Management of Genital Ulcers and Discharges

MOH Clinical Practice Guidelines 1/2009
Levels of evidence and grades of recommendation

Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1**</td>
<td>High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.</td>
</tr>
<tr>
<td>1*</td>
<td>Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.</td>
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<tr>
<td>1</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.</td>
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<tr>
<td>2**</td>
<td>High quality systematic reviews of case control or cohort studies.</td>
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<tr>
<td>2*</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a high probability that the relationship is causal.</td>
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<tr>
<td>2</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.</td>
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<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, case series.</td>
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<tr>
<td>4</td>
<td>Expert opinion.</td>
</tr>
</tbody>
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Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review of RCTs, or RCT rated as 1** and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1*, directly applicable to the target population, and demonstrating overall consistency of results.</td>
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<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2**, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1** or 1*.</td>
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<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2*, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.</td>
</tr>
<tr>
<td>GFP (good practice points)</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
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</table>
Management of Genital Ulcers and Discharges
Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive summary of recommendations</td>
<td>1</td>
</tr>
<tr>
<td>1 Introduction</td>
<td>25</td>
</tr>
<tr>
<td>2 Management of genital ulcers</td>
<td>26</td>
</tr>
<tr>
<td>3 Management of genital discharges</td>
<td>42</td>
</tr>
<tr>
<td>4 Cost-effectiveness issues</td>
<td>71</td>
</tr>
<tr>
<td>5 Clinical quality improvement</td>
<td>72</td>
</tr>
<tr>
<td>References</td>
<td>73</td>
</tr>
<tr>
<td>Self-assessment (MCQs)</td>
<td>90</td>
</tr>
<tr>
<td>Workgroup members</td>
<td>95</td>
</tr>
</tbody>
</table>
Sexually transmitted infections (STIs) remain a public health problem of major significance in most parts of the world. Infection with STIs can lead to acute symptoms, chronic infection and serious delayed consequences such as infertility, ectopic pregnancy and cervical cancer. There has been an increasing trend in the overall STI incidence in Singapore for the past ten years, from 160 cases per 100,000 population in 1998 to 251 cases per 100,000 population in 2007.

Genital ulcers and genital discharge are commonly seen symptoms of STIs. The incidence of genital ulcer disease is on the rise in Singapore and the two commonest causes are genital herpes and primary syphilis. In patients presenting with a urethral discharge, gonorrhoea and Chlamydia trachomatis infections are the most common causes in Singapore.

Primary care doctors are often the first contact point for patients with genital ulcers or discharges. According to the results of a survey on STI management practices among GPs in 2006 and 2007, it was found that the overall medical management of STI by primary care physicians was acceptable. However, there was variation in terms of medications and ordering relevant investigations for their patients. It is therefore timely to develop this first national guideline that incorporates the best available evidence from the scientific literature, to assist our doctors in the management of genital ulcers and discharge.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES
Management of genital ulcers

D It is recommended that the following diagnostic approach be taken in any patient with genital ulcers or discharges (pg 27):

A. Patient history:
   1. Lesion history: prodrome, initial presentation (especially presence of vesicles), duration of lesion, pain, symptoms of urethritis, other systemic symptoms, use of systemic or topical remedies, any history of similar symptoms in the past or partners with similar symptoms.
   2. Medical history: HIV status, skin conditions, drug allergies, and medications.
   3. Sexual history: gender of partners, number of partners, venue for meeting partners, commercial sex exposure, partners with symptoms or signs, partners with known HSV or recent syphilis diagnosis.
   4. Travel history: geographical area where sexual intercourse has taken place.

B. Physical exam:
   1. Lesion: examine for appearance, distribution, number, size, induration, depth, and tenderness.
   2. Genital exam: examine genital and perianal area for other lesions.
   3. Lymph node(s): note number and location of enlarged nodes, size, tenderness, presence of bubo.
   4. General exam: thorough examination of oral cavity and skin of torso, palms and soles. In patients with syphilis, this would include an examination of the cardiovascular and neurological systems.

Grade D, Level 4

A A diagnosis based only on the patient’s medical history and physical examination frequently may be inaccurate. Ideally, all patients who have genital ulcers should be evaluated with a serologic test for syphilis and a diagnostic evaluation for genital herpes; if chancroid is suspected, the patient should be referred to a specialist for evaluation and a test for *Haemophilus ducreyi* (pg 29).

Grade A, Level 1+
HIV and serologic testing for syphilis should be performed on all patients who have STIs presenting with genital ulcers, as well as tests for herpes simplex infection where appropriate. Locally, genital herpes and syphilis are the two most likely infective etiologies. Non-infective causes may need to be considered (pg 29).

Grade B, Level 2++

The clinician should treat for the diagnosis considered most likely, on the basis of clinical presentation and epidemiologic circumstances. In some instances, treatment must be initiated for additional conditions because of diagnostic uncertainty (pg 29).

Grade B, Level 2++

Successful management of STI-associated syndromes requires that staff are respectful of patients and are not judgmental. Examination must be done in appropriate surroundings where privacy can be ensured and confidentiality guaranteed. Patients should be educated and counseled on their condition as well as safer sex (pg 29).

GPP

Management of herpes simplex virus (HSV) infection

In performing serology for HSV infection, assays that detect the type-specific glycoproteins gG1 (HSV 1) and gG2 (HSV 2) should be used (pg 31).

Grade B, Level 2++

Treatment of first episode genital herpes (pg 32)

1. A Acyclovir 200 mg orally 5 times daily for 5 to 10 days.

   Grade A, Level 1++

   OR

2. A Acyclovir 400 mg orally tid for 5 to 10 days.

   Grade A, Level 1++

   OR

3. A Valacyclovir 500 mg/1g orally bid for 5 to 10 days.

   Grade A, Level 1++

   OR

4. B Famciclovir 250 mg orally tid for 5 to 10 days.

   Grade B, Level 2++
For episodic treatment of recurrent herpes, the patient should be provided with a supply of drug or a prescription for the medication with instructions to self-initiate treatment immediately when symptoms begin (pg 32).

Grade C, Level 2+

Treatment of recurrent genital herpes (pg 32)

1. Acyclovir 200 mg orally 5 times daily or 400 mg orally tid or 800 mg orally bid for 5 days.
   Grade A, Level 1++

   OR

2. Acyclovir 800 mg tid orally for 2 days.
   Grade A, Level 1++

   OR

3. Valacyclovir 500 mg orally bid or 1000 mg orally once a day for 5 days.
   Grade A, Level 1++

   OR

4. Valacyclovir 500 mg bid for 3 days.
   Grade A, Level 1++

   OR

5. Famiciclovir 125 mg orally bid for 5 days.
   Grade A, Level 1++

   OR

6. Famiciclovir 1 g bid orally for 1 day.
   Grade A, Level 1++

Suppressive therapy reduces the frequency of genital herpes recurrences and may be considered in patients who have frequent recurrences (i.e. 6 or more recurrences per year) (pg 33).

Grade C, Level 2+

Suppressive treatment of recurrent genital herpes (pg 33)

1. Acyclovir 400 mg orally bid.
   Grade A, Level 1+

   OR

2. Valacyclovir 500 mg orally od.
   Grade A, Level 1+
3. **A** Valacyclovir 1000 mg orally od (for > 10 recurrences in 1 year).  

**Grade A, Level 1+**

OR

4. **A** Famiclovir 250 mg orally bid.  

**Grade A, Level 1+**

C Physicians should stop suppressive treatment of genital herpes after 9 to 12 months to see if recurrence occurs and continued prophylaxis is warranted (pg 34).  

**Grade C, Level 2+**

**Treatment of genital herpes in HIV-infected patients (pg 34)**

1. **A** Acyclovir 400 mg orally tid for 7 to 10 days.  

**Grade A, Level 1+**

OR

2. **A** Valacyclovir 1 g orally bid for 7 to 10 days.  

**Grade A, Level 1+**

OR

3. **A** Famiclovir 500 mg orally bid for 7 to 10 days.  

**Grade A, Level 1+**

**Suppressive treatment of genital herpes in HIV-infected patients (pg 34)**

1. **A** Acyclovir 400 mg to 800 mg orally bid or tid.  

**Grade A, Level 1+**

OR

2. **A** Valacyclovir 500 mg orally bid.  

**Grade A, Level 1+**

OR

3. **A** Famiclovir 500 mg orally bid.  

**Grade A, Level 1+**
Management of genital herpes in pregnancy

First episode genital herpes – 1st and 2nd trimester acquisition

C Management should be in line with the clinical condition with the use of either oral or intravenous acyclovir (pg 35).

Grade C, Level 2+

C Vaginal delivery is anticipated in women who present with first episode genital herpes in the first and second trimesters as the risk for transmission to the neonate at delivery is low (pg 35).

Grade C, Level 2+

First episode genital herpes – 3rd trimester acquisition

C Caesarean section should be offered to all women presenting with first-episode genital herpes lesions at the time of delivery, or within 6 weeks of the expected date of delivery or onset of labour (pg 35).

Grade C, Level 2+

Recurrent genital herpes in pregnancy

C If there are no genital lesions at the onset of labour, Caesarean section to prevent neonatal herpes is not indicated (pg 36).

Grade C, Level 2+

A For women with a history of recurrent genital herpes, who would opt for caesarean delivery if HSV lesions were detected at the onset of labour, daily suppressive acyclovir given from 36 weeks of gestation until delivery may be given to reduce the likelihood of HSV lesions at term) (pg 36).

Grade A, Level 1+

B Counselling for genital herpes is important and should include (pg 36):
  • Information on natural history of disease, potential for recurrent attacks, role of asymptomatic shedding in sexual transmission
  • Abstinence from sexual activity during prodromal symptoms or when lesions are present
  • Advice to inform current and new sexual partners of genital herpes
  • Use of condoms with new or uninfected partners, particularly in first 12 months after first attack
• Information on anti-viral treatment available
• Risk of neonatal infection: women with a history of genital herpes or whose partners have history of genital herpes should inform their obstetrician early in pregnancy

Management of primary syphilis

Treatment of primary syphilis (pg 37)

1. 
   Benzathine Penicillin G 2.4 million units i/m weekly x single dose.
   (For primary syphilis, most authorities administer a single dose, while some might use two doses for secondary syphilis).
   
   OR

2. 
   Aq. Procaine Penicillin G 600,000 units i/m daily x 10 days.

Penicillin-allergic patients (pg 38)

1. 
   Doxycycline 100 mg orally bid x 14 days.
   
   OR

2. 
   Erythromycin 500 mg orally qid x 14 days.
   
   OR

3. 
   Azithromycin 500 mg orally od x 10 days.

C For HIV-infected individuals, either the same treatment as in non-HIV infected individuals or 3 doses of Benzathine Penicillin G 2.4 million units i/m weekly are recommended (pg 38).

C HIV-positive individuals with primary syphilis should be referred to an appropriate expert for follow up (pg 38).

B Oral doxycycline is the preferred oral alternative in all patients in view of its more favourable dosing intervals and low cost (pg 38).
The treatment guidelines listed refer to management of primary syphilis. For late latent syphilis, syphilis of unknown duration, congenital syphilis or neurosyphilis, the treatment recommendations are different and relevant expert advice should be sought (pg 38).

The same quantitative nontreponemal tests [i.e rapid plasma regain (RPR) or Venereal Disease Research Laboratory (VDRL)] should be repeated during follow up; the DSC Clinic follows up patients for a total period of two years (tests are repeated at 3 months; 6 months; 12 months; 18 months; 24 months) (pg 38).

A sustained fourfold or greater increase in RPR/VDRL titres suggests re-infection or treatment failure. Following treatment of early syphilis, RPR/VDRL should demonstrate a decrease in titre within 6 months. In particular, patients treated with non-penicillin based regimens should be followed up to look for signs of treatment failure (pg 38).

Since treponemal tests remain positive for life following effective treatment, proper documentation is necessary to prevent unnecessary retreatment. Patients should be given a letter documenting their treatment (pg 39).

Reinfection or relapse should be retreated preferably with supervised treatment schedules to ensure compliance, and sexual partners should be rescreened. These patients could also be referred to the relevant experts (pg 39).

All pregnant women should be screened for syphilis at the initial antenatal visit. Women who had documented treatment for syphilis in the past do not need retreatment during current or subsequent pregnancies if there is no clinical evidence of syphilis and the RPR/VDRL titre is negative or serofast in low titre compared to previous results (pg 39).
For penicillin-allergic patients, erythromycin is given in dosage schedules as recommended for the treatment of non-pregnant patients. However, as erythromycin exhibits poor penetration across the placental barrier, the infant should be routinely treated with penicillin at birth. For these patients, retreatment with doxycycline can be considered after delivery when breastfeeding has been stopped (pg 40).

Grade D, Level 4

Women treated for early syphilis during pregnancy should have monthly rapid plasma regain (RPR) or Venereal Disease Research Laboratory (VDRL) for the remainder of the current pregnancy (pg 40).

Grade C, Level 2+

Management of chancroid

Locally, chancroid is uncommon. Any suspected case should be referred to a specialist for evaluation, as routine laboratory tests are not widely available (pg 40).

Grade D, Level 4

Treatment of chancroid (pg 40-41)

1. **A** Azithromycin 1 g orally x single dose.  
   **Grade A, Level 1+**

   OR

2. **B** Ceftriaxone 250 mg i/m x single dose.  
   **Grade B, Level 2++**

   OR

3. **B** Ciprofloxacin 500 mg bid x 3 days.  
   **Grade B, Level 2++**

Management of lymphogranuloma venereum

Locally, lymphogranuloma venereum (LGV) is uncommon. Any suspected case should be referred to a specialist for evaluation, as routine laboratory tests are not widely available (pg 41).

Grade D, Level 4
Treatment of lymphogranuloma venereum (pg 41)

1. **C** Doxycycline 100 mg bid x 21 days.  
   **Grade C, Level 2+**

OR

2. **C** Erythromycin 500 mg qid x 21 days.  
   **Grade C, Level 2+**

Management of genital discharges

**B** Patients presenting with genital discharges should also be screened for HIV and syphilis (pg 42).

**Grade B, Level 2++**

**GPP** The following diagnostic approach is recommended (pg 42-43):

A. **Patient history:**
   1. **History of discharge:** onset, duration, colour, odour, association with micturition, dysuria, itch, rash, chronicity, involvement of sites (urethra, vagina, pharynx, rectum, eye), other systemic symptoms (fever, joint pain, ophthalmic symptoms), use of systemic or topical remedies, any history of similar symptoms in the past or partners with similar symptoms.
   2. **Medical history:** diabetes, HIV status, skin conditions, drug allergies, current & previous medications, menstrual history, obstetric history
   3. **Sexual history:** gender of partners, number of partners, venue for meeting partners, commercial sex exposure, partners with symptoms or signs, partners with known genital discharge diagnosis.
   4. **Travel history:** geographical area where sexual intercourse has taken place.

B. **Physical examination:**
   1. **Lesion:** appearance and character of discharge, consistency, odour.
   2. **Genital exam:** external genitalia and peri-anal area for inflammation and other lesions.
   3. **Lymph node(s):** note number and location of enlarged nodes, size, tenderness.
   4. **General exam:** thorough examination of oral cavity and eyes/joints as necessary. In males, 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.

Genital discharges in males

D All patients who have confirmed or suspected urethritis should be tested for gonorrhoea and chlamydia (pg 45).

Grade D, Level 4

B Because of high specificity (>99%) and sensitivity (>95%), a Gram stain of a male urethral specimen that demonstrates polymorphonuclear leukocytes with intracellular Gram-negative diplococci is presumptive of infection with *N.gonorrhoeae* in symptomatic men. Thus it is recommended that urethral smears be obtained in symptomatic men to aid in diagnosis (pg 46).

Grade B, Level 2++

Chlamydia and gonorrhoea in women

B Microscopical examination of Gram-stained smears of endocervical discharge can be used as a point of care test to provide an immediate presumptive diagnosis of gonorrhoea (pg 46).

Grade B, Level 2++

B Gonococcal complement fixation test are not recommended for the diagnosis of gonorrhea. Serological tests are not recommended for the diagnosis of acute chlamydial infections (pg 47).

Grade B, Level 2++
## Complications of genital discharges

### Syndromic management of urethral symptoms in males (pg 48)

<table>
<thead>
<tr>
<th>Urethral symptoms present</th>
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</thead>
<tbody>
<tr>
<td>Presence of sexually transmitted urethral infection</td>
</tr>
<tr>
<td>This is indicated if any one of the following are present:</td>
</tr>
<tr>
<td>- History - risk of sexually transmitted infection present (e.g. unprotected oral, vaginal, anal sex)</td>
</tr>
<tr>
<td>- Examination - presence of urethral discharge and meatitis</td>
</tr>
<tr>
<td>- Laboratory - raised polymorphonuclear leucocytes (PML) on Gram-stained smear</td>
</tr>
</tbody>
</table>

Diagnosis of gonorrhoea is likely if there is -

- Thick purulent discharge
- Short incubation period (2-7 days)
- Gram-negative intracellular diplococci seen on Gram-stain microscopy

If *any* one of the above points are present -

- Send urethral swab for gonococcal culture
- Send urethral swab or first catch urine for nucleic-acid amplification test (NAAT) for *Chlamydia trachomatis*
- Treat for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*
- Review in 14 days

If none of the above points are present -

- Send urethral swab for gonococcal culture
- Send urethral swab or first catch urine for NAAT for *Chlamydia trachomatis*
- Treat for *Chlamydia trachomatis*
- Review in 14 days

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### Treatment of gonorrhoea

- **Uncomplicated infection in adults - urethral, endocervical & rectal infection (pg 49)**

1. **A** Ceftriaxone 250 mg intramuscular single dose.  
   
   **Grade A, Level 1+**

   OR

2. **A** Cefixime 400 mg orally single dose.  
   
   **Grade A, Level 1+**

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Alternative regimens (pg 49)

1. **A** Cefotaxime 1 g intramuscular single dose.  
   \[\text{Grade A, Level 1+}\]
   \[\text{OR}\]

2. **A** Spectinomycin 2 g intramuscular single dose (for patients with \(\beta\)-lactam allergy).  
   \[\text{Grade A, Level 1+}\]

   **B** All patients with gonorrhoea should be given concurrent treatment for Chlamydia (pg 49).  
   \[\text{Grade B, Level 2++}\]

• **Pharyngeal infection** (pg 49)

   **B** Ceftriaxone 250 mg intramuscular single dose with anti-chlamydia therapy (refer to section 3.7).  
   \[\text{Grade B, Level 2++}\]

   **B** The fluoroquinolones (e.g. ciprofloxacin, ofloxacin, norfloxacin) should NOT be used as >70% of isolates in Singapore are resistant.  
   \[\text{Grade B, Level 2++}\]

• **Gonococcal infection in pregnancy** (pg 49-50)

   **A** Cephalosporins in the recommended dosages are safe and effective in pregnancy.  
   \[\text{Grade A, Level 1+}\]

   **A** Spectinomycin can be administered to pregnant women who are unable to tolerate cephalosporins.  
   \[\text{Grade A, Level 1+}\]

   **B** Simultaneous treatment for chlamydial infection with azithromycin 1g single dose orally or erythromycin 500 mg orally qid x 7 to 14 days is advocated for pregnant women receiving treatment of gonorrhoea.  
   \[\text{Grade B, Level 2++}\]

**D** **Follow-up** (pg 50)

Patients should be instructed to abstain from sexual intercourse until 7 days after therapy is initiated. After this period sexual activity can be
resumed provided their symptoms have resolved and sex partners have been screened and treated.
- The test-of-cure is recommended for all sites and assessment for post-gonococcal urethritis (PGU) should be performed after 14 days.
- All treatments are less effective at eradicating pharyngeal infection and test-of-cure is strongly recommended following treatment of infection at this site.
- Serologic tests for syphilis and HIV should also be performed at the initial visit; if negative they should be repeated at 3 months after the last risky exposure.
- Education on STIs and safer sex advice should be regularly reinforced.

**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 (pg 50).

**Treatment of Chlamydia trachomatis infection**

- **Uncomplicated urethral, endocervical, pharyngeal or rectal infections in adults (pg 50-51)**
  1. **A** Doxycycline 100 mg orally bid x 7 days.  
     *Grade A, Level 1++*
     OR
  2. **A** Azithromycin 1 g orally single dose.  
     *Grade A, Level 1++*
     OR
  3. **A** Erythromycin 500 mg orally qid x 7 days or 500 mg orally bid x 14 days.  
     *Grade A, Level 1+
     OR
  4. **B** Ofloxacin 200 mg orally bid or 400 mg orally od x 7 days.  
     *Grade B, Level 2++*
• **Chlamydia trachomatis infection in pregnancy (pg 51)**

1. **A** Erythromycin 500 mg orally qid x 7 days or 250 mg orally qid x 14 days.  
   Grade A, Level 1+

   OR

2. **A** Amoxicillin 500 mg orally tid x 7 days.  
   Grade A, Level 1+

   OR

3. **A** Azithromycin 1 g orally single dose.  
   Grade A, Level 1+

**Follow up**

**D** A test-of-cure is not necessary when treatment with doxycycline or azithromycin has been completed, unless symptoms persist or re-infection is suspected. Test-of-cure is however recommended after 4 weeks for infections in pregnant women, or when erythromycin was used. Non-culture tests (e.g. NAAT) done within 4 weeks of completing treatment may yield false positive tests due to persistence of chlamydial antigens (pg 51).  

Grade D, Level 4

**Management of sex partners**

**D** 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 (pg 52).  

Grade D, Level 4

**D** Sex partners of asymptomatic male patients and of females within the last 90 days (or the most recent sex partner if the last contact was >90 days) should be screened and treated for chlamydial infection (pg 52).  

Grade D, Level 4
Treatment of non-gonococcal urethritis (NGU)

Management of sex partners

**D** Sex partners of men with non-gonococcal urethritis (NGU) within the last 60 days should be screened and treated. These partners should also be examined to exclude other associated STI (pg 52).

Grade D, Level 4

Management of recurrent or chronic NGU

- **D** Obtain objective evidence of urethritis, e.g. presence of urethral discharge or pus cells on urethral smear. If patient has no objective evidence, consider reassurance only.
- Exclude drug adherence failure or re-infection from untreated partner or a new partner.
- Consider referral to a specialist for further evaluation.

(pg 53)

Grade D, Level 4

Vaginal discharge

**B** In women of reproductive age complaining of vaginal discharge the commonest cause is physiological, but infective and other causes should be excluded (pg 53).

Grade B, Level 2++

**B** A spontaneous complaint of abnormal vaginal discharge is most commonly due to a vaginal infection, and rarely, it may be the result of mucopurulent STI-related cervicitis. The symptom of abnormal vaginal discharge is highly indicative of vaginal infection, but poorly predictive for cervical infection. To ensure a cost-effective approach, risk assessment should therefore be done before investigations and treatment is provided (pg 54).

Grade B, Level 2++

**B** Where resources permit, one should consider the use of laboratory tests to screen women with vaginal discharge. Such screening could be applied to all women with discharge as well as to those with a positive risk assessment (pg 55).

Grade B, Level 2++
Investigation of a woman with vaginal discharge is indicated if (Table 2) (pg 55):
1. She is deemed to be at high risk of sexually transmitted infections (STI).
2. She has symptoms suggestive of upper genital tract infection (e.g. abdominal pain, dyspareunia or fever).
3. She has previous treatment which failed.
4. She is postnatal, post-miscarriage, or post-abortion.
5. She is within 3 weeks of insertion of intrauterine contraceptive device.
6. Requested by the patient.

Table 2  Investigations for vaginal discharges

<table>
<thead>
<tr>
<th>Site</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulval fissures and erythema</td>
<td>▪ Microscopy for yeasts</td>
</tr>
<tr>
<td></td>
<td>▪ Culture for yeasts</td>
</tr>
<tr>
<td></td>
<td>▪ Herpes simplex virus (if multiple vesicles or ulcers present)</td>
</tr>
<tr>
<td>Vagina</td>
<td>▪ Wet preparation to detect Trichomonas vaginalis (posterior fornix)</td>
</tr>
<tr>
<td></td>
<td>▪ Gram stain to detect clue cells and yeasts (lateral walls)</td>
</tr>
<tr>
<td></td>
<td>▪ Culture for Trichomonas vaginalis and yeasts (lateral walls and posterior walls)</td>
</tr>
<tr>
<td></td>
<td>▪ Amine ‘sniff’ test (if available)</td>
</tr>
<tr>
<td></td>
<td>▪ Vaginal pH (if available)</td>
</tr>
<tr>
<td>Cervix</td>
<td>▪ Gram-stain for pus cells, Gram-negative intracellular diplococci</td>
</tr>
<tr>
<td></td>
<td>▪ Culture Neisseria gonorrhoeae</td>
</tr>
<tr>
<td></td>
<td>▪ Nucleic-acid amplification test (NAAT) for Chlamydia trachomatis</td>
</tr>
</tbody>
</table>

Not all women with vaginal discharge require investigation. Empirical treatment can be given after taking a clinical and sexual history if (pg 56):
1. The woman is at low risk of STI.
2. She has no symptoms to suggest upper genital tract infection.
3. She can return for follow-up if symptoms do not resolve.

Grade B, Level 2++
A woman of reproductive age complaining of vaginal discharge should be investigated if (pg 56):
1. She is deemed to be at high risk of sexually transmitted infections (STI).
2. She has symptoms suggestive of upper genital tract infection (e.g. abdominal pain, dyspareunia or fever).
3. She has previous treatment which failed.
4. She is postnatal, post-miscarriage, or post-abortion.
5. She is within 3 weeks of insertion of intrauterine contraceptive device.
6. Investigation is requested by the patient.

The major causes for vaginal discharge include candidiasis, bacterial vaginosis, trichomoniasis, *Chlamydia trachomatis* and gonococcal infection. Depending on the physician assessment of the patient’s risk factors, syndromic management may be directed against one or all of these common causes (pg 56).

**Treatment of bacterial vaginosis (pg 59)**

Indications for treatment:
1. All symptomatic women with bacterial vaginosis, pregnant or non pregnant.

Grade A, Level 1+

2. Asymptomatic women with bacterial vaginosis before surgical procedures.

Grade A, Level 1+

Patients with bacterial vaginosis should avoid vaginal douching, use of shower gels, antiseptic agents or shampoo in the bath (pg 59).

Grade D, Level 3

**Recommended regimens for bacterial vaginosis (pg 60):**

1. Clindamycin cream 2% (5 g) intravaginally daily x 3 days or Clindamycin site-released (SR) cream 2% (5 g) intravaginally x single application.

Grade A, Level 1+

OR

2. Clindamycin 300 mg orally bid x 7 days.

Grade A, Level 1+
3. **A** Metronidazole gel 0.75% (5 g) intravaginally daily x 5 days.  
   *Grade A, Level 1*

   **OR**

4. **A** Metronidazole pessary (500 mg) intravaginally bid x 7 days or daily x 14 days.  
   *Grade A, Level 1*

   **OR**

5. **A** Metronidazole 400 mg orally bid x 7 days.  
   *Grade A, Level 1*

   **OR**

6. **A** Tinidazole 2 g orally single dose.  
   *Grade A, Level 1*

**Note:**

1. **A** Metronidazole 2 g orally single dose therapy is the least effective for bacterial vaginosis and is no longer recommended.  
   *Grade A, Level 1*

2. Intravaginal metronidazole gel and clindamycin cream have similar efficacy.

3. Metronidazole is less active against lactobacilli than clindamycin. However, clindamycin is more active than metronidazole against most of the bacteria associated with bacterial vaginosis. Clindamycin reduces vaginal Mobiluncus to a greater extent than metronidazole.

4. Clindamycin vaginal creams and suppositories may be oil-based and might weaken latex condoms.

**A** If bacterial vaginosis causes vaginal discharge in pregnancy, it should be treated as for non-pregnant women (pg 61).  
*Grade A, Level 1*

**Recommended regimens for pregnant women (pg 61)**

1. **A** Clindamycin cream 2% (5 g) intravaginally daily x 3 days or Clindamycin-sustained released (SR) cream 2% (5 g) intravaginally x single application.  
   *Grade A, Level 1*

   **OR**
2. **A** Clindamycin 300 mg orally bid x 7 days.  

    Grade A, Level 1+

    OR

3. **A** Metronidazole pessary (500 mg) intravaginally bid x 7 days or daily x 14 days.  

    Grade A, Level 1+

    OR

4. **A** Metronidazole 400 mg orally bid x 7 days. (Avoid in first trimester*).  

    Grade A, Level 1+

Note:

1. *Metronidazole crosses the placental barrier. Although it has been given to pregnant women without apparent complication or teratogenicity, it is advisable to withhold oral or vaginal metronidazole during the first trimester of pregnancy.

2. In three trials, intravaginal clindamycin cream was administered at 16-32 weeks’ gestation, and an increase in adverse events (e.g., low birth-weight and neonatal infections) was observed in newborns. Therefore, intravaginal clindamycin cream should only be used during the first half of pregnancy.

**Suggested suppressive therapy for recurrent bacterial vaginosis** (pg 62):

1. **A** Metronidazole gel 0.75% (5 g) twice weekly for 4-6 months.  

    Grade A, Level 1+

    OR

2. **C** Metronidazole 400 mg orally bid for 3 days at the start and end of menstruation.  

    Grade C, Level 2+

**Suggested maintenance regime for recurrent bacterial vaginosis:**

**B** Acetic acid vaginal gel use at the time of menstruation and following unprotected sexual intercourse to maintain acidic vaginal pH (pg 62).  

    Grade B, Level 2+

**Follow up**

**D** Follow-up is not necessary if symptoms resolve. A test of cure is not required (pg 62).  

    Grade D, Level 4
Treatment of candidiasis

D Avoid local irritants (e.g. perfumed vaginal douch), scented panty-liners and tight fitting synthetic clothing (pg 63).

Grade D, Level 4

Treatment for uncomplicated acute vulvovaginal candidiasis

A Both vaginal or oral antifungals (azoles) can be used in the treatment of uncomplicated acute vulvovaginal candidiasis (pg 63).

Grade A, Level 1+

Recommended regimens for uncomplicated acute vulvovaginal candidiasis (pg 63-64):

1. A Butoconazole1-sustained released (SR) cream site 2% (5 g) intravaginally x single application.

   Grade A, Level 1+

   OR

2. A Clotrimazole pessary 200 mg intravaginally daily x 3 days or 100 mg or 1% cream (5 g) intravaginally daily x 7 days or 500 mg x single application.

   Grade A, Level 1+

   OR

3. A Fluconazole 150 mg orally single dose.

   Grade A, Level 1+

   OR

4. A Isoconazole pessary 600 mg intravaginally x single application.

   Grade A, Level 1+

   OR

5. A Itraconazole 200 mg orally bid x 1 day.

   Grade A, Level 1+

   OR

6. A Miconazole pessary 200 mg intravaginally daily x 3 days or 100 mg or 2% cream (5 g) intravaginally daily x 7 days.

   Grade A, Level 1+

   OR

7. A Nystatin pessary 100,000 U daily x 14 days.

   Grade A, Level 1+
Note:
1. All topical and oral azole therapies give a clinical and mycological cure rate of 80-90% in uncomplicated vulvovaginal candidiasis. Nystatin preparations give 70-90% cure rate.
2. The treatment choice is the personal preference, availability and affordability as well as familiarity of the clinician with the treatment.
3. Topical azole creams and suppositories may be oil-based and might weaken latex condoms.
4. Topical azole treatment may cause vulvo-vaginal irritation and this should be considered if symptoms worsen.

**Follow up**

Follow-up is not necessary if symptoms resolve. A test of cure is not required (pg 64).

**Treatment of recurrent vulvovaginal candidiasis**

Clinicians should be aware of psychosexual problems and depression, which can occur in women with recurrent vaginal infections (pg 65).

**Recommended regimens for recurrent vulvovaginal candidiasis**

*Induction regimens*

1. **A** Fluconazole 150 mg orally every 72 hours x 3 doses.  
   Grade A, Level 1+
   
   OR

2. **C** Topical imidazole therapy x 7-14 days according to symptomatic response.  
   Grade C, Level 2+

*Maintenance regimens*

1. **B** Clotrimazole pessary 500 mg intravaginally once a week or 200 mg intravaginally twice a week.  
   Grade B, Level 2++
   
   OR

2. **B** Fluconazole 150 mg orally once a week.  
   Grade B, Level 2++
Note:

1. **B** Maintenance therapy should last 6 months. 90% of women should remain disease-free during treatment.

   **Grade B, Level 2++**

2. **C** For women who have relapses between doses, consider twice-weekly 150 mg fluconazole or 50 mg fluconazole daily.

   **Grade C, Level 2+**

**D** Monitor the liver function test when the woman is on regular oral azole treatment (pg 66).

   **Grade D, Level 4**

**Candidiasis in pregnancy**

**B** Symptomatic candidiasis in pregnancy should be treated with topical azole therapy only. Longer courses (seven days) are recommended. Oral azole therapy is contraindicated (pg 67).

   **Grade B, Level 2+**

**Non-albicans candidiasis**

**Treatment (pg 67)**

**C** Nystatin pessaries or nonfluconazole azole drug (oral or topical) are the first line treatment for non-albicans infection.

   **Grade C, Level 2+**

   **OR**

**C** Consider Amphotericin B vaginal suppositories 50 mg once a day for 14 days.

   **Grade C, Level 2+**

**Trichomoniasis**

**Management of sex partners**

**D** 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 (pg 68).

   **Grade D, Level 4**
Patients should be advised to avoid sexual intercourse (including oral sex) until they and their partner(s) have completed treatment and follow-up (pg 68).

Grade D, Level 4

Screening for coexisting sexually transmitted infections should be undertaken in both the patients and their partners (pg 68).

Grade D, Level 4

Women should be informed that *T. vaginalis* is a STI and partner management and treatment is recommended for all partners in the last 2 months (pg 68).

Grade C, Level 2+

**Treatment of trichomoniasis**

**Recommended regimen for trichomoniasis** (pg 69):

1. **A** Metronidazole 2 g orally x single dose.

   Grade A, Level 1+

   OR

2. **A** Metronidazole 400 mg orally bid x 7 days.

   Grade A, Level 1+

   OR

3. **A** Tinidazole 2 g orally single dose.

   Grade A, Level 1+

**Note:**

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

   Grade D, Level 4

2. The recommended metronidazole regimes have resulted in cure rates of 90-95%.

**Trichomoniasis in pregnancy**

Although the use of metronidazole in pregnancy has not been shown to be teratogenic or mutagenic in all stages of pregnancy or breastfeeding, caution should be advised for use in the first trimester. Metronidazole pessaries may be used to provide symptomatic relief but have lower cure rates than the oral regimes (pg 69).

Grade D, Level 4
D Treatment of *Trichomonas vaginalis* relieves symptoms of vaginal discharge in pregnant women and might prevent respiratory or genital infection of the newborn and further sexual transmission. Clinicians should counsel patients regarding the potential risks and benefits of treatment (pg 69).

**Grade D, Level 4**

A It is reasonable to delay therapy in asymptomatic pregnant women until after 37 weeks’ gestation. In addition, these pregnant women should be provided careful counseling regarding condom use and the continued risk of sexual transmission (pg 70).

**Grade A, Level 1+**

**Follow up**

A Follow-up is unnecessary for asymptomatic patients. Patients with persistent symptoms should be retreated with metronidazole 400 mg orally bid for 7 days (pg 70).

**Grade A, Level 1+**

A If treatment failure occurs repeatedly, the patient can be treated with high dose oral metronidazole 2 g daily for 3 days (pg 70).

**Grade A, Level 1+**

**Cost-effectiveness issues**

**GPP** Doctors should consider efficacy, adverse side effects, dosing frequency, and cost to the patient when recommending treatments. For compliance issues, single dose therapies are generally recommended (pg 71).

**GPP**

B Male patients complaining of urethral discharge and/or dysuria should be examined for discharge. The major pathogens causing urethral discharge are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. In the syndromic management of a patient with urethral discharge, treatment should adequately cover these two organisms and has been found to be cost-effective. Where reliable laboratory facilities are available, a distinction may be made between the two organisms (pg 71).

**Grade B, Level 2++**
1 Introduction

1.1 Background information

These clinical practice guidelines have been produced to familiarize doctors with the key features of the common sexually transmitted causes of genital ulcers and discharges, to identify “red flags” that indicate a need to refer the patient to a specialist, and to provide an overview to evidence-based management of the various causes. The guidelines are not intended to be a comprehensive review of all aspects of genital ulcerative disease or discharge, or sexually transmitted diseases.

1.2 Development of guidelines

These guidelines have been produced by a team comprising dermatologists, obstetricians/gynaecologists, infectious disease physicians, urologists, pathologists with an interest in laboratory diagnosis of sexually transmitted infections, as well as general practitioners.

1.3 Objectives

The main objective of these guidelines is to promote evidence-based management of the common sexually transmitted causes of genital ulcers and discharges. These guidelines will assist all doctors who manage patients presenting with genital ulcers and discharges, in particular primary care physicians, as well as dermatologists, obstetricians and gynaecologists and infectious disease physicians.

1.4 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 5 years after publication, or when new evidence appears that requires updating of the recommendations.
2 Management of genital ulcers

2.1 Introduction

The incidence of genital ulcer disease is on the rise in Singapore. This is shown by the increase in notifications of patients seen at the Department of STI Control Clinic (DSC) as well as from physicians in hospital and general practice.¹

Genital ulcer disease is associated with an increased risk for HIV infection.² The physician must also be aware that two or more infections can coexist in a patient presenting with genital ulcers, and a thorough evaluation of the possible causes should be undertaken. Counselling and contact tracing, as far as possible, should also be done. These management guidelines will cover the common sexually transmitted infections causing genital ulcer disease.

2.2 Definition

Genital ulcer disease is defined as an ulcerative, erosive, pustular or vesicular genital lesion(s) with or without regional lymphadenopathy, caused by either sexually transmitted infections (STIs) or non-STI-related infections or conditions.

Aetiology of genital ulcer disease

A. STI-related

The two commonest STIs which cause genital ulcerative disease are:
1. Genital herpes (HSV-1 or HSV-2) which is the leading cause, and
2. Primary syphilis
   Other diseases such as Chancroid, Granuloma inguinale and Lymphogranuloma venereum (due to Chlamydia trachomatis serotypes L1, 2 or 3) are uncommon in Singapore.
B. Non-STI related infections or conditions

<table>
<thead>
<tr>
<th>Bullous dermatoses</th>
<th>Non-bullous dermatoses</th>
<th>Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Non-autoimmune</td>
<td>• Nonspecific vulvitis/balanitis</td>
<td>• Squamous cell carcinoma</td>
</tr>
<tr>
<td>1. Contact dermatitis</td>
<td>• Apthous ulcers</td>
<td>• Vulval intraepithelial neoplasia</td>
</tr>
<tr>
<td>2. Erythema multiforme</td>
<td>• Erosive lichen planus</td>
<td>• Erythroplasia of Queyrat</td>
</tr>
<tr>
<td>(commonly HSV-related)</td>
<td>• Lichen sclerosus</td>
<td>Less common:</td>
</tr>
<tr>
<td>• Auto-immune</td>
<td>• Behcet’s disease</td>
<td>• Extramammary Paget’s disease</td>
</tr>
<tr>
<td>3. Pemphigus</td>
<td>• Pyoderma gangrenosum</td>
<td>• Basal cell carcinoma</td>
</tr>
</tbody>
</table>

2.3 Clinical approach to genital ulcers

It is recommended that the following diagnostic approach be taken in any patient with genital ulcers or discharges:

A. **Patient history**:
   1. **Lesion history**: prodrome, initial presentation (especially presence of vesicles), duration of lesion, pain, symptoms of urethritis, other systemic symptoms, use of systemic or topical remedies, any history of similar symptoms in the past or partners with similar symptoms.
   2. **Medical history**: HIV status, skin conditions, drug allergies, and medications.
   3. **Sexual history**: gender of partners, number of partners, venue for meeting partners, commercial sex exposure, partners with symptoms or signs, partners with known HSV or recent syphilis diagnosis.
   4. **Travel history**: geographical area where sexual intercourse has taken place.

B. **Physical exam**:
   1. **Lesion**: examine for appearance, distribution, number, size, induration, depth, and tenderness.
   2. **Genital exam**: examine genital and perianal area for other lesions.
   3. **Lymph node(s)**: note number and location of enlarged nodes, size, tenderness, presence of bubo.
4. **General exam**: thorough examination of oral cavity and skin of torso, palms and soles. In patients with syphilis, this would include an examination of the cardiovascular and neurological systems.

**Table 1 Clinical features of some causes of genital ulcers**

<table>
<thead>
<tr>
<th></th>
<th>Genital Herpes</th>
<th>Primary Syphilis</th>
<th>Chancroid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aetiologic agent</strong></td>
<td>HSV-1 &amp; HSV-2</td>
<td><em>T. pallidum</em></td>
<td><em>H. ducreyi</em></td>
</tr>
<tr>
<td></td>
<td>- most common cause</td>
<td></td>
<td>- uncommon locally</td>
</tr>
<tr>
<td><strong>Incubation period</strong></td>
<td>2-7 days</td>
<td>10-90 days</td>
<td>3-10 days</td>
</tr>
<tr>
<td></td>
<td>(avg. 21 days)</td>
<td>(avg. 4-7 days)</td>
<td></td>
</tr>
<tr>
<td><strong>Initial lesions</strong></td>
<td>Papule → vesicle*</td>
<td>Papule</td>
<td>Papule or pustule</td>
</tr>
<tr>
<td><strong>Presenting lesion</strong></td>
<td>Vesicles</td>
<td>Chancre</td>
<td>Ulcer/bubo</td>
</tr>
<tr>
<td><strong>Number and distribution of lesions</strong></td>
<td>Multiple*, may coalesce. Bilateral in primary; unilateral in recurrent.</td>
<td>Usually one</td>
<td>Single or multiple</td>
</tr>
<tr>
<td><strong>Diameter</strong></td>
<td>1-2 mm</td>
<td>5-15 mm</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Edges</strong></td>
<td>Erythematous</td>
<td>Sharply demarcated, elevated, round, or oval</td>
<td>Undermined, ragged, irregular</td>
</tr>
<tr>
<td><strong>Depth</strong></td>
<td>Superficial</td>
<td>Superficial or deep</td>
<td>Excavated, deep</td>
</tr>
<tr>
<td><strong>Base</strong></td>
<td>Serous, erythematous, nonvascular</td>
<td>Smooth, non-purulent, relatively nonvascular</td>
<td>Necrotic, generally purulent, bleeds easily</td>
</tr>
<tr>
<td><strong>Induration</strong></td>
<td>None</td>
<td>Usually present</td>
<td>None</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>Common, often with prodrome of tingling*</td>
<td>Uncommon*</td>
<td>Common, severe</td>
</tr>
<tr>
<td><strong>Lymphadenopathy</strong></td>
<td>Usually present in primary infection, and absent in recurrences</td>
<td>Firm, non-tender, bilateral</td>
<td>Tender, may suppurate, usually unilateral</td>
</tr>
</tbody>
</table>


*Useful in differential diagnosis.
C. **Laboratory testing**

**A**

A diagnosis based only on the patient’s medical history and physical examination frequently may be inaccurate. Ideally, all patients who have genital ulcers should be evaluated with a serologic test for syphilis and a diagnostic evaluation for genital herpes; if chancroid is suspected, the patient should be referred to a specialist for evaluation and a test for *Haemophilus ducreyi*.\(^5,6,7\)

*Grade A, Level 1*+

**B**

HIV and serologic testing for syphilis should be performed on all patients who have STIs presenting with genital ulcers, as well as tests for herpes simplex infection where appropriate. Locally, genital herpes and syphilis are the two most likely infective etiologies. Non-infective causes may need to be considered.\(^8,9\)

*Grade B, Level 2++*

D. **Management**

Clinicians often have to treat patients before test results are available because early treatment decreases the possibility of ongoing transmission and because successful treatment of genital herpes depends on prompt initiation of therapy.

**B**

The clinician should treat for the diagnosis considered most likely, on the basis of clinical presentation and epidemiologic circumstances. In some instances, treatment must be initiated for additional conditions because of diagnostic uncertainty.\(^5\)

*Grade B, Level 2++*

**GPP**

Successful management of STI-associated syndromes requires that staff are respectful of patients and are not judgmental. Examination must be done in appropriate surroundings where privacy can be ensured and confidentiality guaranteed. Patients should be educated and counseled on their condition as well as safer sex.

*GPP*

Even after complete diagnostic evaluation, at least 25% of patients who have genital ulcers have no laboratory-confirmed diagnosis.\(^5\)
A syndromic approach to management of genital ulcers has proven to be cost-effective in resource poor settings; however it has not been shown to be applicable in the local context.\textsuperscript{8,9}

2.4 Management of specific genital ulcer diseases

2.4.1 Management of herpes simplex virus (HSV) infection

2.4.1.1 Clinical features

Genital herpes is caused by HSV type 1 or 2. First episode genital herpes is often severe, presenting with multiple grouped vesicles, which rupture easily leaving painful erosions and ulcers. In the male, the lesions occur mainly on the prepuce and sub-preputial areas of the penis; in females on the vulva, vagina and cervix. Healing of uncomplicated lesions takes 2 to 4 weeks.

Recurrent attacks are less severe than the first episode. Groups of vesicles or erosions develop on a single anatomical site and these usually heal within 10 days.

The majority of persons with HSV infection have mild, often unrecognised or sub-clinical disease and are unaware of the infection. They may nevertheless shed the virus intermittently in the genital tract and thus transmit the infection to their partners unknowingly.

2.4.1.2 Laboratory investigations

- Viral isolation in cell culture:
  This is considered the ‘Gold standard’. The test is both sensitive and specific, but sensitivity declines as lesions heal; viral typing is possible.\textsuperscript{10-12}

The swab used for sampling the cells at the bases of ulcers should be sent in viral transport medium, which can be obtained from the laboratories performing the test. Do not use calcium alginate swabs, however cotton-, rayon-, or dacron-tipped swabs are suitable. Insert the swab into the viral transport medium, break off the stick and screw-cap the bottle securely. The sample then needs to be dispatched to the laboratory at 4°C using an ice pack. If delay is anticipated, refrigerate at 4°C, do not freeze. Time
taken for a positive result (HSV type 1 or 2) ranges from 1 to 7 days, and for a negative result 7 days.

OR

- **HSV antigen detection:**
  By Direct Immunofluorescence techniques.
  The swab used for sampling the cells at the base of ulcers can be sent in a sterile container with 1 to 2 mL of sterile saline added to prevent drying of the swab. Refrigerate sample at 4°C until transfer to the laboratory, do not freeze. Results may be available in 1 to 2 days. HSV type is reported if the test is positive.

OR

- **PCR detection of viral nucleic acid:**
  Highest sensitivity; viral typing possible\(^{11,12}\); but expensive and not widely available. Use only Dacron-tipped swabs and send swab in swab sheath without any media. Refrigerate sample at 4°C until transfer to the laboratory, do not freeze. Dispatch to the laboratory at 4°C using an ice pack. Results are available in 2 to 4 days.

**What about serology?**

The role of **Type-specific serological tests (TSST):**

Many commercial tests for HSV antibodies are not type specific and are of **NO** value in the management of genital herpes.\(^{13-16}\)

Accurate type-specific assays for HSV antibodies must be based on the HSV-specific glycoprotein G1 for the diagnosis of infection with HSV-1 and glycoprotein G2 for the diagnosis of HSV-2.

**B** In performing serology for HSV infection, assays that detect the type-specific glycoproteins gG1 (HSV 1) and gG2 (HSV 2) should be used.

*Grade B, Level 2++*

The presence of specific IgG to HSV indicates previous exposure.
The use of TSST may be useful in certain specific situations, such as confirming a diagnosis of genital herpes in a person with a typical history of recurrent ulcers but negative cultures, counselling of sexual partners of infected persons, detection of unrecognized infection and for seroepidemiological studies.\textsuperscript{16}

Because almost all HSV-2 infections are sexually acquired, type-specific HSV-2 antibody indicates anogenital infection, but the presence of HSV-1 antibody does not distinguish anogenital from orolabial infection.

2.4.1.3 Treatment

Treatment of first episode genital herpes

1. \textcolor{blue}{A} Acyclovir 200 mg orally 5 times daily for 5 to 10 days.\textsuperscript{17}

   \textbf{Grade A, Level 1++}

   OR

2. \textcolor{blue}{A} Acyclovir 400 mg orally tid for 5 to 10 days.\textsuperscript{17}

   \textbf{Grade A, Level 1++}

   OR

3. \textcolor{blue}{A} Valacyclovir 500 mg/1g orally bid for 5 to 10 days.\textsuperscript{18}

   \textbf{Grade A, Level 1++}

   OR

4. \textcolor{blue}{B} Famciclovir 250 mg orally tid for 5 to 10 days.\textsuperscript{5}

   \textbf{Grade B, Level 2++}

Recurrent genital herpes

Most recurrent attacks are mild and can be managed with general measures/supportive therapy.

Management should be decided together with the patient and can be divided into episodic or suppressive treatment.

Episodic treatment – Effective episodic treatment of recurrent herpes requires initiation of therapy during the prodrome or within 1 day of lesion onset.

\textbf{C} For episodic treatment of recurrent herpes, the patient should be provided with a supply of drug or a prescription for the medication
with instructions to self-initiate treatment immediately when symptoms begin.\textsuperscript{13} 

\textbf{Treatment of recurrent genital herpes}

1. A Acyclovir 200 mg orally 5 times daily or 400 mg orally tid \textit{or} 800 mg orally bid for 5 days.\textsuperscript{19} 

\textit{OR}

2. A Acyclovir 800 mg tid orally for 2 days.\textsuperscript{20} 

\textit{OR}

3. A Valacyclovir 500 mg orally bid \textit{or} 1000 mg orally once a day for 5 days.\textsuperscript{21} 

\textit{OR}

4. A Valacyclovir 500 mg bid for 3 days.\textsuperscript{22,23} 

\textit{OR}

5. A Famciclovir 125 mg orally bid for 5 days.\textsuperscript{24} 

\textit{OR}

6. A Famciclovir 1 g bid orally for 1 day.\textsuperscript{25} 

\textbf{Suppressive treatment}

\textbf{C} Suppressive therapy reduces the frequency of genital herpes recurrences and may be considered in patients who have frequent recurrences (i.e. 6 or more recurrences per year).\textsuperscript{13} 

\textbf{Suppressive treatment of recurrent genital herpes}

1. A Acyclovir 400 mg orally bid.\textsuperscript{26,27} 

\textit{OR}

2. A Valacyclovir 500 mg orally od.\textsuperscript{28}
OR

3. **A** Valacyclovir 1000 mg orally od (for > 10 recurrences in 1 year).\(^5,29^\)

   Grade A, Level 1+

OR

4. **A** Famiclovir 250 mg orally bid.\(^30^\)

   Grade A, Level 1+

C Physicians should stop suppressive treatment of genital herpes after 9 to 12 months to see if recurrence occurs and continued prophylaxis is warranted.\(^13^\)

Grade C, Level 2+

**Treatment of genital herpes in HIV-infected patients**\(^31^\)

1. **A** Acyclovir 400 mg orally tid for 7 to 10 days.\(^32^\)

   Grade A, Level 1+

   OR

2. **A** Valacyclovir 1 g orally bid for 7 to 10 days.\(^32\)

   Grade A, Level 1+

   OR

3. **A** Famiclovir 500 mg orally bid for 7 to 10 days.\(^33^\)

   Grade A, Level 1+

**Suppressive treatment of genital herpes in HIV-infected patients**

1. **A** Acyclovir 400 mg to 800 mg orally bid or tid.\(^34^\)

   Grade A, Level 1+

   OR

2. **A** Valacyclovir 500 mg orally bid.\(^32,35^\)

   Grade A, Level 1+

   OR

3. **A** Famiclovir 500 mg orally bid.\(^36^\)

   Grade A, Level 1+
2.4.1.4 Management of genital herpes in pregnancy

Neonatal herpes is a rare but serious condition, caused by herpes simplex virus type 1 or herpes simplex virus type 2. Neonatal herpes is almost always acquired by direct contact with infected maternal secretions at birth.\textsuperscript{37,38}

The most severe form of the disease is disseminated infection with multiple organ involvement, where mortality is around 30% and 17% have long-term neurologic sequelae.\textsuperscript{37}

The risk of transmission to a neonate is high (30-50%) in women who acquire genital herpes late in pregnancy and low (<1%) in women with recurrent genital herpes at term or who acquire genital herpes during the first half of pregnancy.\textsuperscript{38}

Although acyclovir is not licensed for use in pregnancy, there is substantial clinical experience supporting its safety.\textsuperscript{39}

**First episode genital herpes – 1\textsuperscript{st} and 2\textsuperscript{nd} trimester acquisition**

\textbf{C} Management should be in line with the clinical condition with the use of either oral or intravenous acyclovir.\textsuperscript{40} \hspace{1cm} \textbf{Grade C, Level 2+}

\textbf{C} Vaginal delivery is anticipated in women who present with first episode genital herpes in the first and second trimesters as the risk for transmission to the neonate at delivery is low.\textsuperscript{40} \hspace{1cm} \textbf{Grade C, Level 2+}

**First episode genital herpes – 3rd trimester acquisition**

\textbf{C} Caesarean section should be offered to all women presenting with first-episode genital herpes lesions at the time of delivery, or within 6 weeks of the expected date of delivery or onset of labour.\textsuperscript{41-43} \hspace{1cm} \textbf{Grade C, Level 2+}
Recurrent genital herpes in pregnancy

**C** If there are no genital lesions at the onset of labour, Caesarean section to prevent neonatal herpes is not indicated.\(^{40-43}\)

*Grade C, Level 2+*

**A** For women with a history of recurrent genital herpes, who would opt for caesarean delivery if HSV lesions were detected at the onset of labour, daily suppressive acyclovir given from 36 weeks of gestation until delivery may be given to reduce the likelihood of HSV lesions at term.\(^{44-47}\)

*Grade A, Level 1+

**B** **Counselling for genital herpes is important and should include**:  
- Information on natural history of disease, potential for recurrent attacks, role of asymptomatic shedding in sexual transmission  
- Abstinence from sexual activity during prodromal symptoms or when lesions are present  
- Advice to inform current and new sexual partners of genital herpes  
- Use of condoms with new or uninfected partners, particularly in first 12 months after first attack  
- Information on anti-viral treatment available  
- Risk of neonatal infection: women with a history of genital herpes or whose partners have history of genital herpes should inform their obstetrician early in pregnancy

*Grade B, Level 2++*

### 2.3.2 Management of primary syphilis

#### 2.3.2.1 Clinical features

Primary syphilis is characterised by an ulcer (chancre) and regional lymphadenopathy. A chancre typically occurs in the anogenital region, and presents as a solitary, painless and indurated ulcer with a clean base discharging clear serum.\(^{49}\) However, atypical features may be present; these include multiple lesions, presence of pain, and occurrence on extragenital sites.\(^{50}\)
2.3.2.2 Laboratory investigations

Serological Tests

I Non-Treponemal Tests – rapid plasma regain (RPR) and/or Venereal Disease Research Laboratory (VDRL)
A positive RPR/VDRL test needs to be confirmed by a treponemal test. RPR/VDRL may become negative if treatment is instituted early in the disease. However treatment of late infections often results in a persistently positive result - or a serological scar.

II Treponemal Tests (confirmatory)
- The Treponema Pallidum Haemagglutination Assay (TPHA) and the Treponema Pallidum Particle Agglutination (TPPA) test are the most widely used confirmatory tests.
- The treponemal EIA test is also a specific test for syphilis, but most experts recommend performing either TPHA or TPPA as an additional confirmatory test if the EIA result is positive.
- Once positive, specific tests tend to remain positive even after the syphilis has been successfully treated. The titres of treponemal tests are not useful in monitoring treatment response.

2.3.2.3 Treatment

Treatment of primary syphilis

1. Benzathine Penicillin G 2.4 million units i/m weekly x single dose. (For primary syphilis, most authorities administer a single dose, while some might use two doses for secondary syphilis).\textsuperscript{51,52} 
   Grade B, Level 2++
   OR

2. Aq. Procaine Penicillin G 600,000 units i/m daily x 10 days.\textsuperscript{53-55} 
   Grade B, Level 2++
Penicillin-allergic patients

1. Doxycycline 100 mg orally bid x 14 days.\textsuperscript{56-58} \textsuperscript{Grade B, Level 2++}

OR

2. Erythromycin 500 mg orally qid x 14 days.\textsuperscript{59,60} \textsuperscript{Grade B, Level 2++}

OR

3. Azithromycin 500 mg orally od x 10 days.\textsuperscript{61} \textsuperscript{Grade B, Level 1+}

\textbf{C} For HIV-infected individuals, either the same treatment as in non-HIV infected individuals or 3 doses of Benzathine Penicillin G 2.4 million units i/m weekly are recommended.\textsuperscript{9} \textsuperscript{[0]} \textsuperscript{Grade C, Level 2+}

\textbf{C} HIV-positive individuals with primary syphilis should be referred to an appropriate expert for follow up.\textsuperscript{9} \textsuperscript{Grade C, Level 2+}

\textbf{B} Oral doxycycline is the preferred oral alternative in all patients in view of its more favourable dosing intervals and low cost.\textsuperscript{58} \textsuperscript{Grade B, Level 2++}

\textbf{GPP} The treatment guidelines listed refer to management of primary syphilis. For late latent syphilis, syphilis of unknown duration, congenital syphilis or neurosyphilis, the treatment recommendations are different and relevant expert advice should be sought. 

\textbf{2.3.2.4} Follow-up

\textbf{C} The same quantitative nontreponemal tests (i.e RPR or VDRL) should be repeated during follow up; the DSC Clinic follows up patients for a total period of two years (tests are repeated at 3 months; 6 months; 12 months; 18 months; 24 months).\textsuperscript{9,53} \textsuperscript{Grade C, Level 2+}

\textbf{C} A sustained fourfold or greater increase in RPR/VDRL titres suggests re-infection or treatment failure. Following treatment of early syphilis, RPR/VDRL should demonstrate a decrease in titre within 6
months. In particular, patients treated with non-penicillin based regimens should be followed up to look for signs of treatment failure.9,53

**Grade C, Level 2+**

**C** Since treponemal tests remain positive for life following effective treatment, proper documentation is necessary to prevent unnecessary retreatment. Patients should be given a letter documenting their treatment.9

**Grade C, Level 2+**

**D** Reinfection or relapse should be retreated preferably with supervised treatment schedules to ensure compliance, and sexual partners should be rescreened. These patients could also be referred to the relevant experts.9

**Grade D, Level 4**

### 2.3.2.5 Management of sexual contacts

Partner notification, or “contact tracing”, is the process of learning from persons with STIs about their sexual partners and helping to arrange for evaluation and treatment of those partners. Many persons benefit from partner notification; thus patients with STIs should be encouraged to make partners aware of potential risk and urge them to seek diagnosis and treatment.

At risk partners are those who have been exposed within the following periods – 3 months plus duration of symptoms for primary syphilis.

There is clear evidence that involving index patients in shared responsibility for the management of sexual partners improves outcomes.62

**Syphilis in pregnancy**

Penicillin is the drug of choice in the same dosage schedule as for non-pregnant individuals.

**D** All pregnant women should be screened for syphilis at the initial antenatal visit. Women who had documented treatment for syphilis in the past do not need retreatment during current or subsequent pregnancies if there is no clinical evidence of syphilis and the
RPR/VDRL titre is negative or serofast in low titre compared to previous results.\footnote{9}

**D** For penicillin-allergic patients, erythromycin is given in dosage schedules as recommended for the treatment of non-pregnant patients. However, as erythromycin exhibits poor penetration across the placental barrier, the infant should be routinely treated with penicillin at birth. For these patients, retreatment with doxycycline can be considered after delivery when breastfeeding has been stopped.\footnote{9}

**Grade D, Level 4**

Doxycycline is contraindicated in pregnancy.

**C** Women treated for early syphilis during pregnancy should have monthly RPR/VDRL for the remainder of the current pregnancy.\footnote{9}

**Grade C, Level 2+**

### 2.4.3 Management of chancroid

#### 2.4.3.1 Clinical features

Chancroid is caused by *Haemophilus ducreyi*. It is characterised by genital ulceration and lymphadenitis with progression to bubo formation. The incubation period ranges from 3 to 10 days. There may be single or multiple ulcers, which are not indurated, bordered by ragged undermined edges and have a necrotic base and purulent exudate, and are typically painful.\footnote{63}

**D** Locally, chancroid is uncommon. Any suspected case should be referred to a specialist for evaluation, as routine laboratory tests are not widely available.\footnote{1}

**Grade D, Level 4**

#### 2.4.3.2 Treatment of chancroid

1. **A** Azithromycin 1 g orally x single dose.\footnote{64}

**Grade A, Level 1+**

OR
2. **B** Ceftriaxone 250 mg i/m x single dose.\(^{65}\)  
   **Grade B, Level 2++**  
   OR  
3. **B** Ciprofloxacin 500 mg bid x 3 days.\(^{66}\)  
   **Grade B, Level 2++**

### 2.4.4 Management of lymphogranuloma venereum

#### 2.4.4.1 Clinical features

Lymphogranuloma venereum (LGV) is a systemic disease caused by one of three invasive serovars L1, L2 or L3 of *Chlamydia trachomatis*.

Rectal exposure in women or men who have sex with men might result in proctocolitis (including mucoid and/or hemorrhagic rectal discharge, anal pain, constipation, fever, and/or tenesmus). LGV is an invasive, systemic infection, and if it is not treated early, LGV proctocolitis might lead to chronic, colorectal fistulas and strictures.\(^{60}\) There have been recent outbreaks described among men who have sex with men in Western Europe and the United States.\(^{67,68}\)

**D** Locally, lymphogranuloma venereum (LGV) is uncommon. Any suspected case should be referred to a specialist for evaluation, as routine laboratory tests are not widely available.\(^1\)  
   **Grade D, Level 4**

#### 2.4.4.2 Treatment of lymphogranuloma venereum

1. **B** Doxycycline 100 mg bid x 21 days.\(^{69}\)  
   **Grade C, Level 2+**  
   OR  
2. **B** Erythromycin 500 mg qid x 21 days.\(^{69}\)  
   **Grade C, Level 2+**
3 Management of genital discharges

3.1 Introduction

In patients presenting with a urethral discharge, gonorrhoea and *Chlamydia trachomatis* infections are the most common causes in Singapore.\(^7\) A spontaneous complaint of abnormal vaginal discharge is most commonly due to a vaginal infection, and less commonly may be the result of mucopurulent STI-related cervicitis.

Genital discharges are associated with an increased risk for acquiring HIV infection.\(^7\) Two or more infections may coexist in a patient presenting with a genital discharge, therefore a thorough evaluation of the possible causes should be undertaken. As far as possible, counselling and contact tracing should be done. There may be a need to treat the contact epidemiologically. These management guidelines will cover the common infections causing genital discharges.

Patients presenting with genital discharges should also be screened for HIV and syphilis.\(^8,9\)

3.2 Diagnostic approach

The following diagnostic approach is recommended:

A. Patient history:
   1. **History of discharge**: onset, duration, colour, odour, association with micturition, dysuria, itch, rash, chronicity, involvement of sites (urethra, vagina, pharynx, rectum, eye), other systemic symptoms (fever, joint pain, ophthalmic symptoms), use of systemic or topical remedies, any history of similar symptoms in the past or partners with similar symptoms.
   2. **Medical history**: diabetes, HIV status, skin conditions, drug allergies, current & previous medications, menstrual history, obstetric history
   3. **Sexual history**: gender of partners, number of partners, venue for meeting partners, commercial sex exposure, partners with symptoms or signs, partners with known genital discharge diagnosis.
   4. **Travel history**: geographical area where sexual intercourse has taken place.
B. Physical examination:
1. Lesion: appearance and character of discharge, consistency, odour.
2. Genital exam: external genitalia and peri-anal area for inflammation and other lesions.
3. Lymph node(s): note number and location of enlarged nodes, size, tenderness.
4. General exam: thorough examination of oral cavity and eyes/joints as necessary. In males, 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.

3.3 Genital discharges in males

Urethritis is a common cause of genital discharges in males.

Clinical features

Symptoms of urethritis include discharge, dysuria, and intra-urethral itch/discomfort. 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 a more likely diagnosis. Nevertheless urethral infections due to sexually-transmitted pathogens may be asymptomatic.
Causes of sexually transmitted urethritis in males

<table>
<thead>
<tr>
<th>Causes of sexually transmitted urethritis in males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common causes</td>
</tr>
<tr>
<td>- Neisseria gonorrhoeae</td>
</tr>
<tr>
<td>- Chlamydia trachomatis</td>
</tr>
<tr>
<td>Other causes</td>
</tr>
<tr>
<td>- Ureaplasma urealyticum</td>
</tr>
<tr>
<td>- Mycoplasma genitalium</td>
</tr>
<tr>
<td>- Trichomonas vaginalis</td>
</tr>
<tr>
<td>- Herpes simplex virus</td>
</tr>
<tr>
<td>- Adenovirus infection</td>
</tr>
<tr>
<td>- Neisseria meningitidis</td>
</tr>
<tr>
<td>- Non-specific urethritis (NSU)</td>
</tr>
</tbody>
</table>

**Gonococcal urethritis** has a shorter incubation period (2-7 days) than NGU 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 urinary tract infection and Herpes simplex virus. The remainder (20-30%) have no detectable organisms (non-specific urethritis).
## Approach to diagnosis of urethral discharges

<table>
<thead>
<tr>
<th>Diagnosis Clinical feature</th>
<th>Gonorrhoea</th>
<th>Non-gonococcal urethritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nature of discharge</td>
<td>Purulent</td>
<td>Clear, whitish</td>
</tr>
<tr>
<td></td>
<td>Profuse</td>
<td></td>
</tr>
<tr>
<td>Clinical complications</td>
<td>Epididymo-orchitis</td>
<td>Epididymo-orchitis</td>
</tr>
<tr>
<td></td>
<td>Prostatitis</td>
<td>Prostatitis</td>
</tr>
<tr>
<td></td>
<td>Disseminated gonococcal infection (DGI)</td>
<td>Reiter’s Disease</td>
</tr>
<tr>
<td>Urethral smear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram stain Polymorph</td>
<td>+/++</td>
<td>+/+ (&gt; 5 wbc/μl)</td>
</tr>
<tr>
<td>Gram negative intracellular diplococci</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Culture/nucleic-acid amplification test (NAAT)</td>
<td><em>N. gonorrhoeae</em></td>
<td><em>C. trachomatis</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>U. urealyticum</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>M. genitalium</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>M. hominis</em></td>
</tr>
</tbody>
</table>

### Investigations in males:

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.

**D** All patients who have confirmed or suspected urethritis should be tested for gonorrhoea and chlamydia.\(^9\)

*Grade D, Level 4*

Testing for chlamydia is strongly recommended because of the increased utility and availability of highly sensitive and specific testing methods and because a specific diagnosis might enhance partner notification/management and improve compliance with treatment, especially in the exposed partner.\(^72\)
Because of high specificity (>99%) and sensitivity (>95%), a Gram stain of a male urethral specimen that demonstrates polymorphonuclear leukocytes with intracellular Gram-negative diplococci is presumptive of infection with *N. gonorrhoeae* in symptomatic men. Thus it is recommended that urethral smears be obtained in symptomatic men to aid in diagnosis.\(^{72,73}\)

Microscopy is not suitable for pharyngeal or rectal specimens where many other bacteria are present including Gram-negative cocci belonging to other genera.\(^{73}\)

Cultures and PCR detection for *Ureaplasma urealyticum* and *Mycoplasma genitalium* are not routinely performed.

Acute 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.

### 3.4 Chlamydia and gonorrhoea in women

**Chlamydia trachomatis**

*C. trachomatis* is a common bacterial STI in women. It is usually asymptomatic (in 80% of women). However, women may present with vaginal discharge (due to cervicitis), abnormal bleeding (postcoital or intermenstrual), lower abdominal pain, dyspareunia or dysuria. Risk factors for *C. trachomatis* are: age <25 years, a new sexual partner or more than one partner in the last year.\(^{74-76}\)

**Neisseria gonorrhoeae**

*N. gonorrhoeae* is another common bacterial STI in women. Up to 50% of women with *N. gonorrhoeae* will complain of vaginal discharge. The discharge is due to cervicitis rather than vaginitis. *N. gonorrhoeae* may coexist with other genital tract pathogens such as Trichomonas, Candida and *C. trachomatis*.\(^{77}\)

Microscopical examination of Gram-stained smears of endocervical discharge can be used as a point of care test to provide an immediate presumptive diagnosis of gonorrhoea.\(^{73}\)
Microscopy of endocervical smears in women has a sensitivity of between 30-50%

Blood tests such as the gonococcal complement fixation test (GC-CFT) are not useful for the diagnosis of gonorrhea. Serological tests are also not useful in the diagnosis of acute chlamydial infections because of cross-reactivity between chlamydial species, and the high prevalence of Chlamydia antibodies in high risk populations.

**B Gonococcal complement fixation test are not recommended for the diagnosis of gonorrhea. Serological tests are not recommended for the diagnosis of acute chlamydial infections.**

**Grade B, Level 2++**

### 3.5 Complications of genital discharges

**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 causes.

**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.

**Pelvic inflammatory disease** (PID) may occur in untreated females. As PID can cause serious sequelae such as infertility & ectopic pregnancy as a result of tubal damage, investigation AND treatment is warranted. Chronic pelvic pain may also occur.

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.
### Syndromic management of urethral symptoms in males

#### Urethral symptoms present

Presence of sexually transmitted urethral infection

This is indicated if any one of the following are present:

- History - risk of sexually transmitted infection present (e.g. unprotected oral, vaginal, anal sex)
- Examination - presence of urethral discharge and meatitis
- Laboratory - raised polymorphonuclear leucocytes (PML) on Gram-stained smear

#### Diagnosis of gonorrhoea is likely if there is -

- Thick purulent discharge
- Short incubation period (2-7 days)
- Gram-negative intracellular diplococci seen on Gram-stain microscopy

If *any* one of the above points are present -

- Send urethral swab for gonococcal culture
- Send urethral swab or first catch urine for nucleic-acid amplification test (NAAT) for *Chlamydia trachomatis*
- Treat for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*
- Review in 14 days

If none of the above points are present -

- Send urethral swab for gonococcal culture
- Send urethral swab or first catch urine for NAAT for *Chlamydia trachomatis*
- Treat for *Chlamydia trachomatis*
- Review in 14 days

---

3.6 Treatment of gonorrhoea

- **Uncomplicated infection in adults - urethral, endocervical & rectal infection**

  1. **A** Ceftriaxone 250 mg intramuscular single dose.\(^{78-80}\)  
     Grade A, Level 1+

     OR

  2. **A** Cefixime 400 mg orally single dose.\(^{78-80}\)  
     Grade A, Level 1+

  **Alternative regimens**

  1. **A** Cefotaxime 1 g intramuscular single dose.\(^{72,78,79,81}\)  
     Grade A, Level 1+

     OR

  2. **A** Spectinomycin 2 g intramuscular single dose (for patients with β-lactam allergy).\(^{72,78,79,81}\)  
     Grade A, Level 1+

  **B** All patients with gonorrhoea should be given concurrent treatment for Chlamydia.\(^{82}\)  
     Grade B, Level 2++

- **Pharyngeal infection**

  **B** Ceftriaxone 250 mg intramuscular single dose\(^{79,83}\) with anti-chlamydia therapy (refer to section 3.7).  
     Grade B, Level 2++

  **B** The fluoroquinolones (e.g. ciprofloxacin, ofloxacin, norfloxacin) should NOT be used as >70% of isolates in Singapore are resistant.\(^{70}\)  
     Grade B, Level 2++

- **Gonococcal infection in pregnancy**

  **A** Cephalosporins in the recommended dosages are safe and effective in pregnancy.\(^{84-86}\)  
     Grade A, Level 1+
Spectinomycin can be administered to pregnant women who are unable to tolerate cephalosporins.\textsuperscript{84-86} \textbf{Grade A, Level 1+}

Simultaneous treatment for chlamydial infection with azithromycin 1g single dose orally or erythromycin 500 mg orally qid x 7 to 14 days is advocated for pregnant women receiving treatment of gonorrhoea.\textsuperscript{84-86} \textbf{Grade B, Level 2++}

**Follow-up**\textsuperscript{9}
- Patients should be instructed to abstain from sexual intercourse until 7 days after therapy is initiated. After this period sexual activity can be resumed provided their symptoms have resolved and sex partners have been screened and treated.
- The test-of-cure is recommended for all sites and assessment for post-gonococcal urethritis (PGU) should be performed after 14 days.
- All treatments are less effective at eradicating pharyngeal infection and test-of-cure is strongly recommended following treatment of infection at this site.
- Serologic tests for syphilis and HIV should also be performed at the initial visit; if negative they should be repeated at 3 months after the last risky exposure.
- Education on STIs and safer sex advice should be regularly reinforced. \textbf{Grade D, Level 4}

**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.\textsuperscript{9} \textbf{Grade B, Level 2++}

### 3.7 Treatment of *Chlamydia trachomatis* infection

- **Uncomplicated urethral, endocervical, pharyngeal or rectal infections in adults**
  - 1. **A** Doxycycline 100 mg orally bid x 7 days.\textsuperscript{71,72} \textbf{Grade A, Level 1++}

  OR
2. **A** Azithromycin 1 g orally single dose.\textsuperscript{71,72} \hspace{2cm} \textbf{Grade A, Level 1++}

OR

3. **A** Erythromycin 500 mg orally qid x 7 days or 500 mg orally bid x 14 days.\textsuperscript{71,72} \hspace{2cm} \textbf{Grade A, Level 1+}

OR

4. **A** Ofloxacin 200 mg orally bid or 400 mg orally od x 7 days.\textsuperscript{71,72} \hspace{2cm} \textbf{Grade B, Level 2++}

- \textbf{Chlamydia trachomatis infection in pregnancy}

Pregnant women whose sexual partners have non-gonococcal urethritis (NGU) should be examined, screened for other STI, and treated on epidemiological grounds.

1. **A** Erythromycin 500 mg orally qid x 7 days or 250 mg orally qid x 14 days.\textsuperscript{87-89} \hspace{2cm} \textbf{Grade A, Level 1+}

OR

2. **A** Amoxicillin 500 mg orally tid x 7 days.\textsuperscript{87-89} \hspace{2cm} \textbf{Grade A, Level 1+}

OR

3. **A** Azithromycin 1 g orally single dose.\textsuperscript{87-89} \hspace{2cm} \textbf{Grade A, Level 1+}

\textbf{Follow up}

\textbf{D} A test-of-cure is not necessary when treatment with doxycycline or azithromycin has been completed, unless symptoms persist or re-infection is suspected. Test-of-cure is however recommended after 4 weeks for infections in pregnant women, or when erythromycin was used. Non-culture tests (e.g. NAAT) done within 4 weeks of completing treatment may yield false positive tests due to persistence of chlamydial antigens.\textsuperscript{9} \hspace{2cm} \textbf{Grade D, Level 4}
Management of sex partners

D 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.\textsuperscript{9} 

\textbf{Grade D, Level 4}

D Sex partners of asymptomatic male patients and of females within the last 90 days (or the most recent sex partner if the last contact was >90 days) should be screened and treated for chlamydial infection.\textsuperscript{9}

\textbf{Grade D, Level 4}

3.8 Treatment of non-gonococcal urethritis (NGU)

Recommended regimens
(See treatment of \textit{Chlamydia trachomatis} above).

Management of sex partners

D Sex partners of men with non-gonococcal urethritis (NGU) within the last 60 days should be screened and treated. These partners should also be examined to exclude other associated STI.\textsuperscript{9}

\textbf{Grade D, Level 4}

At least 30\% of consorts of men with NGU have chlamydial infections of the cervix and 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.\textsuperscript{90}

Management of recurrent or chronic NGU

This is empirically defined as persistent or recurrent symptoms of urethritis occurring 4 to 6 weeks following treatment of acute NGU and occurs in up to 30\% of patients. There is no consensus of opinion for either the diagnosis or the management of this condition. 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.

- **D** Obtain objective evidence of urethritis, e.g. presence of urethral discharge or pus cells on urethral smear. If patient has no objective evidence, consider reassurance only.
- Exclude drug adherence failure or re-infection from untreated partner or a new partner.
- Consider referral to a specialist for further evaluation.\(^9\)

**Grade D, Level 4**

### 3.9 Vaginal discharge

Vaginal discharge is the commonest genital symptom in women. The causes can be physiological or pathological.

#### 3.9.1 Physiological vaginal discharge

Pre-menopausal women may 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.

The causes of physiological vaginal discharge are listed in Table 1.

**B** In women of reproductive age complaining of vaginal discharge the commonest cause is physiological, but infective and other causes should be excluded.\(^91,92\)

**Grade B, Level 2++**
Table 1 Causes of vaginal discharge

1. Physiological
   - Hormonal factors:
     - Variation during the menstrual cycle
     - Hormonal contraception
     - Pregnancy
     - Lactational atrophic vaginitis
     - Postmenopausal atrophic vaginitis
   - Sexual arousal

2. Pathological
   Infective causes
   - Vaginal causes (Commonest causes):
     - Bacterial Vaginosis
     - Vulvovaginal candidiasis
     - Trichomonas vaginalis
   - Cervical causes:
     - *Chlamydia trachomatis*
     - *Neisseria gonorrhoeae*

   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, intrauterine contraceptive device
   - Cervical polyps
   - Genital (Cervical, Endometrial or vaginal) neoplasia
   - Endometritis

3.9.2 How should a woman with vaginal discharge be investigated?

When a woman presents with a complaint of vaginal discharge, her clinician should consider if and when investigations are required.

A spontaneous complaint of abnormal vaginal discharge is most commonly due to a vaginal infection, and rarely, it may be the result of mucopurulent STI-related cervicitis. The symptom of abnormal vaginal discharge is highly indicative of vaginal infection, but poorly predictive for cervical infection. To ensure a cost-effective approach,
risk assessment should therefore be done before investigations and treatment is provided.\textsuperscript{91,92}

\textbf{Grade B, Level 2++}

\textbf{B} Where resources permit, one should consider the use of laboratory tests to screen women with vaginal discharge. Such screening could be applied to all women with discharge as well as to those with a positive risk assessment.\textsuperscript{91,92}

\textbf{Grade B, Level 2++}

\textbf{GPP} Investigation of a woman with vaginal discharge is indicated if (Table 2):
1. She is deemed to be at high risk of sexually transmitted infections (STI).
2. She has symptoms suggestive of upper genital tract infection (e.g. abdominal pain, dyspareunia or fever).
3. She has previous treatment which failed.
4. She is postnatal, post-miscarriage, or post-abortion.
5. She is within 3 weeks of insertion of intrauterine contraceptive device.
6. Requested by the patient.

\textbf{GPP}

\textbf{Table 2}   \textbf{Investigations for vaginal discharges}

<table>
<thead>
<tr>
<th>Site</th>
<th>Investigations</th>
</tr>
</thead>
</table>
| Vulval fissures and erythema      | ▪ Microscopy for yeasts  
▪ Culture for yeasts  
▪ Herpes simplex virus (if multiple vesicles or ulcers present) |
| Vagina                           | ▪ Wet preparation to detect Trichomonas vaginalis (posterior fornix)  
▪ Gram stain to detect clue cells and yeasts (lateral walls)  
▪ Culture for Trichomonas vaginalis and yeasts (lateral walls and posterior walls)  
▪ Amine ‘sniff’ test (if available)  
▪ Vaginal pH (if available) |
| Cervix                           | ▪ Gram-stain for pus cells, Gram-negative intracellular diplococci  
▪ Culture \textit{Neisseria gonorrhoeae}  
▪ Nucleic-acid amplification test (NAAT) for \textit{Chlamydia trachomatis} |
The presence of vaginal discharge, in itself, is a poor predictor of STI.\textsuperscript{93}

A sexual history should be taken to assess the risk of STI when the patient has vaginal discharge.

Risk factors of STIs are: age <25 years, change of new sexual partner in the last year or more than one sexual partner in the last year.\textsuperscript{74-76}

\textcolor{blue}{B} Not all women with vaginal discharge require investigation. Empirical treatment can be given after taking a clinical and sexual history if:
1. The woman is at low risk of STI.
2. She has no symptoms to suggest upper genital tract infection.
3. She can return for follow-up if symptoms do not resolve.\textsuperscript{28}

\textbf{Grade B, Level 2++}

\textcolor{blue}{B} A woman of reproductive age complaining of vaginal discharge should be investigated if \textsuperscript{94}.
1. She is deemed to be at high risk of sexually transmitted infections (STI).
2. She has symptoms suggestive of upper genital tract infection (e.g. abdominal pain, dyspareunia or fever).
3. She has previous treatment which failed.
4. She is postnatal, post-miscarriage, or post-abortion.
5. She is within 3 weeks of insertion of intrauterine contraceptive device.
6. Investigation is requested by the patient.

\textbf{Grade B, Level 2++}

\textbf{3.9.3 Infections and vaginal discharge}

Vaginal infections due to bacterial vaginosis, Trichomoniasis vaginalis and vulvovaginal candidiasis commonly present with vaginal discharge (Table 3).

\textcolor{blue}{B} The major causes for vaginal discharge include candidiasis, bacterial vaginosis, trichomoniasis, \textit{Chlamydia trachomatis} and gonococcal infection. Depending on the physician assessment of the patient’s risk factors, syndromic management may be directed against one or all of these common causes.\textsuperscript{91,92}

\textbf{Grade B, Level 2++}
3.9.3.1 Bacterial vaginosis

Bacterial vaginosis is characterised by an overgrowth of predominantly anaerobic organisms (Gardnerella vaginalis, Mycoplasma hominis and Mobiluncus species) in the vagina, leading to replacement of lactobacilli and an increase in pH from less than 4.5 to as high as 7.0. Spontaneous onset and remission of bacterial vaginosis can occur. Whilst bacterial vaginosis is not considered a sexually transmitted disease, it is more common amongst sexually active than non-sexually active women.95

Bacterial vaginosis presents with complaints of an unpleasant fishy smelling vaginal discharge; however, it can be asymptomatic. Bacterial vaginosis is not associated with itch, soreness or irritation. A malodorous, white-grey, thin homogeneous discharge is often visible and adherent to the introitus.

Diagnosis is made by the Amsel criteria or with a Gram stained vaginal smear (Hay/Ison or Nugent Criteria).

**Amsel Criteria**96

Bacterial vaginosis is confirmed on the basis of fulfillment of three or more of the four Amsel criteria:
1. Thin, homogenous, white vaginal discharge
2. Vaginal pH >4.5
3. Clue cells on microscopy of wet mount
4. Positive amine test (addition of potassium hydroxide to a wet preparation of vaginal secretion releases a fishy odour).

**Hay / Ison Criteria**97

Grade 1 (Normal): Lactobacillus morphotypes predominate.
Grade 2 (Intermediate): Mixed flora with some Lactobacilli present, but Gardnerella or Mobiluncus morphotypes also present
Grade 3 (bacterial vaginosis): Predominantly Gardnerella and/or Mobiluncus morphotypes. Few or absent Lactobacilli.

**Nugent Criteria**98

Nugent score is derived from estimating the relative proportions of bacterial morphotypes to give a score between 0 and 10. A score of <
4 is normal and 4-6 is intermediate. Bacterial vaginosis is diagnosed if Nugent score is > 6.

Note:
1. Menses, semen, cervical secretions or douching may affect the pH, a weak positive “sniff test” may be produced by menstrual blood or semen.
2. Isolation of Gardnerella vaginalis cannot be used to diagnose bacterial vaginosis because it can be cultured from the vagina of normal women.

Special groups

Pregnancy

In pregnancy, bacterial vaginosis is associated with late miscarriage, preterm delivery, preterm premature rupture of membranes, and postpartum endometritis.

Three randomized controlled studies showed a reduction in the incidence of preterm birth following screening for and treatment of bacterial vaginosis with metronidazole in women with a history of prior idiopathic preterm birth or second trimester loss. Unfortunately, the studies used different treatment regimes.

Some randomized controlled studies and systematic reviews showed that treatment was not beneficial or even harmful and increased the rate of preterm delivery in both low-risk as well as high-risk groups.

Thus, current evidence is insufficient to evaluate the balance of benefits and harms of screening for bacterial vaginosis in pregnant women at high risk for preterm delivery. In asymptomatic pregnant women at high risk for preterm delivery, studies are lacking, and evidence is therefore poor, for the benefits or harms of screening for bacterial vaginosis.

Women undergoing elective termination of pregnancy (TOP)

Bacterial vaginosis is associated with post-TOP endometritis and pelvic inflammatory disease (PID). Screening and treating bacterial
vaginosis reduce the incidence of subsequent endometritis and PID.\textsuperscript{109,111}

Table 3  **Symptoms and signs of common infections for vaginal discharge**

<table>
<thead>
<tr>
<th></th>
<th><strong>Bacterial vaginosis</strong></th>
<th><strong>Vulvovaginal candidiasis</strong></th>
<th><strong>Trichomonas vaginalis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Thin homogeneous</td>
<td>Thick curdish discharge</td>
<td>Scanty to profuse</td>
</tr>
<tr>
<td></td>
<td>discharge</td>
<td></td>
<td>yellow greenish discharge</td>
</tr>
<tr>
<td></td>
<td>Fishy smell</td>
<td>Non-offensive smell</td>
<td>Offensive smell</td>
</tr>
<tr>
<td></td>
<td>No itch</td>
<td>Vulval itch or soreness</td>
<td>Vulval itch</td>
</tr>
<tr>
<td><strong>Signs</strong></td>
<td>Discharge coating</td>
<td>Vulval erythema</td>
<td>Vulva and vagina</td>
</tr>
<tr>
<td></td>
<td>vagina</td>
<td></td>
<td>inflammation</td>
</tr>
<tr>
<td></td>
<td>No vulval</td>
<td>Presence of satellite</td>
<td>“Strawberry” cervix (seen</td>
</tr>
<tr>
<td></td>
<td>inflammation or</td>
<td>lesions</td>
<td>in 2% cases)</td>
</tr>
<tr>
<td></td>
<td>erythema</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vaginal pH</strong></td>
<td>$\geq 4.5$</td>
<td>$&lt; 4.5$</td>
<td>$\geq 4.5$</td>
</tr>
</tbody>
</table>

**Treatment of bacterial vaginosis**

Indications for treatment:

1. **A** All symptomatic women with bacterial vaginosis, pregnant or non pregnant.\textsuperscript{112,113}
   
   **Grade A, Level 1+**

2. **A** Asymptomatic women with bacterial vaginosis before surgical procedures.\textsuperscript{112,113}
   
   **Grade A, Level 1+**

**General Measures**

**D** Patients with bacterial vaginosis should avoid vaginal douching, use of shower gels, antiseptic agents or shampoo in the bath.\textsuperscript{112}

**Grade D, Level 3**
**Recommended regimens for bacterial vaginosis:** 112,113

1. **A** Clindamycin cream 2% (5 g) intravaginally daily x 3 days or Clindamycin site-released (SR) cream 2% (5 g) intravaginally x single application.

   **OR**

2. **A** Clindamycin 300 mg orally bid x 7 days.

   **OR**

3. **A** Metronidazole gel 0.75% (5 g) intravaginally daily x 5 days.

   **OR**

4. **A** Metronidazole pessary (500 mg) intravaginally bid x 7 days or daily x 14 days.

   **OR**

5. **A** Metronidazole 400 mg orally bid x 7 days.

   **OR**

6. **A** Tinidazole 2 g orally single dose.

**Note:**

1. **A** Metronidazole 2 g orally single dose therapy is the least effective for bacterial vaginosis and is no longer recommended. 106

   **Grade A, Level 1+**

2. Intravaginal metronidazole gel and clindamycin cream have similar efficacy.

3. Metronidazole is less active against lactobacilli than clindamycin. However, clindamycin is more active than metronidazole against most of the bacteria associated with bacterial vaginosis. Clindamycin reduces vaginal Mobiluncus to a greater extent than metronidazole. 114-116

4. Clindamycin vaginal creams and suppositories may be oil-based and might weaken latex condoms. 117
Bacterial vaginosis in pregnancy

A If bacterial vaginosis causes vaginal discharge in pregnancy, it should be treated as for non-pregnant women.\textsuperscript{118} 

\textbf{Recommended regimens for pregnant women.}\textsuperscript{119}

1. \textbf{A} Clindamycin cream 2% (5 g) intravaginally daily x 3 days or Clindamycin-sustained released (SR) cream 2% (5 g) intravaginally x single application.

\hspace{1cm} \textbf{OR}

2. \textbf{A} Clindamycin 300 mg orally bid x 7 days.

\hspace{1cm} \textbf{OR}

3. \textbf{A} Metronidazole pessary (500 mg) intravaginally bid x 7 days or daily x 14 days.

\hspace{1cm} \textbf{OR}

4. \textbf{A} Metronidazole 400 mg orally bid x 7 days. (Avoid in first trimester*).

\textbf{Note:}

1. *Metronidazole crosses the placental barrier. Although it has been given to pregnant women without apparent complication or teratogenicity, it is advisable to withhold oral or vaginal metronidazole during the first trimester of pregnancy.

2. In three trials, intravaginal clindamycin cream was administered at 16-32 weeks’ gestation, and an increase in adverse events (e.g., low birth-weight and neonatal infections) was observed in newborns. Therefore, intravaginal clindamycin cream should only be used during the first half of pregnancy.\textsuperscript{99,120,121}

Recurrent bacterial vaginosis

Recurrence of bacterial vaginosis occurs within 3 months of treatment in 15-30\% of women. There are few published studies evaluating the optimal approach to women with frequent recurrences of bacterial vaginosis.\textsuperscript{122}
Suppressive regimes may be considered but evidence to support their effectiveness is limited.

**Suggested suppressive therapy for recurrent bacterial vaginosis:**

1. **A** Metronidazole gel 0.75% (5 g) twice weekly for 4-6 months.  
   *Grade A, Level 1+

   OR

2. **C** Metronidazole 400 mg orally bid for 3 days at the start and end of menstruation.  
   *Grade C, Level 2+

**Suggested maintenance regime for recurrent bacterial vaginosis:**

**B** Acetic acid vaginal gel use at the time of menstruation and following unprotected sexual intercourse to maintain acidic vaginal pH.  
*Grade B, Level 2+

**Follow up**

**D** Follow-up is not necessary if symptoms resolve. A test of cure is not required.  
*Grade D, Level 4

**Management of sex partners**

No clinical counterpart is recognised in males and screening and treatment has not shown to be beneficial for the male partner.

Although some studies reported a high incidence of bacterial vaginosis in female partners of lesbian women with bacterial vaginosis, no studies have as yet investigated the value of treating partners of lesbian women simultaneously.  

3.9.3.2 **Vulvovaginal candidiasis**

Vulvovaginal candidiasis is caused by Candida albicans in the majority of cases (80-92%). The non-albicans species include *C. glabrata, C.tropicalis, C.krusei, C.parapsilosis,* and *Saccharomyces cerevisiae.*  

62
Vulvovaginal candidiasis commonly presents with vulval itch or soreness with a curd-like vaginal discharge. Occasionally, it can be associated with superficial dyspareunia or external dysuria. Clinically, the woman may have signs of erythema and excoriation over the vulva or vagina with a curdy discharge. Satellite lesions may be seen.

The risk factors include pregnancy, diabetes mellitus, prolonged corticosteroid therapy, antibiotics treatment, and immunosuppression.

Laboratory tests include Gram-stain or wet mount (saline or 10% Potassium hydrochloride) of swabs from the vulva/vaginal wall which reveal budding yeast cells and pseudohyphae (sensitivity 60%), vaginal pH 4-4.5 and culture on Sabouraud medium.

**Note:**
1. Isolation of Candida species in the absence of symptoms and signs does not suggest infection and is not an indication for treatment as 10-20% of women during reproductive years may be colonized with Candida species.
2. None of the above symptoms or signs is pathognomonic for vulvovaginal candidiasis.
3. The symptoms and signs are no guide to the underlying causative species.\(^{128,129}\)

**Treatment of candidiasis**
Treatment is indicated for symptomatic patients.

Avoid local irritants (e.g. perfumed vaginal douche), scented panty-liners and tight fitting synthetic clothing.\(^{130,131}\)

**Grade D, Level 4**

**Treatment for uncomplicated acute vulvovaginal candidiasis**

Both vaginal or oral antifungals (azoles) can be used in the treatment of uncomplicated acute vulvovaginal candidiasis.\(^{32}\)

**Grade A, Level 1+**

**Recommended regimens for uncomplicated acute vulvovaginal candidiasis:**\(^{132}\)

1. Butoconazole1-sustained released (SR) cream site 2% (5 g) intravaginally x single application.

**Grade A, Level 1+**
2. A Clotrimazole pessary 200 mg intravaginally daily x 3 days or 100 mg or 1% cream (5 g) intravaginally daily x 7 days or 500 mg x single application.  
   Grade A, Level 1+

OR

3. A Fluconazole 150 mg orally single dose.  
   Grade A, Level 1+

OR

4. A Isoconazole pessary 600 mg intravaginally x single application.  
   Grade A, Level 1+

OR

5. A Itraconazole 200 mg orally bid x 1 day.  
   Grade A, Level 1+

OR

6. A Miconazole pessary 200 mg intravaginally daily x 3 days or 100 mg or 2% cream (5 g) intravaginally daily x 7 days.  
   Grade A, Level 1+

OR

7. A Nystatin pessary 100,000 U daily x 14 days.  
   Grade A, Level 1+

Note:
1. All topical and oral azole therapies give a clinical and mycological cure rate of 80-90% in uncomplicated vulvovaginal candidiasis. Nystatin preparations give 70-90% cure rate.
2. The treatment choice is the personal preference, availability and affordability as well as familiarity of the clinician with the treatment.
3. Topical azole creams and suppositories may be oil-based and might weaken latex condoms.\textsuperscript{117}
4. Topical azole treatment may cause vulvo-vaginal irritation and this should be considered if symptoms worsen.\textsuperscript{129,133-136}

Follow up

GPP Follow-up is not necessary if symptoms resolve. A test of cure is not required.\textsuperscript{132}
Management of sex partners

There is no evidence to support the treatment of asymptomatic male sexual partners in either episodic or recurrent vulvovaginal candidiasis.137,138

Recurrent vulvovaginal candidiasis

This is defined as 4 or more episodes of symptomatic vulvovaginal candidiasis in a year. There may be partial resolution of symptoms between episodes. Positive microscopy or a moderate/heavy growth of Candida should be documented on at least two episodes.

5% of women with acute vulvovaginal candidiasis will develop recurrent vulvovaginal candidiasis. It is usually due to C albicans although C.glabrata and other non-albicans species are observed in 10-20% of patients with recurrent vulvovaginal candidiasis.139,140

Patients must be evaluated for any predisposing factors. These include uncontrolled diabetes mellitus, immunosuppression, high oestrogen state (e.g. use of oral contraceptive pill and hormonal replacement therapy), disturbance of normal vagina flora (e.g. use of broad-spectrum antibiotics) and corticosteroid use.

Treatment of recurrent vulvovaginal candidiasis

GPP Clinicians should be aware of psychosexual problems and depression, which can occur in women with recurrent vaginal infections.

The principle of therapy involves an induction regimen to ensure clinical remission, followed immediately by a maintenance regimen.

Recommended regimens for recurrent vulvovaginal candidiasis:132,138-140

Induction regimens

1. A Fluconazole 150 mg orally every 72 hours x 3 doses.

OR

65
2. **C** Topical imidazole therapy x 7-14 days according to symptomatic response.  

*Grade C, Level 2+

**Maintenance regimens**

1. **B** Clotrimazole pessary 500 mg intravaginally once a week or 200 mg intravaginally twice a week.  

*Grade B, Level 2++

OR

2. **B** Fluconazole 150 mg orally once a week.  

*Grade B, Level 2++

**Note:**

1. **B** Maintenance therapy should last 6 months. 90% of women should remain disease-free during treatment.\(^{132,139,140}\)  

*Grade B, Level 2++

2. **C** For women who have relapses between doses, consider twice-weekly 150 mg fluconazole or 50 mg fluconazole daily.\(^{132,139,140}\)  

*Grade C, Level 2+

**D** Monitor the liver function test when the woman is on regular oral azole treatment.\(^{141}\)  

*Grade D, Level 4

**Alternative treatment for vulvovaginal candidiasis.**

**Probiotics/Lactobacillus**

There is insufficient evidence to support the use of oral or vaginal lactobacillus to prevent vulvovaginal candidiasis although there are anecdotal reports of benefit.\(^{142,143}\)

**Special groups**

**Candidiasis in pregnancy**

Asymptomatic colonization with Candida species is more common (30-40%).

Colonisation with Candida species is not associated with low birth weight or premature delivery. Thus, no treatment is necessary for asymptomatic colonization.
Symptomatic candidiasis in pregnancy should be treated with topical azole therapy only. Longer courses (seven days) are recommended. Oral azole therapy is contraindicated. \textsuperscript{144-146}  

\textbf{Candidiasis in diabetes mellitus}  
Glycaemic control should be optimized. There is an increased prevalence of non-albicans species, in particular \textit{C glabrata}.  

For treatment of symptomatic women with \textit{C glabrata} isolated, boric acid 600 mg intravaginal suppository once a day for 14 days is as effective as a single dose of fluconazole 150 mg, and either may be used. \textsuperscript{145-149}  

\textbf{Candidiasis in HIV infection}  
Vulvovaginal candidiasis occurs more frequently and with greater persistence in women with HIV infection. Treat with conventional methods. \textsuperscript{150,151}  

\textbf{Non-albicans Candidiasis}  
The majority of non-albicans infection is due to \textit{Candida glabrata} and is susceptible to available azoles. \textit{Candida krusei} is intrinsically resistant to fluconazole.  

The optimal treatment of non-albicans vulvovaginal candidiasis remain unknown. Non-albicans infection may require longer courses (7-14 days).  

\textbf{Treatment}  

\textbf{C} Nystatin pessaries or nonfluconazole azole drug (oral or topical) are the first line treatment for non-albicans infection. \hspace{1cm} \textsuperscript{Grade C, Level 2+}  

\hspace{1cm} \textbf{OR}  

\textbf{C} Consider Amphotericin B vaginal suppositories 50 mg once a day for 14 days. \textsuperscript{152-154} \hspace{1cm} \textsuperscript{Grade C, Level 2+}
3.9.3.3  Trichomoniasis

Trichomoniasis is caused by *Trichomonas vaginalis*, a protozoan that causes vaginitis in women. It infects the vagina, urethra and paraurethral glands. In adults, transmission is almost exclusively sexually transmitted.

10-50% of infected women can be asymptomatic. Predominant symptoms are yellow-green and offensive discharge, vulval itch or dysuria.

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” which occurs in 2% of infected patients.\textsuperscript{155-157}

Laboratory tests include direct microscopy of the wet mount of vaginal secretions mixed with normal saline (sensitivity 70%). A swab taken from the posterior fornix of vagina and cultured on Feinberg-Whittington media is the most sensitive (sensitivity > 90%) and specific for trichomoniasis.\textsuperscript{158-160}

**Management of sex partners**

\textbf{D} 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.\textsuperscript{9}  
\hspace{1cm} \textit{Grade D, Level 4}

\textbf{D} Patients should be advised to avoid sexual intercourse (including oral sex) until they and their partner(s) have completed treatment and follow-up.\textsuperscript{9}  
\hspace{1cm} \textit{Grade D, Level 4}

\textbf{D} Screening for coexisting sexually transmitted infections should be undertaken in both the patients and their partners.\textsuperscript{9}  
\hspace{1cm} \textit{Grade D, Level 4}

\textbf{C} Women should be informed that *T. vaginalis* is a STI and partner management and treatment is recommended for all partners in the last 2 months.\textsuperscript{161}  
\hspace{1cm} \textit{Grade C, Level 2+}
Treatment of trichomoniasis
Both symptomatic and asymptomatic patients should be treated.

Recommended regimen for trichomoniasis: 161

1. **A** Metronidazole 2 g orally x single dose.  
   Grade A, Level 1+
   OR

2. **A** Metronidazole 400 mg orally bid x 7 days.  
   Grade A, Level 1+
   OR

3. **A** Tinidazole 2 g orally single dose.  
   Grade A, Level 1+

Note:
1. **D** Metronidazole gel is not recommended because it is less efficacious (< 50%). 72  
   Grade D, Level 4

   2. The recommended metronidazole regimes have resulted in cure rates of 90-95%.

Trichomoniasis in pregnancy
Trichomonas infection has been associated with premature rupture of the membranes, preterm delivery and low birthweight. However, data do not suggest that metronidazole treatment results in a reduction in perinatal morbidity. 162,163

**D** Although the use of metronidazole in pregnancy has not been shown to be teratogenic or mutagenic in all stages of pregnancy or breastfeeding, caution should be advised for use in the first trimester. Metronidazole pessaries may be used to provide symptomatic relief but have lower cure rates than the oral regimes. 72  
Grade D, Level 4

**D** Treatment of *Trichomonas vaginalis* relieves symptoms of vaginal discharge in pregnant women and might prevent respiratory or genital infection of the newborn and further sexual transmission. Clinicians should counsel patients regarding the potential risks and benefits of treatment. 72  
Grade D, Level 4
It is reasonable to delay therapy in asymptomatic pregnant women until after 37 weeks’ gestation. In addition, these pregnant women should be provided careful counseling regarding condom use and the continued risk of sexual transmission.\textsuperscript{164,165}

**Follow up**

Follow-up is unnecessary for asymptomatic patients. Patients with persistent symptoms should be retreated with metronidazole 400 mg orally bid for 7 days.\textsuperscript{161}

**If treatment failure occurs repeatedly, the patient can be treated with high dose oral metronidazole 2 g daily for 3 days.**\textsuperscript{161}
4 Cost-effectiveness issues

GPP Doctors should consider efficacy, adverse side effects, dosing frequency, and cost to the patient when recommending treatments. For compliance issues, single dose therapies are generally recommended.

B Male patients complaining of urethral discharge and/or dysuria should be examined for discharge. The major pathogens causing urethral discharge are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. In the syndromic management of a patient with urethral discharge, treatment should adequately cover these two organisms and has been found to be cost-effective. Where reliable laboratory facilities are available, a distinction may be made between the two organisms.\(^{166,167}\)

Grade B, Level 2++
5 Clinical quality improvement

The following clinical quality improvement parameters, based on recommendations in these guidelines, are proposed:

1. Every patient presenting with genital discharges and/or ulcers should have a sexual history taken and sexual risk assessment evaluation (pg 27).

2. All patients should be educated and counseled on their condition, and be encouraged to adopt safer sexual behaviours (pg 29).

3. Patients with gonorrhoea should be treated with the recommended antibiotics, and specifically should not be treated with quinolones (pg 49).

4. Patients with gonorrhoea should be concurrently given treatment for *Chlamydia trachomatis* (pg 49).

5. Patients with syphilis should be treated with parenteral penicillin unless there is a contraindication (pg 37).

6. Partner notification should be encouraged in all patients diagnosed with an STI (39).
References


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74


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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to “judge” your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose “True” or “False.”

1. Genital ulceration:
   A) increases the risk for HIV acquisition  
   B) occurs in lichen planus  
   C) is most commonly caused by Treponema pallidum  
   D) may occur as a result of a drug allergy

2. Regarding genital herpes:
   A) it is transmitted only when the patient is symptomatic  
   B) culture specimens should be frozen at 0°C before dispatch to the laboratory  
   C) caesarian section should be routinely offered to all pregnant women with a history of the disease  
   D) acyclovir should not be used in pregnancy

3. In primary syphilis:
   A) the presence of a painful genital ulcer excludes the diagnosis  
   B) a persistently positive TPHA test after treatment indicates failure of therapy  
   C) intramuscular benzathine penicillin 2.4 MU single dose is the treatment of choice  
   D) doxycycline is an alternative to intramuscular penicillin injection in pregnancy.
4. A 25-year-old male complains of clear urethral discharge 3 days after unprotected sexual intercourse with a sex worker. Possible causes include:
   A) Chlamydia trachomatis □ □
   B) Herpes simplex virus □ □
   C) Trichomonas vaginalis □ □
   D) Ureaplasma urealyticum □ □

5. Chlamydia trachomatis
   A) causes symptomatic vaginal discharge in 80% of infected women □ □
   B) may lead to an acute epididymo-orchitis □ □
   C) is diagnosed by presence of gram-negative diplococci in a urethral smear □ □
   D) sex partners of symptomatic male patients within the last 60 days should be screened and treated for infection □ □

6. A 20-year-old female presents with a 1-week history of an itchy vaginal discharge. She has had 2 different sexual partners in the past 6 months and requests STI screening. The following investigations should be done:
   A) culture for Neisseria gonorrhoeae □ □
   B) blood test for Chlamydia trachomatis IgG □ □
   C) Neisseria gonorrhoeae Complement fixation test □ □
   D) Culture for Trichomonas vaginalis □ □

7. A 30-year-old male presents with a 3-day history of a profuse, purulent urethral discharge after unprotected sexual intercourse with a casual female partner. He declines any investigations. You should treat him with:
   A) ciprofloxacin 500 mg bid for 3 days □ □
   B) intramuscular ceftriaxone 250 mg single dose □ □
   C) intramuscular benzathine penicillin 2.4MU single dose □ □
   D) azithromycin 1g orally single dose □ □
8. Regarding bacterial vaginosis:
   A) it occurs only in sexually active women
   B) it is associated with preterm delivery
   C) it is recommended that all symptomatic women be treated
   D) male partners of patients should be routinely screened and treated
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## Workgroup members

The members of the workgroup, who were appointed in their personal professional capacity, are:

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<thead>
<tr>
<th>Position</th>
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<tr>
<td>Chairman</td>
<td>Dr Tan Hiok Hee</td>
<td>Head, Dept of STI Control Clinic / Senior Consultant Dermatologist National Skin Centre</td>
</tr>
<tr>
<td>Members</td>
<td>Dr Ngan Cheng Lai, Cecilia</td>
<td>Senior Consultant Microbiologist Immunology &amp; Serology Section Dept of Pathology Singapore General Hospital</td>
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<tr>
<td></td>
<td>Dr Lim Fong Seng</td>
<td>Family Physician NHG Polyclinics</td>
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<td>Dr Cheong Wai Kwong</td>
<td>Consultant Dermatologist Specialist Skin Clinic (S) Pte Ltd</td>
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<td>Dr Asok Kurup</td>
<td>Senior Consultant Department of Infectious Diseases Singapore General Hospital</td>
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<tr>
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<td>Dr Toh Khai Lee</td>
<td>Senior Consultant Urologist &amp; Deputy Head Dept of Urology Tan Tock Seng Hospital</td>
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**Prof Chan Kum Wah, Roy**
Senior Consultant and Director, National Skin Centre / Adj Professor, Dept of Epidemiology and Public Health, Yong Loo Lin School of Medicine

**Dr Priya Sen**
Consultant, National Skin Centre / Deputy Head, Dept of STI Control Clinic

**Dr Chio Tze-Wei, Martin**
Consultant, National Skin Centre

**Dr Tan Thiam Chye**
Assistant Professor, Duke-NUS Graduate Medical School / Associate Consultant, Dept of Obstetrics and Gynaecology KK Women's and Children’s Hospital

**A/Prof Goh Lee Gan**
Associate Professor, Dept of COFM Yong Loo Lin School of Medicine / President, College of Family Physicians, Singapore
Subsidiary editors:

Dr Pwee Keng Ho  
Deputy Director (Health Technology Assessment)  
Health Services Research & Evaluation Division  
Ministry of Health

Ms Celeste Ong  
Assistant Manager (Health Technology Assessment)  
Health Services Research & Evaluation Division  
Ministry of Health

Acknowledgement:

Dr Edwin Chan Shih-Yen  
Head of Evidence-Based Medicine  
and  
Director of the Singapore Branch, Australasian Cochrane Centre  
Clinical Trials & Epidemiology Research Unit

Dr Pradeep Paul  
Clinical Trials & Epidemiology Research Unit  
Singapore Branch of the Australasian Cochrane Centre
Management of Genital Ulcers and Discharges

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