

UNIT NO. 3

APPROACH TO MANAGEMENT OF GENITAL DISCHARGE

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ABSTRACT

Symptoms of urethritis in males include discharge, dysuria, and urethral itch. Syndromic management can be applied to urethritis in males in view of the relatively short list of pathogens, fairly specific clinical features, and small number of differential diagnoses. In females, the commonest genital symptoms are abnormal vaginal discharge and vulval itch. A speculum examination should always be undertaken in a woman presenting with discharge or itch. The appearance of the vaginal mucosa and the cervix, and the nature and quantity of discharge should be observed. Such information provides a guide to the diagnosis and treatment.

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URETHRITIS IN MALES

Clinical features

Table 1 shows the causes of sexually transmitted urethritis in males. Symptoms of urethritis include discharge, dysuria, and urethral itch. The quantity of discharge ranges from minimal to profuse, and it may be continuous or intermittent. The colour and consistency of the discharge ranges from clear, mucoid, white, mucopurulent, to frankly purulent. The presence of a urethral discharge is almost always indicative of urethral infection. Dysuria in sexually active young to middle-aged men often indicates a urethral infection, whereas in older men a urinary tract infection is more likely diagnosis. The presence of visible threads in a first-catch urine (FCU) specimen is suggestive of anterior urethritis. Nevertheless, urethral infections due to sexually-transmitted pathogens are often asymptomatic. Table 2 shows the approach to the diagnosis of urethral discharge.

Table 1. Causes of sexually transmitted urethritis in males

Common causes

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*

Other causes

- *Ureaplasma urealyticum*
- *Mycoplasma genitalium*
- *Trichomonas vaginalis*
- Herpes simplex virus
- Adenovirus infection
- *Neisseria meningitidis*
- Non Specific Urethritis (NSU)

Table 2. Approach to diagnosis of urethral discharge

Diagnosis	Gonorrhoea	Non-gonococcal urethritis
Clinical features		
Nature of discharge	purulent, profuse	clear, whitish
Clinical complications	Epididymo-orchitis Prostatitis Disseminated Gonococcal infection	Epididymo-orchitis Prostatitis Reiter's disease
Urethral smear Gram stain Polymorphs Gram negative i/c diplococci	+ /+++ +	+ /++ (>5 wbcs/hpf) —
Culture/NAAT	<i>N. gonorrhoea</i>	<i>C. trachomatis</i> <i>U. urealyticum</i> <i>M. genitalium</i> <i>M. hominis</i>

Gonococcal urethritis has a shorter incubation period (2-7 days) than other forms of urethritis, and is characterised clinically by a profuse purulent discharge from the affected genital site (> 80% in male urethritis, up to 50% in female cervicitis), often accompanied by local pain or discomfort. However, asymptomatic infection occurs in 10% of urethral infection, > 50% of cervical infection, > 90% of pharyngeal and rectal infection.

Non-gonococcal urethritis (NGU) refers to any urethritis from which *N. gonorrhoeae* cannot be detected or isolated. NGU often has milder symptoms, with scant discharge, and a longer incubation period (7-21 days). Urethritis which is not caused by *N. gonorrhoeae* may be due to *Chlamydia trachomatis* (up to 50%) and other organisms (10% to 20%) including *Ureaplasma urealyticum*, *Mycoplasma genitalium*, *Trichomonas vaginalis*, bacterial UTI and *Herpes simplex virus*. The remainder (20-30%) have no detectable organisms (non-specific urethritis).

Examine the penis carefully, retract the foreskin if present, inspect the meatus for inflammation, and look for urethral discharge. If there is no discharge visible, gently 'milk' the urethra towards the meatus. A cotton-tipped swab is used to collect a sample of the discharge. This is smeared on a glass microscope slide, allowed to dry in the air and sent for Gram-staining and microscopy. A sample is also placed in appropriate transport medium for gonococcal culture. A second specimen of discharge or a urine sample can be sent for a NAAT for Chlamydia. Cultures and PCR detection for *Ureaplasma urealyticum* and *Mycoplasma genitalium* are not routinely performed.

Small amounts of discharge may have been washed away if the patient has recently voided. In such cases the patient should be asked to return 4 hours after holding his urine when the laboratory tests can be performed.

NGU is diagnosed when there are 5 or more polymorphic leucocytes (PML) present per high-power field in 5 or more fields using high power (1000x) oil immersion microscopic examination of a properly prepared urethral smear.

Complications

Epididymo-orchitis due to retrograde spread of urethral infection is a relatively uncommon but well-known complication of untreated urethritis. *N. gonorrhoeae* and *C. trachomatis* are the commonest causative agents.

Reactive arthritis or Reiter's syndrome (the classic triad of arthritis, conjunctivitis, and urethritis; sometimes with circinate balanitis and keratoderma blennorrhagica) is most frequently triggered by *Chlamydia trachomatis* urethritis.

Syndromic management

Syndromic management can be applied to urethritis in males in view of the relatively short list of pathogens, fairly specific clinical features and small number of differential diagnoses. See Table 3.

Table 3. Syndromic management of urethral symptoms in males

Urethral symptoms present
A. Presence of sexually transmitted urethral infection This is indicated if any one of the following are present: - History – Risk of sexually transmitted infection present - Examination – Presence of urethral discharge and meatitis - Laboratory – Raised polymorphonuclear leucocytes (PML) on Gram-stained smear - Visible threads in first catch urine specimen, PML in smear of sediment
B. Diagnosis of gonorrhoea is likely if there is: - Thick purulent discharge - Short incubation period - Gram stain microscopy shows Gram-negative intracellular diplococci If any one of the points is present: - Send swab for gonococcal culture - Send swab or first catch urine for NAAT for <i>Chlamydia trachomatis</i> - Treat for <i>Neisseria gonorrhoeae</i> and <i>Chlamydia trachomatis</i> - Review in 14 days If none of points is present: - Send swab for gonococcal culture - Send swab or first catch urine for NAAT for <i>Chlamydia trachomatis</i> - Treat for <i>Chlamydia trachomatis</i> - Review in 14 days

VAGINAL DISCHARGE

Table 4 shows the causes of vaginal discharge. Abnormal vaginal discharge and vulval itch are the commonest genital symptoms in women.

Physiological vaginal discharge

Pre-menopausal women have normal physiological discharge

that is cyclical in nature. The quantity of physiological discharge will vary from minimal during parts of the cycle but profuse at other times.

Sexually transmitted infections and vaginal discharge

Vaginal infections due to trichomoniasis, candidiasis, and bacterial vaginosis (BV) commonly present with vaginal discharge. Pathogens that infect the cervix on the other hand (*N. gonorrhoeae*, *C. trachomatis*, *M. genitalium*) are not consistently associated with an abnormal vaginal discharge.

Vulvovaginal candidiasis presents with features that include vulval itch and burning, a curd-like vaginal discharge, superficial dyspareunia, and dysuria. Factors facilitating germination of *Candida* result in invasion and symptomatic disease, e.g. pregnancy, diabetes mellitus, corticosteroid therapy, antibiotics, and immunosuppression. Laboratory tests include Gram-stain or wet mount (saline or 10% KOH) of swabs from the vulva/vaginal wall will reveal budding yeast cells and pseudohyphae (sensitivity 60%), vaginal pH 4 – 4.5, and culture on Sabouraud media. Isolation in the absence of symptoms and negative direct smear is not an indication for treatment.

Table 4. Causes of vaginal discharge

Physiological - Hormonal factors: - Variation during the menstrual cycle - Hormonal contraception - Pregnancy - Lactational atrophic vaginitis - Postmenopausal atrophic vaginitis - Cervical ectropion - Sexual arousal
Infective causes - Vaginal causes: - Candidiasis - Bacterial vaginosis - Trichomoniasis - Herpes simplex virus - Staphylococcus aureus (toxic shock) - Streptococcal species - Cervical causes: <i>Chlamydia trachomatis</i> <i>Neisseria gonorrhoeae</i> <i>Mycoplasma genitalium</i> <i>Herpes simplex virus</i>
Non-infective Inflammatory causes: - Irritant contact dermatitis, e.g. topical medications, lubricants - Allergic contact dermatitis, e.g. latex
Other causes of discharge: - Foreign body, e.g. retained tampon, IUCD - Retained products of conception - Cervical polyps - Cervical or endometrial neoplasia - Endometritis

Bacterial vaginosis (BV) is a condition that results from a decrease in hydrogen peroxide-producing lactobacilli, an increase in mixed flora, and a rise in vaginal pH. Diagnosis is based on fulfillment of specific clinical and laboratory criteria.

The following have been shown to be associated with a higher risk of BV:

- κ sexually active woman,
- κ higher number of recent and lifetime partners,
- κ recent change in sexual partner,
- κ lack of condom use,
- κ cunnilingus, and
- κ lesbian.

BV presents with complaints of an unpleasant odour or abnormal vaginal discharge; women often have a history of recurrent symptoms. A malodorous, white-grey, thin discharge is often visible and adherent to the introitus. However, the discharge can be scant and the odour barely noticeable. Diagnosis is made on the basis of fulfillment of three or more of Amsel's criteria:

- κ Vaginal pH >4.5
- κ Homogeneous white vaginal discharge
- κ Clue cells on Gram stain of vaginal secretions (epithelial cells coated in gram-variable coccobacilli are the most reliable predictor of BV)
- κ Positive amine test (addition of potassium hydroxide to a wet preparation of vaginal secretions releases a fishy odour).

Note:- Menses, semen, cervical secretions or douching may affect the pH, a weak positive "sniff test" may be produced by menstrual blood or semen.

Trichomoniasis is caused by *Trichomonas vaginalis* (TV), a protozoa that can cause vaginitis in women and urethritis in men and women. It infects the vagina, urethra, Bartholin's and Skene's glands in women. Predominant symptoms are a yellow-green discharge and vulval itch. On examination, the vulva may be erythematous or excoriated, the vagina inflamed, and small cervical haemorrhages and ulcers can give the classical appearance of the 'strawberry cervix'. *Trichomonas* infection has been associated with premature rupture of the membranes and preterm delivery in pregnant women. Laboratory tests include direct microscopy of a wet mount of vaginal secretions mixed with normal saline that will show the trichomonas about the size of white blood cells moving with a jerky motion (sensitivity 60-70%), and culture on Feinberg-Whittington media (sensitivity > 90%).

STIs that infect the cervix are not consistently associated with an abnormal vaginal discharge. *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, herpes simplex virus, and *Mycoplasma genitalium* infect the cervix. While a STI screen should always be conducted in women presenting with vaginal symptoms, cervical infections – unless longstanding – are more likely to present with symptoms of upper genital tract infection, or to be asymptomatic.

A speculum examination should always be undertaken in a woman presenting with discharge or itch. The appearance of the vaginal mucosa and the cervix, and the nature and quantity of discharge should be observed. See Table 5. Table 6 shows the investigations for vaginal discharge.

Table 5. Approach to the diagnosis of vaginal discharge

Cause Features	Normal	Gonorrhoea	Chlamydia	Candidiasis	Tichomonas	Bacterial vaginosis
Physical examination	Mild, white, milky discharge	Purulent discharge from cervix	Purulent discharge from cervix	Thick white cheesy plaques, erythema of vulva and perineum	Profuse, frothy grey to yellowish/ green discharge. Erythema of vulvae, perineum, and cervix	Profuse grey, smooth, watery discharge which may contain bubbles. Vaginal walls and vulva not inflamed
Vaginal pH	<4.5	>5	>5	<4.5	>4.5	>4.5
Wet film microscopy						
Lactobacilli	+	-	-	+	+/-	-
Polymorphs	-	++	++	-	++	++
Trichomonads	-	-	-	-	++	-
Clue cells	-	-	-	-	-	+
Pseudohyphae and budding yeast cells	-	-	-	+	-	-

Table 6. Investigations for vaginal discharge

Site	Investigations
Vulval fissures and erythema	▫ Microscopy for yeasts ▫ Culture for yeasts ▫ Herpes simplex virus (if vesicles or erosions present)
Vagina	▫ Wet preparation to detect TV ▫ Gram stain to detect clue cells and yeasts ▫ Culture for TV and yeasts ▫ Amine 'sniff' test ▫ Vaginal pH
Cervix	▫ Gram-stain for pus cells, Gram-negative intracellular diplococci ▫ Culture <i>Neisseria gonorrhoeae</i> ▫ NAAT for <i>Chlamydia trachomatis</i>

TREATMENT OF GONORRHOEA

Uncomplicated infection in adults - urethral, endocervical and rectal infection

1. Ceftriaxone 250 mg i/m single dose [A]
- or
2. Cefixime 400 mg orally single dose [A]

Alternative Regimens

1. Cefotaxime 1 g i/m single dose [A]
- or
2. Spectinomycin 2 g i/m single dose [A]

With anti-chlamydia therapy

The fluoroquinolones (e.g. ciprofloxacin, ofloxacin, norfloxacin) are contraindicated as > 50% of isolates in Singapore and the region are resistant.

Gonococcal infection in pregnancy

Cephalosporins [A] in the recommended dosages are safe and effective in pregnancy. Spectinomycin [A] can be administered to women who are unable to tolerate cephalosporins. Simultaneous treatment for chlamydial infection with erythromycin 500 mg orally qid x 7 to 14 days is advocated.

Pharyngeal infection

Ceftriaxone 250 mg i/m single dose [B] with anti-chlamydia therapy.

Follow up

- Test-of-cure is not routinely necessary if recommended regimens are given unless there is persistence of symptoms or re-exposure.
- All treatments are less effective at eradicating pharyngeal infection and test-of-cure is recommended following treatment of infection at this site.
- In DSC Clinic test-of-cure and assessment for post-gonococcal urethritis (PGU) is performed after 14 days.
- Serologic tests for syphilis and HIV should be performed; if negative they should be repeated at 3 months after the last risky exposure.

Management of sex partners

Sexual contacts in the preceding 60 days should be traced, screened and treated on epidemiologic grounds. If the last sexual exposure was > 60 days, the patient's most recent partner should be treated.

TREATMENT OF CHLAMYDIA TRACHOMATIS INFECTION

Uncomplicated urethral, endocervical, pharyngeal or rectal infections in adults

1. Doxycycline 100 mg orally bid x 7 days [1a, A]
- or
2. Azithromycin 1 g orally single dose [1a, A]
- or
3. Erythromycin 500 mg orally qid x 7 days or 500 mg orally bid x 14 days [1b, A]
- or
4. Ofloxacin 200 mg orally bid or 400 mg orally od x 7 days [1b, A]

Chlamydia trachomatis infection in pregnancy

Risk factors for *Chlamydia trachomatis* infection during pregnancy include young age (< 25 years), past history of other STI, new sex partner within the last 3 months, and multiple sex partners. Pregnant women whose sexual partners have NGU should be examined, screened for other STI, and treated on epidemiological grounds.

1. Erythromycin 500 mg orally qid x 7 days or 500 mg orally bid x 14 days [1a, A]
- or
2. Amoxicillin 500 mg orally tid x 7 days [1a, A]
- or
3. Azithromycin 1 g orally single dose (clinical data suggests this is safe in pregnancy) [1a, A]

Follow up

A test-of-cure is not necessary when treatment with a tetracycline or azithromycin has been completed, unless symptoms persist or reinfection is suspected. Test-of-cure is however recommended after 4 weeks for infections in infants, children and pregnant women, or when erythromycin was used. Non-culture tests done within 4 weeks of completing treatment may yield false positive tests due to persistence of chlamydial antigens.

Management of sex partners

Sex partners of symptomatic male patients within the last 60 days (or the most recent sex partner if the last contact was > 60 days) should be screened and treated for chlamydial infection epidemiologically. The look-back period for contacts of female patients and asymptomatic males is longer e.g. 3 months.

TREATMENT OF NGU

Recommended regimens

See treatment of *Chlamydia trachomatis* above.

Follow up

Patients are advised to return 2 weeks after completion of treatment for evaluation of symptoms and signs, tests-of-cure, patient education, and partner notification interviews. HIV and syphilis serology are repeated at 3 months.

Management of sex partners

Sex partners of men with NGU within the last 60 days should be screened and treated. These partners should also be examined to exclude other associated STI. At least 30% of consorts of men with NGU have chlamydial infections of the cervix. Such women are at risk of developing upper genital tract infections, which are often asymptomatic and have the potential sequelae of ectopic pregnancy, infertility, and chronic pelvic inflammatory disease.

Management of recurrent or chronic NGU

About 30% of patients with NGU have recurrent or chronic symptoms 4 to 6 weeks after initiation of treatment. Persistent chlamydial infection is only rarely detected. There is evidence that ureaplasmas and *M. genitalium* may be important in the aetiology of chronic NGU. Some men with recurrent or persistent NGU are anxious, obsessional, and hypochondriacal. There may also be an association with guilt over a perceived inappropriate sexual episode.

- Obtain objective evidence of urethritis, e.g. presence of urethral discharge or pus cells on urethral smear. If patient has objective evidence, consider reassurance only.
 - Exclude drug adherence failure or re-infection from untreated partner or a new partner.
 - Azithromycin 1 g orally single dose [C]
(if initially treated with Doxycycline and vice versa).
- or
- Erythromycin 500 mg orally qid x 2 weeks together with Metronidazole 200 mg orally tid x 7 days (for *T. vaginalis*)
 - Not cured
Doxycycline 100 mg orally bid x 4 to 6 weeks [C]
- or
- Erythromycin 500 mg orally qid x 4 to 6 weeks [C]
 - Not cured
Exclude prostatitis, urethral stricture and intraurethral lesions

Normal findings

- No further antimicrobial treatment, observe and reassure
- Avoid repeated courses of antimicrobials and over investigation.
- Urological investigations usually normal unless patient has urinary flow problems.

Explain and reassure the patient that :

- physical sequelae of persistent NGU such as infertility are slight
- risk of transmission is low because repeated courses of antibiotics would have eliminated infective causes
- symptoms should usually resolve with time
- most recurrences arise independent of resumption of sexual activity

TREATMENT OF CANDIDIASIS

Treatment is indicated for symptomatic patients. It is not recommended for asymptomatic patients with a positive culture because 10-20% of women harbour *Candida* species or other yeasts in the vagina in the absence of symptoms.

General advice

Avoid local irritants (e.g. perfumed products) and tight fitting clothing [IV, C]

Uncomplicated vulvovaginal candidiasis (UVC)

1. Clotrimazole vaginal tablet 200 mg daily x 3 days or 500 mg single dose or 100 mg or cream (1%) 5g intravaginally daily x 7 days [II, A]
- or
2. Miconazole nitrate vaginal tablet 200 mg daily x 3 days [II, A]
- or
3. Econazole nitrate ovule 150 mg intravaginally nightly x 3 days [II, A]
- or
4. Nystatin pessary 100,000 U daily x 7 to 14 days [II, A]
- or
5. Fluconazole 150mg orally single dose [II, A]

Candidiasis in pregnancy

Only topical azole therapy should be given. Longer courses may be necessary. Oral azole therapy is contraindicated. [II, B]

Recurrent vulvovaginal candidiasis

This is defined as 4 or more episodes of symptomatic vulvovaginal candidiasis annually. Patients must be evaluated for any predisposing factors e.g. uncontrolled diabetes mellitus, immunosuppression and corticosteroid use. Repeated courses of treatment may be required. Systemic treatment may be indicated for resistant/recurrent candidiasis:

Induction Regimens

1. Ketoconazole 200 mg orally daily x 10-14 days [II, B]
- or
2. Itraconazole 100 mg orally bid x 1-3 days [II, B]
- or
3. Fluconazole 150 mg orally single dose [II, B]

Maintenance Regimens

1. Fluconazole 100mg orally once a week x 6 months [II, B]
- or
2. Clotrimazole pessary 500mg once a week x 6 months [II, B]
- or
3. Itraconazole 400mg once a month x 6 months [II, B]

TREATMENT OF BACTERIAL VAGINOSIS

Indications for treatment:

- 1) All symptomatic women, pregnant or non pregnant [A].
- 2) Asymptomatic pregnant women with high risk for preterm delivery [A].
- 3) Asymptomatic women before surgical abortion procedures [A].

- 4) Women who do not volunteer symptoms may elect to take treatment if offered. They may report a beneficial change in their discharge following treatment.

General Measures

Patients should be asked to avoid vaginal douching, use of shower gels, antiseptic agents or shampoo in the bath [C]

Recommended regimens

1. Metronidazole 400 mg orally bid x 7 days [A]
or
2. Clindamycin cream 2% one full applicator (5g) intravaginally at bedtime x 7 days [A]
or
3. Metronidazole gel 0.75% one full applicator (5g) intravaginally once a day x 5 days [A]

Alternative regimens

1. Clindamycin 300 mg orally bid x 7 days [A]
or
2. Clindamycin ovules 100 mg intravaginally once at bedtime x 3 days

Notes: - Metronidazole 2 g single dose therapy is the least effective for BV and is no longer a recommended

BV in Pregnancy

1. Metronidazole 400 mg orally bid x 7 days [A]
or
2. Clindamycin 300 mg bid orally x 7 days [A]

Recurrent BV

There are few published studies evaluating the optimal approach to women with frequent recurrences of BV. Possible approaches are:

- Suppressive therapy: Metronidazole gel 0.75% twice weekly for 4-6 months [Ia]
- Metronidazole 400mg orally bid for 3 days at the start and end of menstruation (combined with fluconazole 150mg as a single dose if there is a history of candidiasis also) [III]
- Maintenance therapy involving acetic acid vaginal gel use at the time of menstruation and following unprotected sexual intercourse [Ib]

Follow-up

Follow-up is not necessary if symptoms resolve. For high-risk pregnant women, a one month follow-up visit is recommended to evaluate if treatment is successful. Alternative regimens can be given for recurrent disease. Long term maintenance regimens are not recommended.

Management of sex partners

No clinical counterpart is recognised in males and screening and treatment has not shown to be beneficial for the patient or the male partner. Although studies have reported a high incidence of BV in female partners of lesbian women with BV [II], no studies have as yet investigated the value of treating partners of lesbian women simultaneously.

TREATMENT OF TRICHOMONIASIS

Both symptomatic and asymptomatic patients should be treated.

Recommended regimen

1. Metronidazole 2 g orally single dose [Ib, A]
or
2. Metronidazole 400 mg orally bid x 7 days [Ib, A]
or
3. Tinidazole 2 g orally single dose.

Metronidazole gel is not recommended because it is less efficacious (< 50%).

Treatment in pregnancy

Metronidazole in pregnancy has not been shown to be teratogenic or mutagenic and can be used during all stages of pregnancy or breastfeeding. Imidazole and metronidazole pessaries may be used to provide symptomatic relief, but systemic metronidazole is needed for eradication of infection.

Follow-up

Follow-up is unnecessary for asymptomatic patients. Patients with persistent symptoms should be retreated with metronidazole 400 mg bid for 7 days. If treatment failure occurs repeatedly, the patient can be treated with a single 2 g dose of metronidazole once a day for 3-5 days.

Management of sex contacts

Sex partners should be encouraged to come for examination and be treated on epidemiological grounds.

REFERENCES

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LEARNING POINTS

- o NGU is diagnosed when there are 5 or more polymorphic leucocytes (PML) present per high-power field in 5 or more fields using high power (1000x) oil immersion microscopic examination of a properly prepared urethral smear.
- o About 30% of patients with NGU have recurrent or chronic symptoms 4 to 6 weeks after initiation of treatment.
- o Factors facilitating germination of *Candida* result in invasion and symptomatic disease, e.g. pregnancy, diabetes mellitus, corticosteroid therapy, antibiotics, and immunosuppression.
- o Metronidazole in pregnancy has not been shown to be teratogenic or mutagenic and can be used during all stages of pregnancy or breastfeeding.