UNIT NO. 5

THE MANAGEMENT OF PATIENTS PRESENTING WITH GENITAL DISCHARGE

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ABSTRACT

The approach to the management of genital discharge in men and women differ due to the varying presentations and aetiologies for each. In women, non-sexually transmitted causes are typically, physiological, bacterial vaginosis and candidiasis. In men, chlamydia and gonorrhoea are the most frequent causes of urethritis. A thorough history and examination should be conducted as they provide a guide to diagnosis and treatment. Investigations are particularly important in women to confirm or exclude sexually transmitted infections which are often asymptomatic. Where a sexually transmitted infection is suspected, patients should be counselled regarding abstaining until treatment completion, notification and treatment of sex partners to reduce onward transmission and re-infection, and safe sex practices.

Keywords:
Sexually Transmitted Infection, gonorrhoea, chlamydia, vaginal discharge, urethritis

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INTRODUCTION

The approach to the management of genital discharge in men and women differ due to the varying presentations and aetiologies for each. As such, they will be considered separately. The treatment of only the more common causes and uncomplicated sexually transmitted infections of the genital tract in adults will be discussed.

VAGINAL DISCHARGE

Vaginal discharge is a common presenting complaint among omen. Many women at some point in their lives perceive their vaginal discharge to be abnormal. The most common causes of altered vaginal discharge are not sexually transmitted. These are: physiological, bacterial vaginosis (BV) and vulvovaginal candidiasis (VVC). Sexually transmitted infections (STIs) are often asymptomatic, particularly cervical infections with *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Additionally, the presence of vaginal discharge is a poor predictor of STIs. *Trichomonas vaginalis* (TV) is also sexually transmitted, can cause abnormal vaginal discharge but may also be asymptomatic. Nevertheless, STIs must be considered, tested for and treated. Untreated STIs can lead to adverse health sequelae as well as enhancing the risk and transmission of HIV. Other causes of vaginal discharge are shown in Table 1.

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NON-SEXUALLY TRANSMITTED CAUSES OF VAGINAL DISCHARGE

Physiological discharge

It is normal for women of reproductive age to have some degree of vaginal discharge. This is related to hormonal fluctuations of the menstrual cycle. The quantity and characteristics of the discharge vary; around ovulation, the vaginal discharge is thin, clear and slippery (similar to egg white) due to the cervical mucus becoming fertile. Following menstruation, the vaginal discharge tends to be thicker, white and tacky. Normal vaginal discharge is acidic at pH≤4.5 secondary to lactic acid producing lactobacilli, a commensal bacteria (normal vaginal flora). Other commensal organisms include Candida albicans, anaerobic bacteria, staphylococci and streptococci. Abnormal discharge can develop if these "overgrow."

Bacterial vaginosis

BV is the most common cause of abnormal vaginal discharge in women of reproductive age [1]. It may spontaneously occur and resolve, and is associated with the replacement of normal lactobacilli by mixed anaerobic bacteria causing a rise in vaginal pH[2]. BV may be asymptomatic. Typical signs and symptoms are shown in Table 2. Gardnerella vaginalis if frequently found in women with BV but its presence alone is insufficient to diagnose BV due to its presence as a commensal organism in 30-40% of women [3]. BV is not considered a sexually transmitted infection but may be sexually associated (more common in sexually active women, recent change in partner, lack of condom use, cunnilingus, women who have sex with women) [4, 5].

BV is associated with adverse pregnancy outcomes (premature rupture of membranes, preterm labour and birth [6, 7], post-hysterectomy vaginal cuff infection[8], post-termination endometritis [9], and there is growing evidence of its association with increased HIV risk [10, 11].

Vulvovaginal candidiasis

VVC is common and is caused by the overgrowth of yeast, *Candida albicans* in 70-90% of cases and occasionally by other non-albicans species (e.g. *C. glabrata*) [12]. It occurs most frequently when the vagina is exposed to oestrogen making VVC more common during the reproductive years and in pregnancy. It may be precipitated by the use of antibiotics. Predisposing factors include: diabetes mellitus, long-term antibiotic use, steroid use and immunosuppression. Up to 20% of women have colonisation and unless symptomatic, VVC does not necessarily require treatment. Table 2 outlines the signs and symptoms of VVC.

TABLE 1. CAUSES OF ALTERED VAGINAL DISCHARGE

Non-infective

- Physiological
  - Menstrual cycle related
  - Pregnancy
  - Hormonal contraception
  - Sexual arousal
  - Cervical ectropian
  - Lactational and post-menopausal atrophic vaginitis
- Other
  - Foreign body e.g. retained tampon, IUCD
  - Cervical polyp
  - Genital tract malignancy
  - Retained products of conception
  - Fistulae
  - Endometritis
  - Genital dermatitis and allergic reactions

Infective (sexually transmitted)

- Vaginal
  - *Trichomonas vaginalis*
- Cervical
  - *Chlamydia trachomatis*
  - *Neisseria gonorrhoeae*
  - Herpes simplex virus

Infective (non-sexually transmitted)

- Bacterial vaginosis
- *Candida* infections

TABLE 2. SIGNS AND SYMPTOMS OF VAGINAL INFECTION

	Bacterial vaginosis	**Candidiasis**	**Trichomoniasis**
Symptoms	50% asymptomatic	10-20% asymptomatic	10-50% asymptomatic
Discharge	Thin white homogenous, coats vaginal wall and vestibule	Thick white, curd-like, removable plaques on vaginal wall	Scanty to profuse Frothy yellow/green
Odour	Offensive, fishy	Non-offensive	Offensive
Itch	None	Vulval/vaginal itch	Vulval/vaginal itch
Other signs and symptoms	No inflammation Symptoms often more noticeable post-coitally	Superficial dyspareunia Dysuria Vulval/vaginal erythema, oedema Vulval fissuring Satellite lesions	Superficial dyspareunia Dysuria Erythema of vagina, vulva, perineum Cervicitis ("strawberry cervix")
Point-of-care test: vaginal pH	>4.5	≤4.5	>4.5

Note: Blood, semen and cervical mucus may increase the pH.

SEXUALLY-TRANSMITTED CAUSES OF VAGINAL DISCHARGE

Trichomoniasis

Trichomoniasis is caused by the flagellated protozoan, *Trichomonas vaginalis*. In addition to causing vaginitis, it may infect the urethra, Bartholin's and Skene's glands in women. It is almost exclusively sexually transmitted and is less common than BV or VVC. There is an association between TV with premature rupture of membranes, preterm delivery and low birth weight [13].

Chlamydia

Chlamydia trachomatis infection of the cervix is asymptomatic in about 80% of women [14] and is particularly common in sexually active women under the age of 25. Vaginal discharge is not necessarily an indicator of chlamydia. However, a discharge can result from abnormal bleeding (postcoital or intermenstrual) due to cervicitis or endometritis, or purulent cervicitis. Dysuria, pelvic pain and deep dyspareunia may also be experienced (see Table 3).

Complications of chlamydia include pelvic inflammatory disease (PID), ectopic pregnancy, chronic pelvic pain, tubal infertility, reactive arthritis and neonatal infection from vertical transmission.

Gonorrhoea

Gonorrhoea is caused by *Neisseria gonorrhoeae* and is asymptomatic in approximately 50% of women [15]. Abnormal vaginal discharge can result from cervicitis and abnormal bleeding (Table 3). Complications include PID, disseminated gonococcal infection (DGI) and neonatal gonococcal ophthalmia during delivery.

Concomitant infection by chlamydia occurs in up to 40% of women diagnosed with gonorrhoea [15].

include those who:

- Are <25 years of age.
- Have a new sex partner or multiple partners.
- Are not using condoms consistently.
- Have been diagnosed with chlamydia in the past 12 months or have a past history of other STI.
- Have a sex partner who has been diagnosed with an STI.
- Have a sex partner who is at higher risk of having an STI (e.g. is bisexual, has paid sex or other sex partners).

As with any clinical history, the patient should be asked about the onset, duration and characteristics (odour, menstrual cycle association, colour, consistency, precipitating/exacerbating factors) of their symptoms as well as any associated symptoms (e.g. itch, pain, abnormal bleeding, deep dyspareunia) which may provide an indicator to the most likely cause of the vaginal discharge.

TABLE 3. SIGNS AND SYMPTOMS OF CHLAMYDIA AND GONORRHOEA

	Women	Men*
Chlamydia		
Sites	Cervix Other: urethra, conjunctiva, rectum, throat (rare)	Urethra Other: conjunctiva, in MSM -rectum, throat (rare)
Symptoms	70-80% asymptomatic Post-coital/intermenstrual bleeding Vaginal discharge Pelvic pain, deep dyspareunia Dysuria	50% asymptomatic Dysuria Urethral itch or irritation Urethral discharge
Signs	Normal Mucopurulent cervicitis	Normal Urethral discharge – may be scant, clear, whitish or mucopurulent Meatal erythema
Gonorrhoea		
Sites	Cervix Other: urethra, conjunctiva, throat, rectum	Urethra Other: conjunctiva, in MSM – rectum, throat
Symptoms	≥50% asymptomatic Vaginal discharge in ≤50% Lower abdominal pain in ≤25% Dysuria in 10-15% Rarely abnormal bleeding	<10% asymptomatic Urethral discharge in >80% Dysuria in >50%
Signs	Normal Mucopurulent cervicitis	Urethral discharge – profuse, purulent Meatal erythema

Note: In complicated chlamydia or gonorrhoea where the infection has ascended to the upper genital tract, women may have signs of PID – cervical excitation, adnexal tenderness, pelvic tenderness +/- fever. Men may have symptoms of epididymitis/epididymo-orchitis (unilateral testicular pain) with testicular tenderness and swelling.

*Symptoms of non-gonococcal urethritis are as per chlamydial urethritis.

MSM = men who have sex with men; PID=pelvic inflammatory disease

MANAGEMENT OF WOMEN PRESENTING WITH VAGINAL DISCHARGE

1. History

A clinical and sexual history (Table 4) should be taken when a woman presents with a vaginal discharge. The latter is to assess their risk of STIs. Women who are at a higher risk of STIs

2. Examination

The history alone may be a guide to the likely diagnosis but a patient presenting with symptoms should in most cases undergo external genital and speculum examination. The appearance of the vulva, vagina and cervix, and the nature and quantity of the discharge should be observed (Table 2 and 3). If associated pelvic pain or deep dyspareunia are present, bimanual

TABLE 4. SEXUAL HISTORY TAKING – TIPS AND PERTINENT QUESTIONS

Tips

- Ensure that the environment is private so the patient feels comfortable talking.
- Explain why you are asking for personal and sensitive information. Example*: I ask all of my patients these questions when…to work out your risk of infection and to make sure I don't miss anything.*
- Do not make assumptions or judgements about the patient's sexual practices and identity.
- Reassure regarding confidentiality.
- Use patient-appropriate language – avoid medical jargon and technical terms.
- Avoid leading or loaded questions e.g. "You use condoms all the time, don't you?"
- Start with less confrontational questions before progressing onto more sensitive ones.
- Recognise your own biases and do not allow them to interfere.

Some important questions to ask

- *When was the last time you had sex?*
- *Who was it with? Was it a casual or regular partner (how long with regular partner)? Male or female? Have you ever paid for/been paid for sex?*
- *What type of sex -(vaginal, anal, oral, mutual masturbation)- did you have?*
- *Was a condom used? How often do you use condoms? When was the last time you had unprotected sex?*
- *How many sex partners have you had in the last 3 (6 or 12) months?*
- *Have you been diagnosed with an STI before?*

TABLE 5. INVESTIGATIONS FOR VAGINAL DISCHARGE

Site	Investigation
Vulval swab	• Culture for candida • Herpes simplex virus culture or NAAT (if ulcer, erosions or vesicles present)
Vaginal swab	• pH of the vaginal discharge (using narrow-range pH paper) - pH>4.5 for BV and TV, pH≤4.5 for VVC (unless mixed infection) • "Whiff test" using 10% KOH – positive amine odour in BV • Microscopy of Gram-stained vaginal fluid - Spores or pseudohyphae of candida - Clue cells of BV • Wet mount of vaginal fluid - Motile trichomonads of *T. vaginalis* (sensitivity 70% and declines rapidly with transit time) • Culture for *T. vaginalis* and candida
Endocervical swab	• Gram-stain of cervical mucus - Gram-negative intracellular diplococci of gonorrhoea - Pus cells • NAAT* (example, PCR test) - Chlamydia - Gonorrhoea • Culture - Gonorrhoea (test-of-cure and antibiotic sensitivities; much lower sensitivity than NAATs)
First-pass urine	• NAAT - Chlamydia and gonorrhoea

*Note: Serology has NO role in the diagnosis of vaginal and cervical infections. *NAATs are the current gold-standard for the diagnosis of chlamydia and gonorrhoea.*
NAAT = nucleic acid amplification test , PCR = polymerase chain reaction

examination and a pregnancy test should be conducted to exclude ectopic pregnancy and PID.

3. Investigations

A syndromic approach (where no investigations are performed and treatment based on signs and symptoms alone) to the management of women with vaginal discharge is sub-optimal for diagnosing STIs [16] and not recommended in a setting where diagnostic laboratory tests are available except in exceptional circumstances. For example, syndromic management of a patient with uncomplicated vaginal discharge who has never been sexually active or has no risk of STIs would not be unreasonable. An STI screen should always be offered to women who have ever been sexually active, presenting with vaginal

discharge. However, cervical infections are more likely to be asymptomatic or present with symptoms of upper genital tract infection.

Investigations should be conducted according to local protocols and the latest clinical standards (Table 5). High vaginal swabs (HVS) are often used but may be of limited value. Reporting of commensal organisms may lead to overtreatment, and under-diagnosis if other diagnostic criteria are not included such as with BV.

The diagnosis of BV requires the fulfilment of three or more of Amsel's criteria:
1. Vaginal pH>4.5
2. Homogenous white vaginal discharge
3. Clue cells on Gram-stain of vaginal secretions (epithelial cells coated with Gram-variable bacteria)
4. Positive amine test ("whiff test") – addition of KOH to wet preparation of vaginal discharge releases a fishy odour.

HVS may be useful for the diagnosis of BV, VVC, trichomoniasis and other vaginal infections (e.g. streptococcus) in these scenarios:
- Symptoms, signs and pH are not consistent with a specific diagnosis
- Pregnancy, post-partum, post-termination/instrumentation
- Treatment failure
- Recurrent symptoms.

Where a patient with symptoms of uncomplicated vaginal infection declines examination and genital swabs, chlamydia and gonorrhoea NAAT on a urine specimen should still be offered.

4. Treatment

Specific treatments [17] are outlined in Table 6. Patients who have been diagnosed with an STI should be advised to abstain until treatment has been completed and their sex partners assessed and treated as well. Table 7 summarises other management considerations. Presumptive treatment for BV, candidiasis and TV can be provided based on signs and symptoms and pending chlamydia and gonorrhoea results.

Treatment of bacterial vaginosis

Indications for treatment include:
1) Symptomatic women, pregnant or not pregnant.
2) Asymptomatic women with a high risk of pre-term delivery.
3) Asymptomatic women who are planning surgical termination of pregnancy; treatment reduces the incidence of subsequent endometritis and pelvic inflammatory disease.
4) Women who deny abnormal vaginal discharge may elect to take treatment if offered, and may report a beneficial change in their vaginal discharge.

As a general measure, patients should be advised to avoid douching (vaginal cleaning) and the use of shower gels, antiseptics, or shampoos in the bath. Follow-up is not necessary if symptoms resolve. It is recommended, however, for high-risk pregnant women at 1 month to ensure successful treatment. Male sexual partners of women with BV do not require treatment.

Treatment of candidiasis

Treatment of vulvovaginal candidiasis (VVS) is indicated for symptomatic patients but is not necessary for those who are symptom-free. General advice includes the avoidance of local irritants such as soaps and perfumed products, and tight-fitting clothing. Follow-up is not needed for patients whose symptoms resolve. Partner notification is also not required. If the male sexual partner is symptomatic with balanoposthitis, topical antifungal creams will usually treat the infection.

Patients experiencing recurrent VVC which is defined as 4 or more episodes of confirmed symptomatic episodes annually should be evaluated for predisposing factors such as uncontrolled diabetes mellitus, immunosuppression, corticosteroid and long-term antibiotic use. Repeated courses of treatment may be required. Infection by less susceptible Candida species (e.g. *C. glabrata*) may necessitate longer duration of therapy. Oral therapy is usually indicated.

Treatment of trichomoniasis

Unlike BV and VVC, trichomoniasis infection is a sexually transmitted. As such, both symptomatic and asymptomatic patients should be treated. Follow-up is only necessary if patients have persistent or recurrent symptoms. Partner notification is a necessary part of trichomoniasis management; sex partners should be encouraged to be screened and treated on epidemiological grounds. Patient-delivered partner therapy might have a role in partner management for trichomoniasis.

Treatment of chlamydia

The patient and their sex partner/s both need to be treated, the latter based on epidemiological grounds. A test-of-cure is not necessary when treatment with a tetracycline or azithromycin has been completed unless symptoms recur or reinfection is suspected. It *is* recommended for infections in infants, children and pregnant women, or when erythromycin was used. This should be performed no sooner than 4 weeks after the completion of treatment.

Note:
- NAATs performed within 4 weeks of treatment completion may yield false positive results due to the persistence of chlamydial antigens.
- Re-infection rates are high and because of the increased risk of complications in women, rescreening should be offered at 3 to 4 months.

Serology for other STIs (syphilis, HIV and hepatitis B (if no history of vaccination) should be offered and repeated at 3 months after the sexual exposure, if tests were initially negative.

Management of sexual contacts: contact tracing of the patient's sex partners from a minimum of 2-3 months prior to diagnosis should be conducted. Current and recent sex partners should be screened and treated for chlamydia empirically.

TABLE 6. ANTIMICROBIAL TREATMENT OF GENITAL INFECTIONS	
Bacterial vaginosis	
Recommended regimens	Metronidazole 400-500mg orally bid for 5-7 days *OR* Metronidazole 2g single dose (avoid in pregnancy) *OR* Clindamycin cream 2% one full applicator (5g) vaginally at bedtime for 7 days *OR* Metronidazole gel 0.75% one full applicator (5g) vaginally once a day for 5 days
Alternative regimens	Clindamycin 300 mg orally bid for 7 days *OR* Tinidazole 2g orally as single dose
Note:	• *Patients should avoid alcohol during treatment with metronidazole and for 24 hours after as a disulfiram-like reaction may occur.* • *Metronidazole 2g single dose therapy may be slightly less effective at 4 weeks compared to longer treatment.* • *Patients should be advised to take extra contraceptive precautions when cream-based treatment is used as they may weaken latex condoms and diaphragms.* • *There is currently insufficient evidence to recommend the use of probiotic lactobacilli or lactic acid preparations.*
In pregnancy	Metronidazole 400-500mg orally bid for 7 days *OR* Metronidazole 200mg orally tid for 7 days *OR* Clindamycin 300 mg bid orally for 7 days *Note:* • *Avoid metronidazole 2g single does in pregnancy and breastfeeding women.* • *Data is conflicting regarding the usefulness of screening and treating low risk asymptomatic pregnant women. Metronidazole use in the first trimester of pregnancy has not been shown to be teratogenic or mutagenic.* • *Avoid intravaginal clindamycin cream during the 2nd half of pregnancy. Use at 16-32 weeks gestation has been associated with increased adverse events (e.g. low birth weight and neonatal infections).* • *When using clindamycin in breastfeeding women, intravaginal treatment is recommended.*

Recurrent BV	Suppressive treatment may be considered although optimal treatment has not been established. Possible approaches are: metronidazole gel 0.75% twice weekly for 4-6 months *OR* 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) *OR* acidifying vaginal gels at the time of menstruation and following unprotected sexual intercourse.
Candidiasis	
Recommended regimens	Clotrimazole vaginal pessary 200mg daily (inserted at bedtime) for 3 days or 500mg single dose *OR* Miconazole pessary 200mg daily for 3 days *OR* Econazole pessary 150mg daily for 3 days *OR* Fluconazole 150mg orally single dose
Alternative regimens	Clotrimazole pessary 100mg or cream (1%) 5g intravaginally daily for 7 days *OR* Miconazole pessary 100mg or cream (2%) 5g intravaginally daily for 7 days *OR* Miconazole pessary 1200mg as single dose (Many other anti-fungal preparations available).
Note:	• *Oral and topical azoles are equally effective in treating VVC. Azole drugs are more effective than nystatin.* • *Combined anti-fungal and steroid creams applied to the vulva may help with symptomatic relief.*
In pregnancy	Oral anti-fungal therapy is contraindicated in pregnancy; only topical azole therapy should be given. Single-dose treatment is less effective than longer regimens of up to 7 days.
Recurrent candidiasis	*Induction:* Fluconazole 150mg orally as single dose *OR* Itraconazole 100mg orally bid for 1-3 days, followed by: *Maintenance:* Fluconazole 100-200mg orally once a week for 6 months *OR* Clotrimazole pessary 500mg once a week for 6 months *OR* Itraconazole 400mg once a month for 6 months
Note:	• *There are anecdotal reports of oral contraceptive failure with*

	prolonged oral azole therapy. • *Creams and pessaries, being oil-base, may weaken latex condoms.* • *There is a risk of idiosyncratic drug-induced hepatitis with itraconazole.*
Trichomoniasis	
Recommended regimens	Metronidazole 400mg orally bid for 7 days *OR* Metronidazole 2g orally single dose *OR* Tinidazole 2g orally single dose
Note:	• *Metronidazole gel is not recommended because of its low efficacy (<50%).* • *Patients should avoid alcohol during treatment with metronidazole and for 24 hours after (72 hours for tinidazole) as a disulfiram-like reaction may occur.*
In pregnancy	Systemic metronidazole is needed for the eradication of *T. vaginalis* infection. Imidazole and metronidazole pessaries only provide symptomatic relief. The use of metronidazole has not been shown to be teratogenic or mutagenic and can be used throughout pregnancy and breastfeeding although high-doses should be avoided.
Recurrent or persistent	Untreated sexual partners should be treated to prevent re-infection of the patient. Re-treatment should be with metronidazole 400mg bid for 7 days whichever initial regimen was used. If treatment failure occurs repeatedly, the patient should be treated with a single 2g dose of metronidazole once a day for 3-5 days. Such cases may require testing of antibiotic sensitivity.
Chlamydia	
Recommended regimens	***(Uncomplicated cervical, urethral, rectal or throat infections in adults)*** Azithromycin 1g orally single dose (may improve compliance) *OR* Doxycycline 100mg orally bid for 7 days
Alternative regimens	Erythromycin 500mg orally qid for 7 days *OR* Ofloxacin 200 mg orally bid or 400 mg orally od for 7 days *OR* Levofloxacin 500 mg orally once daily for 7 days
In pregnancy	Azithromycin 1 g orally single dose *OR* Erythromycin 500 mg orally qid for 7 days *OR* Amoxicillin 500 mg orally tid for 7 days *Note:* • *Tetracyclines and ofloxacin are contraindicated during pregnancy.*

	• *Mothers of infected infants, and their sex partners should be screened and treated on epidemiological grounds.* • *A test-of-cure at 4 weeks after completion of treatment is recommended for pregnant women.* • *The efficacy of erythromycin treatment is approximately 80%; a second course of therapy may be required.*
Gonorrhoea	
Recommended regimens	***(Uncomplicated cervical, urethral and rectal infections in adults)*** Ceftriaxone 500mg i/m as single dose *PLUS* azithromycin 1-2g as single dose *or* doxycycline 100mg bid for 1-2 weeks
Alternative regimens	Cefotaxime 1g i/m single dose *PLUS* azithromycin 1-2g single dose *or* doxycycline 100mg bid for 1-2 weeks *OR* Spectinomycin 2g i/m single dose *PLUS* azithromycin 1-2g single dose *or* doxycycline 100mg bid for 1-2 weeks
Note:	• *Gonorrhoea treatment should be accompanied with anti-chlamydia therapy.* • *Fluroquinolones (e.g. ciprofloxacin, ofloxacin, norfloxacin) are not to be used; >70% of isolates in Singapore and the region are resistant.* • *Only ceftriaxone (250mg i/m with azithromycin 1g stat or doxycycline 100mg bid for 1 week) should be used to treat pharyngeal gonorrhoea.*
In pregnancy	Ceftriaxone 500mg i/m single dose *PLUS* azithromycin 1g orally single dose *or* erythromycin 500mg orally qid for 7-14 days. *Note:* • *Cephalosporins in the recommended dosages are safe and effective in pregnancy.* • *Spectinomycin can be used in women who are unable to tolerate cephalosporins.*
Non-gonococcal urethritis	
Recommended regimens	Doxycycline 100mg bid orally for 7 days *OR* Azithromycin 1g orally single dose
Alternative regimens	Erythromycin 500mg bid orally for 14 days *OR* Ofloxacin 200mg bid for 7 days *or* 400mg once daily for 7 days

Recurrent or persistent	Azithromycin 1g orally single dose PLUS metronidazole 400mg bid orally for 7 days *OR* Erythromycin 500mg orally qid for 2 weeks PLUS metronidazole 400mg bid orally for 7 days *OR* Moxifloxacin 400mg orally once a day for 10 days PLUS metronidazole 400mg bid orally for 7 days *Note:* • *Diagnosis of recurrence or persistence requires objective evidence of urethritis AND the exclusion of treatment non-compliance or re-infection from untreated/new partner.*

TABLE 7. OTHER MANAGEMENT POINTS FOR VAGINAL AND URETHRAL INFECTIONS

Infection	Contact tracing	Empirical treatment of partner/s	Follow-up
Bacterial vaginosis	Nil	Nil	Nil unless pregnant
Candidiasis	Nil	Nil unless partner symptomatic with candidiasis	Nil
Trichomoniasis	Required	Required	Nil unless symptomatic
Gonorrhoea	Required	Required	Review and test-of-cure at 2 weeks
Chlamydia	Required	Required	Nil unless symptoms, re-infection risk or pregnant
NGU	Required	Required	Review in 2 weeks

Note: 1) All patients suspected of having an STI should be advised to abstain until treated and until current sex partners have been treated. 2) All patients diagnosed with an STI should undergo follow-up serology at 3 months to exclude HIV, syphilis and +/-hepatitis B. 3) Chlamydia re-infection is common; patients should be offered re-testing (distinct from test-of-cure) after 3 months.

Treatment of gonorrhoea

Gonorrhoea treatment should be accompanied with anti-chlamydia therapy. This treats concurrent infection (up to 40%) and there is evidence to suggest that concurrent administration of azithromycin may slow down the possible development of cephalosporin resistant strains of *N. gonorrhoeae*. Drugs that should NOT be used for gonorrhoea treatment in Singapore are listed in Table 8.

Test-of-cure is recommended in all cases of gonorrhoea particularly pharyngeal gonorrhoea (may be more difficult to eradicate) after two weeks. In men, a urethral smear is performed to assess for post-gonococcal urethritis (PGU). Culture is performed at other sites. As for chlamydia, serology for syphilis and HIV (as well as hepatitis B if not vaccinated) should be performed, and if negative, repeated at 3 months from the last risky exposure.

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

URETHRITIS IN MALES

In contrast to the management of vaginal discharge, male urethral infections are far more straight-forward to manage due to the relatively specific clinical features, fewer pathogens and differential diagnoses. Syndromic management is effective in treating men with urethral discharge [16]. The most common causes of urethritis are gonorrhoea and non-gonococcal urethritis (NGU) including chlamydia. Complications of sexually acquired urethritis include epididymo-orchitis, prostatitis, reactive arthritis or Reiter syndrome and DGI with gonorrhoea.

Gonorrhoea infections of the urethra have a short incubation period of usually 2-7 days compared to other causes of male urethritis. The majority of men (80%) will have urethral discharge which is typically profuse and purulent (Table 3). Only 10% of urethral infections are asymptomatic [15]. The presence of Gram-negative intracellular diplococci (GNICD) on microscopy enables a presumptive diagnosis of gonorrhoea.

Non-gonococcal urethritis (NGU) refers to urethritis where *N. gonorrhoea* is not isolated and when there is microscopic evidence

TABLE 8. DRUGS NOT RECOMMENDED FOR THE TREATMENT OF GONORRHOEA INFECTION IN SINGAPORE

The following drugs are either ineffective or have not been adequately evaluated:

- All tetracyclines (they are given as part of anti-chlamydia therapy, not as primary treatment for gonorrhoea)
- All penicillins
- All fluoroquinolones
- Erythromycin
- Rifampicin
- Kanamycin
- Trimethoprim-sulfamethoxazole

of urethritis, defined as ≥5 polymorphonuclear leukocytes (PMLs) per high-power field (HPF) (x1000 magnification) in ≥ 5 fields. Acute NGU, despite being one of the most common STIs in men, has no identifiable pathogen in 20-50% of cases [18]. C. trachomatis accounts for 30-50% [19], Mycoplasma genitalium for 10-30% [20, 21]. Other causes (Table 9) account for a small proportion of cases. Compared to gonorrhoea, NGU has a longer incubation period of (7-21 days or longer) and symptoms may be milder.

About 30% of patients with NGU have recurrent or persistent symptoms 4 to 6 weeks after treatment. There is evidence that *M. genitalium* is has an important role in chronic NGU. Non-compliance to treatment and re-infection from an untreated or new partner should first be excluded.

TABLE 9. PATHOGENS ASSOCIATED WITH URETHRITIS IN MEN

Common causes

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*
- Mycoplasma genitalium (emerging as an increasingly important cause of NGU)

Other causes

- *Trichomonas vaginalis*
- Adenovirus
- Herpes simplex virus
- *Neisseria meningitidis*
- *Ureaplasma urealyticum*
- Other e.g. uropathogens

Note: Urethral symptoms can also be caused by non-infectious agents e.g. chemical irritants, foreign body, trauma.

Management of Men Presenting with Urethritis

A history (Table 4) should be taken and the genitals carefully examined by retracting the foreskin of the penis if the patient is uncircumcised. In the absence of visible urethral discharge, the urethra may need to be gently "milked" toward the meatus. In addition to the history and clinical findings (Table 3), the age of the patient may provide some indicator of the likely cause. STIs are a more common cause of genital symptoms than uropathogens (e.g. *E. coli*) in men under 35 years.

Table 10 summarises the approach and management of men presenting with urethral discharge. Specific treatments for gonorrhoea and chlamydia have been discussed. When the diagnosis of NGU is made treatment should be initiated without waiting for the chlamydia and gonorrhoea results (Table 6). Where microscopy is not available, management should be syndromic covering both gonorrhoea and chlamydia if objective evidence of urethral discharge is present.

Patients should be advised to abstain until treatment has been completed and until their sex partners have undergone screening and treatment.

INDICATIONS FOR REFERRAL TO A SEXUAL HEALTH CLINIC

- Clinician does not feel comfortable or confident with history, diagnosis or management.
- Inadequate investigatory resources available.
- Contact tracing not provided/not available at the practice.
- Patient with recurrent or persistent symptoms.
- Trichomoniasis is suspected.
- Gonorrhoea culture or test-of-cure required.
- Diagnostic uncertainty.
- Complicated infection (PID, epididymo-orchitis).

TABLE 10. APPROACH TO THE MANAGEMENT OF URETHRAL DISCHARGE IN MEN

History

- Sexual history and STI risk assessment (Table 4)
- Relevant symptoms (Table 3)
  - Onset and duration, nature of discharge, associated symptoms
  - Gonorrhoea is more likely with short incubation and thick purulent discharge

Examination

- Meatal inflammation and presence of urethral discharge (may need to gently "milk" urethra towards meatus).
- Discharge of gonorrhoea is typically profuse and purulent; NGU scant to moderate, clear or whitish.

Investigations

- Gram-stain and microscopy of urethral smear of the discharge (ideally patient having not voided in the preceding 4 hours)
  - ≥5 PML/HPF on ≥5 fields in the absence of GNIDC confirms NGU
  - Gram-negative intracellular diplococci indicates gonorrhoea
- Culture of the urethral discharge for gonorrhoea using an appropriate transport medium.
- First-pass urine for chlamydia NAAT or combined chlamydia and gonorrhoea NAAT.

Note:
Testing of Mycoplasma and Ureaplasma are not routinely performed and currently there are no guidelines recommending this. Chlamydia should be tested using a NAAT. Blood tests have no role in the diagnosis of genital chlamydia infection.

Management

- In general, presumptive treatment should be for both gonorrhoea and chlamydia.
- If gonorrhoea is likely or confirmed:
  - Treat for both gonorrhoea and chlamydia
- If gonorrhoea unlikely, or NGU only is confirmed:
  - Treat as per chlamydia
- Advice on contact tracing, abstaining until treated and partner treated, safe sex and follow-up if required (Table 7)

REFERENCES

1. British Association for Sexual Health and HIV Clinical Effectiveness Group. National Guidelines for the Management of Bacterial Vaginosis. 2012. www.bashh.org/documents/4413. Accessed February 20, 2013.
2. Wilson J. Managing recurrent bacterial vaginosis. Sex Transm Infect. 2004; 80: 8-11. http://dx.doi.org/10.1136%2Fsti.2002.002733
3. Faculty of Sexual and Reproductive Healthcare Clinical Guidance and British Association for Sexual Health and HIV. Management of vaginal discharge in non-genitourinary medicine settings. 2011. www.fsrh.org/pdfs/CEUGuidanceVaginalDischarge.pdf Accessed February 20, 2013.
4. Fethers K, Fairley CK, Hocking JS, et al. Sexual risk factors and bacterial vaginosis: a systematic review and meta-analysis. Clin Infect Dis 2008; 47: 1426-1435. http://dx.doi.org/10.1086%2F592974
5. Fethers K, Fairley CK, Morton A, et al. Early sexual experiences and risk factors for bacterial vaginosis. J Infect Dis 2009; 200: 1662-1670. http://dx.doi.org/10.1086%2F648092
6. Hillier S, Nugent RP, Eschenbach DA, et al. Association between bacterial vaginosis and preterm delivery of a low-birth-weight infant. N Engl J Med 1995; 333: 1737-42. http://dx.doi.org/10.1056%2FNEJM199512283332604
7. Hay P, Lamont RF, Taylor-Robinson D, et al. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. BMJ 1994; 308: 295-8. http://dx.doi.org/10.1136%2Fbmj.308.6924.295
8. Soper DE, Bump RC, Hurt WG. Bacterial vaginosis and trichomoniasis vaginitis are risk factors for cuff cellulitis after abdominal hysterectomy. Am J Obstet Gynecol 1990; 163(3):1016-1021. http://dx.doi.org/10.1016%2F0020-7292%2891%2990321-U
9. Larsson PG, Platz-Christensen JJ, Dalaker K, et al. Treatment with 2% clindamycin vaginal cream prior to first trimester surgical abortion to reduce signs of postoperative infection: a prospective, double-blinded, placebo-controlled, multicenter study. Acta Obstet Gynecol Scand 2000; 79(5):390-396. http://dx.doi.org/10.1097%2F00007435-200008000-00002
10. Atashili J, Poole C, Ndumbe PM, et al. Bacterial vaginosis and HIV acquisition: a meta-analysis of published studies. AIDS 2008; 22(12):1493-1501. http://dx.doi.org/10.1097%2FQAD.0b013e3283021a37
11. Schwebke JR. Abnormal vaginal flora as a biological risk factor for acquisition of HIV infection and sexually transmitted diseases. J Infect Dis 2005; 192(8):1315-1317. http://dx.doi.org/10.1086%2F462430
12. Sobel JD, Faro S, Force RW, et al. Vulvovaginal candidiasis: epidemiologic, diagnostic and therapeutic considerations. Am J Obste Gynecol 1998:178: 203-211. http://dx.doi.org/10.1016%2FS0002-9378%2898%2980001-X
13. Cotch MF, Pastorek JG, Nugent RP. Trichomoniasis vaginalis associated with low birth weight and preterm delivery. Sex Transm Dis 1997; 24: 361-2.
14. Horner PJ, Boag F. National guidelines for the management of genital tract infection with Chlamydia trachomatis. Clinical Effectiveness Group. British Association for Sexual Health and HIV. 2006. www.bashh.org/documents/65 Accessed February 20, 2013.
15. Bignell C, FitzGerald M. UK national guideline for the management of gonorrhoea in adults, 2011. Int J STD AIDS 2011; 22: 541–547. DOI: 10.1258/ijsa.2011.011267
16. Pettifor A, Walsh J, Wilkins V, et al. How effective is syndromic management of STDs? A review of current studies. Sex Trans Dis 1999; 27:371-385. http://dx.doi.org/10.1097%2F00007435-200008000-00002

17. Department of STI Control, National Skin Centre. Sexually transmitted infections management guidelines. 2013.
18. Shahmanesh M, Moi H, Lassau F, et al. 2009 European guideline on the management of male non-gonococcal urethritis. Int J STD AIDS 2009; 20: 458-464.
http://dx.doi.org/10.1258%2Fijsa.2009.009143
19. Horner PJ, Thomas B, Gilroy CB, et al. Do all men attending departments of genitourinary medicine need to be screened for non-gonococcal urethritis? Int J STD AIDS 2002; 13:667-73.
http://dx.doi.org/10.1258%2F095646202760326408
20. Taylor-Robinson D. Mycoplasma genitalium – an up-date. Int J STD AIDS 2002; 13: 145-51.
http://dx.doi.org/10.1258%2F0956462021924776
21. Bradshaw C, Tabrizi SN, Timothy R, et al. Etiologies of nongonococcal urethritis: bacteria, viruses and the association with orogenital exposure. J Infect Dis 2006: 193; 336-45.
http://dx.doi.org/10.1086%2F499434

LEARNING POINTS

- **STIs are frequently asymptomatic especially in women.**
- **Most common causes of vaginal discharge are physiological, bacterial vaginosis and vulvovaginal candidiasis.**
- **Most common causes of male urethritis are gonorrhoea and chlamydia.**
- **Gonorrhoea treatment should be accompanied by anti-chlamydial therapy.**
- **With a diagnosis of an STI contact tracing of the patient's sex partners should always be conducted to prevent further transmission, complications of untreated infection and re-infection.**