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Nonspecific Urethritis and Reactive Arthritis

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Abstract. *Nongonococcal urethritis (NGU) is a common sexually transmitted infection most often caused by Chlamydiae and Mycoplasmae. A few other organisms, as well as some nonsexual factors, also contribute to its etiology. NGU can result in considerable physical and psychological morbidity. In a few cases, it can lead to complications like reactive arthirits, and pelvic inflammatory disease, with their attendant morbidities. Correct diagnosis and treatment is therefore imperative in proper management of these cases. While earlier diagnostic support for these infections was limited and expensive, the advent of new methods like the nucleic acid amplification assays (NAA tests) has contributed significantly to better diagnosis. Treatment as per suggested guidelines and follow up of cases and contacts are all crucial in management. Counseling, including advice on behavior change, goes a long way in preventive strategies.*

Urethritis is an inflammation of the urethra caused by organisms which may be sexually or nonsexually transmitted. It is characterized by dysuria and/or a urethral discharge. The finding of >4 PMNLs (pus cells) in a urethral smear is an essential criterion for diagnosing urethritis.

Urethritis is classified as gonococcal or nongonococcal, based on its causative organisms. The major causes of nongonococcal urethritis (NGU) are *Chlamydia trachomatis* and *Ureaplasma urealyticum*. Together they account for >75% of patients. The term nonspecific urethritis is often used in a broad context to mean nongonococcal urethritis, and sometimes in a more restrictive sense, to include only those forms of urethritis in which the well-established causes have been ruled out.

Etiology

Chlamydia trachomatis, the most common cause of NGU, is an obligate intracellular organism infecting columnar epithelium. It has 17 serovars, A—C causing Trachoma, D—K causing urethritis, and L1—L3 causing lymphogranuloma venereum. Chlamydiae exist in two forms: an elementary body, which is the infective form; and a reticulate body, which is the replicating form. Chlamydiae cause 30–50% of NGU and about 60% of postgonococcal urethritis. The infection may be acute or chronic, with slow replication of the organism.[1]

Chlamydial infections are seen in one third to two thirds of women with gonorrhea, and gonorrhea is seen in 20–40% of those with Chlamydia.[2] Chlamydial infections in women involve the cervix and urethra. In the urethra, colonization is seen in 40% of patients, but only one fifth have dysuria. *C. trachomatis* can be recovered from the cervix in 45–90%, and from the urethra in 15–25% of partners of infected males. These women are usually asymptomatic.[3]

U. urealyticum is probably responsible for 10–40% of NGU, although it can also be found in about 60% of normal individuals. It has been recovered from 80% of men with nonchlamydial nongonococcal urethritis.[4]

The mycoplasmas are saprophytes of animals and plants and are the smallest free-living organisms known. There are 50 species in the genus mycoplasma and 2 in ureaplasma. They are cultivated in vitro on broth medium. *M. hominis* is seen to colonize 20% of cases but its pathogenic role is extremely doubtful, because it is also seen in a similar number of normal individuals.[5] *Mycoplasma genitalium*, first isolated from men with NGU more than 20 years ago, causes NGU almost independently of *Chlamydia trachomatis*.[6] It may be associated, perhaps causally, with epididymo-orchitis and reactive arthritis (RA), but there is no substantial evidence that it causes acute or chronic prostatitis. In women, *M. genitalium* is strongly associated with cervicitis and endometritis, and serologically with salpingitis and tubal factor infertility.

Agents other than *C. trachomatis*, *U. urealyticum*, and *M. genitalium* cause 10–20% of NGU cases.[7] The protozoon, *Trichomonas vaginalis* causes Trichomoniasis, which is an infrequent cause of urethritis in males, but a very common one of vaginitis in females. This is due to the spontaneous clearing of urethral colonisation in males. *Trichomonas vaginalis* causes a variable proportion of cases, around 5%. Itching and irritation of the urethra may be prominent symptoms. Infection may be asymptomatic in men.

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Candida can cause urethritis with associated balanitis.

Trichomonas, chlamydiae, and viruses are not normal commensal flora of the lower genital tract, whereas *M. hominis* and *U. urealyticum* are regularly isolated. The bacteria normally present are *Staphylococcus epidermidis* and corynebacteriae in males, and *S. epidermidis*, streptococci, *E.coli*, lactobacilli, and Bacteroides spp. in females.[8] Some cases of urethritis might be due to *Clostridium difficile*, *Branhamella catarrhalis*, *Hemophilus influenzae*, corynebacteria, *Gardnella vaginalis*, Bacteriodes, adenoviruses, and schistosomes; however, these observations do not report the presence of the more frequent causes such as chlamydia and ureaplasma, they may not actually be the true causative agents.

Sometimes, intraurethral syphilitic chancre and condylomata can present with urethral discharge.

Non-sexual causes of urethritis/urethral discharge include

- Bacteria associated with UTI
- Urogenital tuberculosis
- Associated with childhood viral infections
- Stevens Johnson syndrome, Wegener's Granulomatosis
- Secondary to catheterization/other urethral instrumentation,
- Foreign bodies, strictures
- Chemicals, crystalluria, calculi
- Endourethral tumor
- Rigorous urethral stripping.
- Gleet
- Remnants of semen at the meatus, or urinary incontinence misinterpreted as a discharge

Clinical Features

The incubation period for NGU is usually between 1–4 weeks. It tends to be shorter in non-chlamydial infections. The overall prevalence of chlamydial infections in the sexually active age groups is between 5–10%.[9,10] Ten to twenty-five percent of chlamydia-infected men, and a large proportion of women, are asymptomatic, and constitute a hidden source of infection. A single act of vaginal intercourse can transmit gonorrhea in 50–70% of cases whereas with chlamydial infection, the probability is around 20–50%. Repeated contact with an infected individual raises the possibility to 70%.

Gonococcal and nongonococcal urethritis can be differentiated on clinical grounds in 75% of patients.[11] A combination of discharge and dysuria is more suggestive of GU (71%), and the presence of these symptoms separately is more likely to be a feature of NGU.[12] Dysuria is less intense, but its presence in the absence of a discharge is a good indicator of the presence of NGU. Twenty-five to fifty percent of men with chlamydial urethritis are asymptomatic. Symptoms may be minimal in NGU and may wax and wane.

Discharge is mucoid or mucopurulent, may be scanty, and seen only after urethral stripping or early morning.[13] Discharge is less profuse if NGU is caused only by chlamydia. The urethral discharge in patients with chlamydial urethritis is less than in those with nonchlamydial NGU. A small minority of patients (4%) of NGU may have a purulent discharge and a similar proportion of patients with GU have a mucoid discharge. In herpetic urethritis, dysuria is severe with a profuse mucoid discharge, presence of vesicles and ulcers on the skin, and lymphadenopathy.

Symptoms that are not typical of a urethritis are hematuria, fever and chills, frequency, urgency, altered urinary stream, pain in the genitalia/perineum, hematospermia, ejaculatory dysfunction, or growths.[14] Although symptomatology cannot always predict whether upper or lower UTI is present, it could be used as a basis for initiating treatment. A young, sexually active patient with frequency and dysuria but no other symptoms and signs could be considered to have a lower UTI, while another presenting with fever, rigors, dysuria, and loin pain could be having an infection at a higher level, eg, pyelonephritis.

Course of the Disease

In 14–30% of untreated patients, symptoms of NGU resolve within 2 weeks, and 70% are symptom-free by 6 months; however, asymptomatic patients remain infectious. Without treatment, chlamydial urethritis remains infectious for about 15 months. In patients with symptoms, or increased number of PMNL in urethral secretions, one can expect these features to disappear over an unspecified period of time. Without treatment, 95% of GU cases become symptom-free after 6 months. Untreated GU can become chronic and produce small amounts of mucoid discharge called gleet.

Post-Gonococcal Urethritis (PGU).

Patients with Gonococcal urethritis who receive single-dose treatment (quinolones, cephalosporins, or spectinomycin) specific for *N. gonorrhoeae* experience an improvement or resolution of the discharge, but would have a recurrence, albeit more mucoid or mucopurulent, with mild dysuria in 1–2 weeks. This is termed PGU, and is due to simultaneous infection by both *N. gonorrheae* and causative organisms for NGU. Chlamydiae are the most common cause for PGU. Eleven to fifty percent of men with Gonorrhea have coinfection with *C. trachomatis*, and it can be cultured in 75–100% of patients who develop a PGU. It is therefore important to consider dual infection, and pre-emptively treat all cases of GU for NGU as well.

Persistent Urethritis.
This may be due to: (a) non-compliance with Rx; (b) re-exposure to infection; (c) infection with resistant organisms; (d) deep focus of infection (prostatitis); (e) uncommon agents; and (f) Noninfectious causes.

Non-Gonococcal Infections In Women.
The most common manifestations of infection are either a mucopurulent cervicitis (endocervical infection), PID (upper genital tract), or a syndrome similar to bacterial cystitis with dysuria, frequency, urgency, and nocturia. This is frequently seen in women without the presence of bacteria in the urine. This is termed the "acute urethral syndrome." Although *E. coli* can sometimes cause urethritis, this condition is more often due to *Neiserria gonorrheae* and *Chlamydia trachomatis*.[15] This urethral syndrome is probably the clinical counterpart of NGU in women. It can be acute or chronic.

Less often, nongonococcal infections may cause a cervical dysplasia, bartholinitis, bacterial vaginosis (discharge without inflammation), perihepatitis (Fitz-Hugh-Curtis syndrome), periappendicitis, abortion, and infertility. These may be considered sequelae or complications of a primary infection. The causative role of the different organisms in these infections may be variable.[16]

Dysuria in women is more commonly caused by cystitis and vulvovaginitis. Manifestations of a concomitant cervicitis usually overshadow signs and symptoms of urethritis, although careful examination may reveal a urethral discharge in a small number of cases.

The Vaginitis syndromes.
Vaginitis is characterized by a vaginal discharge and irritation, often localized to the introitus. At times it may be difficult to differentiate it from dysuria of urethral origin. A vaginal discharge may be due to a cervicitis, vaginitis, or urethritis, and these conditions may coexist. Infections causing vaginitis usually remain confined to the vaginal mucosa, do not exhibit systemic symptoms, and do not infect the urine or cause pyuria. The four main causes of vaginitis are: (a) trichomoniasis, (b) candidosos, (c) nonspecific vaginitis (bacterial vaginosis), and (d) atrophic vaginitis.

Complications

Local

Although complications are not often seen in patients with nongonococcal urethritis, there may be the rare development of a local spread of infection to the Littre's gland, Tyson's glands, or Cowper's glands. The more important spread is to the epidydimus, seen in about 1% of cases, and to the prostate. Prostatitic involvement is seen in some men with NGU, but is mild and usually asymptomatic. It does not cause urethral discharge. Rarely, a urethral stricture may result.

Ureaplasmas are the cause of a septic arthritis in hypogammaglobulinemic patients.[17]

Reactive Arthritis (RA)

This syndrome is defined as a triad of peripherial arthritis, uveitis, and urethritis occurring concurrently. A more inclusive definition notes the occurrence of an episode of peripheral arthritis of >1-month duration, in association with urethritis or cervicitis. The term reactive arthritis is used in the context of RA, to denote the relationship between a distant focus of infection and an aseptic joint (synovial) inflammation. When this is a focus of a sexually transmitted infection, the term SARA (sexually-acquired reactive arthritis) is used.[18]

RA is mainly triggered by two infections, a sexually transmitted urethritis or a bacterial gastroenteritis. *C. trachomatis* is isolated from 16–44% of cases of RA, and 69% of patients who have urethritis. When examined, post-gonococcal RA accounted for 9% of patients in one series, but 50% of these patients developed a PGU, thereby supporting the likelihood of coexisting *C. trachomatis infection*. It is unlikely that mycoplasma play much of a role in pathogenesis, although *M. genitalium* may be responsible for some cases.

Gastrointestinal pathogens giving rise to a reactive arthritis are Shigella, Salmonella, Yersinia, and Campylobacter, with a few instances of antibiotic-associated colitis and Cryptosporidiosis. It is seen in about 0.25–1.5% of post-dysenteric forms, more often in HLA B27+ individuals. Almost all cases of post-STD RA are male, while about 10% of post-dysenteric forms occur in females. Clinical disease is similar with either etiology.

Rarely, *C. psittaci* and *C. pneumoniae* may cause RA.

Role of Inherited Factors (HLA Linkage).
Because RA was seen to occur in members of the same family, a linkage was quite probable; this was found to be the HLA B_{27} antigen. HLA class I antigens help in the presentation of antigenic determinants to T lymphocytes, and the B_{27} protein may act as a receptor for microbial antigens.

HLA B_{27} antigen is seen in 67–90% of patients as compared to 7–14% of controls. Genetic susceptibility renders a HLA B_{27}+ individual about 40–50 times more likely to develop an arthritis following NGU than a HLA B_{27}-negative individual. The severity of the disease is also greater in those who are positive.

Immunological basis of Reiter's disease[19].
Chlamydiae have been detected in the synovial fluid and eye lesions, which proves dissemination of the organism to distal sites. There are different theories for the pathogenic effect:

1. T-cell stimulation with an increase in CD4 cells, which control chlamydial proliferation.

2. Immune response to chlamydial HSP 60 (heat shock protein), producing inflammatory cytokines.
3. Interplay of TH1 and TH2 cytokine responses, leading to reduced TH1 cytokines and thereby, chlamydial proliferation (persistence). IL-1 and TNF-α can cause cartilage breakdown and bone erosion.
4. Autoantigens. Immune response is directed not against the chlamydial antigen but against some normally expressed protein in the joint that has been altered by the infection. This theory is supported by the lack of efficacy of antimicrobials against *C. trachomatis* in management of RA.

Clinical features[20].

RA is seen in about 1–2% of untreated cases of NGU as a complication. The urethritic component of this condition is usually the presenting feature and it is therefore included in a possible differential diagnosis of urethritis. This urethritis may be mild, and purulent or mucopurulent. Dysuria may not be significant. In females, cervicitis may occur. Urethritis in RA may be infective or noninfective, the type that is seen in patients with enteric infections. This is sometimes termed as "reactive urethritis" to a distinct gut infection. Most cases (up to 80 %) of the GI-induced RA have urethritis.

RA is possibly the most common cause of an inflammatory arthritis in young men. Arthritis usually begins within a month of the urethritis in 80% of cases, but may occur simultaneously or occasionally precede the urethritis in 15%. Knee joints are the most frequently involved, followed by ankles and small joints of the feet. An asymmetrical sacroiliitis is seen in about 66% of cases, more often in those who are HLA B_{27}+. Ankylosing spondylitis is also seen in a significant proportion of these HLA B_{27}+ cases. The arthritis may be prolonged, lasting for months to years. Recurrences are well known, but urethritis may not be a feature of such episodes. Enthesopathy is another feature of RA, with inflammation of tendons and ligament insertions.

Eye involvement is seen in the form of a bilateral conjunctivitis, iritis, keratitis, or an acute unilateral uveitis. These features are usually short-lived.

Cutaneous lesions are an important feature, with 2 well-defined lesions, keratoderma blenorrhagicum and circinate balanitis. Lesions are initially papulosquamous, which then thicken to produce thick, psoriasiform plaques on the soles, termed keratoderma blenorrhagicum, in 10–25% of patients. Circinate balanitis indicates a shallow painless erosion of the glans penis, in about 25–40% of patients. Similar lesions may occur in the oral cavity and vulva.

Incomplete RA consists of only 1 or 2 components of the triad, and is not infrequent. The initial episode of RA lasts between 2–6 months, or sometimes longer. Recurrences are common, and more than 50% of patients get episodes even 15–20 years after the first episode. Joint disability of varying severity is often seen in such patients.

Pelvic Inflammatory Disease

The etiology of PID includes sexually transmitted infections, use of intrauterine contraceptive devices, postabortion, and puerperal infections. A majority of cases are under the age of 25 years. The main symptoms are fever and lower abdominal pain. Seventy-five percent are caused by sexually transmitted infections. Previously, *N. gonorrheae* were implicated (50%); however, *C. trachomatis* has become the most common cause (60%). Fifty to sixty percent of sexual partners of PID sufferers had a genital infection. PID is sometimes considered the female counterpart of NGU in men.

The signs of PID[21] are tenderness of (a) abdomen; (b) cervix and uterus movement; and adnexae. At least one of the following must be present: (a) temperature >38°C; (b) WBC count >10,000/cubic mm; (c) purulent material in peritonial cavity; (d) pelvic abscess; and (e) detection of *N. gonorrheae* or *C. trachomatis*.

Inflammatory changes in PID can involve the endometrium (endometritis) or the Fallopian tubes (salpingitis) or both tubes and ovaries (Salpingo-oophoritis). Chlamydial salpingitis is usually mild and asymptomatic despite severe tubal damage. Infection is usually bilateral. Chlamydiae also result in a chronic form of PID.

Laboratory Diagnosis

Despite the use of all diagnostic tests, 10–30% of NGU has no identifiable cause.[25] For laboratory diagnosis of urethritis, presence of >4 PMNL is the primary criterion for diagnosis. Fifteen or more PMNL in 2 or more of 5 high-power fields (HPFs) of the sediment of the first 10–15 mL of urine can also be utilized as a test.[22] The first voided sample of urine may also show the presence of mucus threads, which indicate urethral infection.[23]

Leukocyte esterase (LE) is an enzyme present in white blood cells. Positive results with dipstick examination indicate presence of >5 WBC/HPF, an indicator of UTI, with a reported sensitivity of 75–90%.[24] Sensitivity is decreased by increased urinary glucose concentration, high urinary specific gravity, and presence of antibiotics in urine.

Diagnostic Techniques for Chlamydiae[26]

The following are commonly employed tests for detecting the presence of the infection: (a) culture; (b) serology; (c) antigen detection by direct immunofluorescence (DFA) or enzyme immunoassay (EIA); and (d)

detection of nucleic acid (DNA) by amplification techniques.

Prior to 1980, the laboratory diagnosis of *C. trachomatis* was limited to few research centers that were equipped to maintain the McCoy cell culture line of mouse fibroblasts. Intracellular inclusion bodies develop within 2–3 days. Because maintaining the culture line was expensive, and the sensitivity of culture was not very high, empiric treatment was preferable. Culture was the earlier "gold standard" for chlamydial detection, which was positive in about 75–85% of cases. With the NAA tests detecting more positives, the actual positivity of culture may only about 60–65%.

Serological testing is done using different techniques: the complement fixation (CF) test, the single L-type immunofluorescence test, the micro-immunofluorescence test (MIF), and the ELISA. The MIF test is the most accurate. In general, a fourfold rise of antibody (both IgM and IgG) in the course of suspected illness is diagnostic of active infection. The rapid serology tests are the least sensitive, with only about 50% positivity rate.

The availability of chlamydial antigen detection tests in the late 1980s greatly enhanced the diagnostic capability for detecting the infection. These tests were based on direct visualization of the chlamydial organism by staining with fluorescein-labeled specific monoclonal antibodies (direct cytologic examination or DFA) or immunohistochemical detection of antigen (EIAs and rapid tests). With the use of monoclonal antibody reagents specific for the major outer membrane protein (MOMP) of *C. trachomatis*, the sensitivity of DFA is 80–90% and the specificity is 98–99% relative to culture. DFA identifies only extracellular particles. EIAs are diagnostic tests based on immunochemical detection of lipopolysaccharide genus-specific antigen. Most commercial tests available today are based on this technology. Sensitivity is lower than other methods (75–80% compared with culture), and the test should be confirmed by a blocking test or another method; it is unsuitable for test of cure. Sensitivity of DIF and EIA for urethritis in men is 70–90%, and cervicitis in women is 90%. Specificity is >95%; however, when compared with the NAA tests, these immunoassays have a low sensitivity of about 60%.

Presently, the test of choice would be the nucleic acid amplification assay (NAAT), which detect the DNA material from the bacterium. Different technical methods are available to amplify DNA. These are: (a) polymerase chain reaction (PCR); (b) ligase chain reaction (LCR); (c) strand displacement amplification (SDA); and (d) transcription-mediated amplification (TMA).

For performing NAA tests, the "first-catch urine" (FCU) is the correct specimen in males, and FCU and vaginal swabs in females. All of these assays are nearly equal in their sensitivity and specificity, and have a much superior performance compared to the earlier immune assays.[27] Their advantage is two-fold: (a) they are the most sensitive of the tests available to detect the organism; and (b) they can be performed on specimens easily obtained without resorting to invasive procedures. The disadvantage of these tests is mainly the cost; they are expensive, and need to be conducted in high volumes so as to be cost effective.

PCR and LCR are the more target nucleotide sequences in the chlamydial plasmids. Because there are 7–10 copies of plasmids per elementary body, the sensitivity of this assay is very high, although on a practical level, at least 10–100 copies of the elementary bodies may be needed for a positive assay. Certain inhibitors are present in the specimens that can influence the sensitivity of NAA tests. Because some of these inhibitors are labile, storage of samples, or subjecting them to freeze/thaw cycles might destroy them.[28]

PCR is a good method for testing a large number of samples because the test is automated. The LCR is a more complicated test and not ideal for more number of samples. LCR is the most sensitive of all the NAA tests, slightly greater than PCR.[29] The specificity of all the NAA assays is nearly 100% and sensitivity is around 90%.

All of the nonculture tests for Chlamydia can detect dead organisms and are therefore are not a test of cure in the initial 2–3 weeks after treatment. Diagnostic tests performed too soon after the end of therapy, ie, up to 3 weeks for *Chlamydia trachomatis*, may be falsely negative.

Specific diagnostic tests for *Ureaplasma urealyticum* and *Mycoplasma genitalium* are not indicated, because the detection of these organisms is often difficult and would not alter therapy. Trichomonas can be detected by doing a wet mount.

Treatment[30–32]

Response to treatment is best in men in whom *C. trachomatis* is the cause of NGU and worst in those patients where neither *C. trachomatis* nor *U. urealyticum* have been detected. Considering the overlap of symptoms and clinical manifestations of GU and NGU and the likelihood of dual infection, it would be reasonable to presumptively treat every case of urethritis for both infections. The WHO, as part of the "syndromic" treatment, recommends this approach. This increases the possibility of organisms resistant to one drug being exposed to another drug to which they are sensitive, thereby ensuring their elimination. This approach is also cost-effective.

Recommended regimens include doxycycline 100 mg twice a day for 7 days or azithromycin 1 g orally in a single dose.

Alternative regimens include (a) erythromycin 500 mg 4 times a day for 7 days, (b) erythromycin 500 mg twice daily for 14 days; (c) ofloxacin 200 mg twice a day or 400 mg once a day for 7 days: or (d) tetracycline 500 mg 4 times a day for 7 days.

Azithromycin and doxycycline are equally efficacious.[33–35] Erythromycin is less efficacious than either. The macrolides are safe in pregnancy. In populations that have erratic health-care-seeking behavior, poor compliance with treatment, or unpredictable follow-up, azithromycin may be more cost-effective because it enables the provision of single-dose directly-observed treatment (DOT). Although susceptible to various broad-spectrum antibiotics, *M. genitalium*-associated diseases are probably best treated with azithromycin[36] or a 3–6 week course of erythromycin. Azithromycin 2g orally is effective against uncomplicated gonococcal infection, but it is expensive and causes gastrointestinal distress; therefore it is not recommended for treatment of gonorrhea. At an oral dose of 1 g, azithromycin is insufficiently effective and is not recommended.

Ofloxacin is similar in efficacy to doxycycline and azithromycin, but it is more expensive to use and offers no advantage with regard to the dosage regimen. A 7-day course of ofloxacin may be useful for tetracycline-resistant species of *U. urealyticum*. Levofloxacin may be substituted in doses of 500 mg once a day for 7 days because its pharmacology and in vitro microbiologic activity are similar to that of ofloxacin. Other quinolones either are not reliably effective against chlamydial infection or have not been adequately evaluated.[37]

Doxycycline failures can be treated with a 7-day course of erythromycin, or a single dose (2 g) of metronidazole for trichomonas. In cases of persistent urethritis when all documentable causes of infection have been excluded, a trial of treatment with either ofloxacin or erythromycin for 3–6 weeks may be given. If the discharge is still persisting, anatomic defects and strictures must be ruled out.

Certain important measures help ensure better treatment of patients and reduced transmission of disease. These would include: (a) dispensing on-site medications for chlamydial infections so as to maximize compliance; (b) first dose of medication to be directly observed; (c) abstinence from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen; (d) abstinence from sexual intercourse until all sex partners are treated, to minimize the risk of reinfection; and (e) assessment and treatment of all contacts. This needs to be handled sensitively, and the confidentiality of the index patient maintained. The duration of "look back" is arbitrary; 4 weeks is suggested for symptomatic men and up to 6 months for asymptomatic men.

Approach to Men with Urethritis[38]

- Obtain a history suggestive of a risk of acquiring a sexually transmitted infection.
- Examine the genitalia, lymph nodes, and related structures for evidence of disease.
- Examine the discharge. This may be expressed by milking the urethra and must be done prior to voiding. There is no role for prostatic massage to express the secretions.
- Make smears from the discharge or from endourethral swabs for microscopic examination and cultures.
- Collect first-catch urine and examine sediment for pus cells. Compare with result from mid-stream urine to determine whether infection is in the urethra or higher.
- Test for other sexually transmitted infections, in particular Syphilis and HIV.
- Treat the infection with the appropriate antibiotics.
- Counsel the patient about sexually transmitted infections.
- Consider vaccine for hepatitis B in individuals deemed to have high-risk behavior.
- Trace all contacts and give correct treatment.

Approach to Women with Urethritis

- Determine whether the discharge is due to urethral or vaginal or cervical involvement from symptoms and physical examination. These infections may occur together.
- Examine the urine. Numerous bacteria indicates an upper UTI.
- Take smears from the vaginal and cervical discharge for microscopy and culture.
- Treat infection with appropriate antibiotic.
- Other steps as for male patients.

Conclusions

Nongonococcal urethral infections are an important and common cause of morbidity in the sexually active age groups. It is important to recognize them, in view of the fact that a number of infections are asymptomatic. Appropriate treatment prevents sequelae such as PID and infertility. Contact tracing and proper treatment is of utmost importance in reducing prevalence of infection in the population.

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