first day as well as at the end of treatment to rule out intrameatal chancre.

TREATMENT

Successful therapeutic results will not follow unless cases are individualized. There are of course routine measures that should be insisted upon; absolutely no sexual excitement or sexual intercourse, avoidance of alcoholic drinks and the examination of sexual mate. Difficulty is often encountered in curing many cases of gonococcal urethritis, if careful observation is made in many instances it will reveal that patient is suffering from urethritis due to nongonococcal causes or an erroneous diagnosis of gonorrhoea was made on the basis of an unsatisfactory gram stain.

We have in our armamentarium many new drugs for the treatment of urinary infections. It is generally agreed that penicillin is the most potent drug so far developed for the treatment of gonococcal infections. In the non-gonococcal urethral and urogenital infections the drug is less impressive. Penicillin is ineffective in 35 per cent of the cases according to Baier². It has proven almost useless against the colon bacillus, and also in cases of mixed infections with the gram negative bacilli. In many cases we have found that the old methods of treatment, mild urethral irrigations with potassium permanganate, 1 to 6000, or the instillations of 1 to 1000 acriflavine solution or 1/2 per cent protargol or 5 per cent of the argyrol group injected into the urethra with a 1/4 ounce syringe and retained for five minutes once or twice daily are often effective. We have also found that penicillin in combination with one of the sulfonamide group is often effective. A synergistic action definitely exists, especially against gram

negative organisms in combination with gram positive cocci. We find that gantrisin is the most serviceable in 1 gm. doses four times daily. It is most effective in infections due to the proteus group according to Carrol, Allen and Flynn¹² of your city.

Mandelic acid and Pyridium may also be used. Pyridium is soothing on the mucosa and on the acute symptoms, burning on urination, frequency and dysuria, especially if due to cocci. It may be given in doses of 2 to 3 tablets t.i.d. Fedder¹³ found that the only remedy effective in his hands, especially in the staphylococcal infections, was neoarspenamine intravenously in .3 to .45 gram doses for from 1 to 3 injections over five to seven days. He states results were often dramatic.

It is most essential that in all stubborn, resistant urethral discharges, obstruction within the urethra should be ruled out. Instrumentation should be avoided, however until the urine in the first glass is clear, or clear with a few shreds for at least 7 days. This avoids complications and exacerbations. If a stricture is suspected the urethra should be carefully explored with a urethral diagnostic acorn bougie (bougie-a-boule), introducing the largest bulb which will pass to the bladder and on withdrawal the bulb will establish the presence of a stricture and its calibre. It is of first importance to restore adequate drainage by gentle, gradual, repeated dilation.

Since the glands of Littre are often infected, a large calibre sound should be passed into the urethra and light massage along the urethra over the sound to dilate the ostia of the glands is most beneficial. The small indurated pockets can often be palpated. We have been able to benefit many stubborn cases even when an obstruction has not been diagnosed by wide dilation, even up to size 30 F., followed by irrigations and the instillation of 1/2 cc. of 1 per cent AgNO₃ solution into the posterior urethra with the Keyes-Ulzman syringe or directly with a urethroscope. Light prostatic massages may be used every five to seven days. if the expressed secretion shows more than 5 to 8 pus cells to the high power lens, continue for twelve to fifteen massages and recheck monthly and repeat if necessary.

In trichomonal vaginitis infection the prostate should be massaged preceded by the instillation of a 1 per cent solution of gentian violet through

a catheter into the bladder, and followed by a bladder irrigation of zephiran solution, 1 to 3000 or potassium permanganate 1 to 6000. Remember that dilatation is most essential in these infections. Cooper and McLean¹⁴ recommended atabrin in 1/2 grain doses three times daily for five days in combination with the above treatment. Liston and Lees¹⁰ recommend strong alkalinization of urine. Strain¹⁵ uses calciummandelate by mouth with success. Remember the importance of treating the sexual mate.

Of the newer drugs streptomycin has been stated to be helpful in the B. Coli, pseudomonas aeruginosa and most of the bacillary type and the streptococci. Pulaski¹⁶ found it an effective remedy in urethritis unaccompanied by prostatitis and it should be used in cases that do not respond to other treatment. He recommends a single intramuscular injection of .5 to 1 gm. and says it will cure 90 to 95 per cent of the cases. "Streptomycin is of no value in the treatment of prostatitis."

Aureomycin, the most recent is rapidly being recognized as the drug of choice in the treatment of mixed infections of the urogenital tract, especially those infections due to escherichia coli and aerobacter aerogenes. Intractability of a genital infection is a special indication for aureomycin. Finland, Collins and Paine¹⁷ treated two cases of nonspecific urethritis refractory to penicillin, the sulfonamides and streptomycin with a course of 9 gm. of aureomycin by mouth for six days with complete disappearance of the urethral discharge and a negative culture and it was their conclusion that it has definite antibacterial action against many organism, including cocci and bacillary forms, especially the streptococci, staphylococci as well as gram positive organism. It is also definitely established that it is most effective against infections caused by the pseudomonas aeruginosa and proteus vulgaris. He recommends 4 grams as the initial dose and then 2 gms. daily for two weeks.

Willcox and Findley⁶ treated four cases. They used 250 mg. capsules, giving 2000 mg. in ten hours in two cases, and in other two cases they gave 1000 mg. in twenty-four hours and found it a satisfactory treatment, especially in the cases showing a pleuropneumonia-like organism. They recommend the routine examination for this organism using the giemsa stain. They found it necessary to repeat the treatment if there was a recurrence.

They found aerobacter aerogenes and streptococcus faecalis susceptible, but that the proteus vulgaris and the pseudomonas pyoscanea were resistant.

CONCLUSIONS

1. No case of urethral discharge should be labeled as gonococcal unless proven by Gram stain or positive culture.

2. Non-gonococcal urethritis is a definite clinical entity increasingly recognized in clinic and private practice.

3. In our opinion, penicillin-resistant gonococcal infection has not been proved and post-penicillin urethral discharges are non-gonococcal.

4. The high incidence of nonspecific urethritis is caused by inadequate treatment of gonococcal urethritis, and old gonococcal infections associated with low grade secondary infections.

5. In the male, chronic non-gonococcal urethritis, strictures of urethra, chronic prostatitis and seminal vesiculitis play a great role in the production of a urethral discharge.

6. The importance of trichomonas vaginitis in the production of a urethral discharge has been emphasized. A chronically infected prostate may harbor the organism and a urethral stricture may be the cause of its persistence.

7. Before therapy of a urethral discharge is instituted a definitive diagnosis should be made.

8. A brief outline of treatment has been given, emphasizing the importance of eradicating infections in prostate and obstructions in the urethra.

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OF INTEREST FROM AFRICA

"The wife of Seretse Khama, a month before she gave birth to a daughter on May 15, was asked by British authorities to accept the services of a white government doctor in place of Dr. Moikangoa, also a government physician, who had been attending her. Said Mrs. Ruth Khama "My doctor is an African and I have no desire to encourage racial discrimination among government officials" . . . The British Colonial Secretary has admitted in Parliament that many Africans died as a result of the famine in Nyasaland earlier this year. He said the number of deaths could not be accurately estimated, but may have been about 200 . . . An African in Uganda, Dr. Levi Lwanga, suddenly became blind while in medical training at a hospital in his country. He learned Braille in English and two vernacular languages, went to England, completed his training, and passed examinations at a London medical school, qualifying as a physiotherapist . . . An African woman in the Belgian Congo has given birth to sextuplets. The mother and all six children are reported to be doing well."

New Africa, May-June, 1950.