SEXUALLY TRANSMITTED INFECTIONS

Management Guidelines
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The DSC STI Management Guidelines are designed to serve as a concise and comprehensive reference manual for doctors, paramedical personnel, medical students and counsellors.

This 6th edition contains updates in all chapters.

Once again, there are key references for each chapter, using the latest available evidence.

In particular, this edition includes updates on issues of antimicrobial resistance in gonorrhoea. There is worldwide concern about decreasing sensitivity to parenteral cephalosporins and in 2012, the British and European authorities have already recommended using a higher dose of intramuscular ceftriaxone, administered together with a night dose of azithromycin, regardless of presence of Chlamydia co-infection. It is hoped that this would delay the development of resistance in the gonococcus. Locally we continue to monitor the trends of antimicrobial resistance in *Neisseria gonorrhoeae*.

There is also a new chapter on vaccinations and the prevention of STIs. Most notably, since the last edition, vaccines that are effective against HPV infection have become widely available. The chapter on HIV infection has been updated to provide the latest information on HIV management and therapeutic regimens. The chapter on non-occupational post exposure prophylaxis against HIV infection has been expanded. We have also added a new table to the annex summarizing the common laboratory tests that are used in screening for STIs.

We hope you will find this book useful and welcome feedback and suggestions on ways to improve it. We would like to thank our co-authors for their valuable contributions, and the staff at DSC clinic for their continued support and excellent work.

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PRINCIPLES OF STI MANAGEMENT

1. TAKING A HISTORY
It is easier to start history taking with questions relating to the medical complaint. For male patients, presenting symptoms are urethral discharge, dysuria, ano-genital sores, rashes or growths. Female symptoms include vaginal discharge, dysuria, anogenital ulcers, rashes or growths. Throat and rectal infections are usually asymptomatic.

The sexual history of a patient with or suspected to have a STI/HIV should include information on:

- Recent sexual exposures – usually the last and second last partner, spouse, casual or regular partner, or sex worker, gender, whether local or overseas
- Type of sexual exposure - vaginal, anal or oral
- Use of condoms – for vaginal, anal, oral sex
- Use of other contraceptives
- Previous STI

It should be noted that a reliable history is only possible in a setting of privacy, confidentiality and if the healthcare provider has a non-judgmental attitude.

Other relevant medical information should include:

- Prior treatment, including traditional medications
- Self medication
- Drug allergies
- Menstrual, gynaecologic and obstetric history in females

After an accurate history is obtained you will be able to ascertain the patient's risk of contracting a STI/HIV and to order the relevant laboratory investigations.

2. PHYSICAL EXAMINATION
The anogenital and inguinal regions should be exposed and carefully examined in good lighting. Males can be examined lying on the examination couch (preferred) or standing up. Females should be examined in the lithotomy position. Proctoscopic examination should be performed on males and females who practice anal intercourse. If indicated, a general examination should be performed when there is the suspicion of syphilis, Reiter's disease, disseminated gonococcal infection and HIV infection.

3. LABORATORY INVESTIGATIONS
The correct use of laboratory tests in STI includes:

- Obtaining adequate specimens for direct smears, cultures and other detection methods e.g. molecular detection.
- Ordering the appropriate blood tests.
- Proper storage and transport of the specimens.
- Accurate interpretation of the test results.
Tests of little or doubtful value should not be performed; these include serology tests for chlamydia and gonorrhoea, and non type specific serological tests for herpes simplex virus. There are increasing examples of point-of-care rapid tests for HIV, syphilis, chlamydia and gonorrhoea. While convenient they need to be used only when their performance has been adequately evaluated. Rapid tests for HIV and syphilis are generally accurate; those for chlamydia and gonorrhoea are not as accurate.

4. MAKING A DIAGNOSIS
Accurate diagnosis is based on:
- A good history
- A thorough physical examination and
- Performing appropriate laboratory tests

History and physical examination are often the basis of reaching a diagnosis in primary healthcare settings like general practitioners’ clinics. Making an aetiological diagnosis is usually possible in referral centres and hospitals with adequate laboratory backup. It must be remembered that clinical syndromes (e.g. urethritis and genital ulcer disease) may be polymicrobial in aetiology. All patients with a STI should be screened for other infections; in particular they should be offered tests for syphilis and HIV infection.

5. TREATMENT
Treatment regimens must be efficacious, safe, easy to comply with, affordable, preferably given in a single dose, easily administered; and it should be provided as far as possible on the patient’s first visit.

Treatment is thus often based on clinical diagnosis only e.g. urethral discharge, vaginal discharge, and genital ulcers. It is often not possible to have an aetiological diagnosis at the first visit. In these situations it is important to ensure that the medications used are effective against all the major pathogens that may be causes of the syndrome. Wherever possible an aetiological diagnosis should be confirmed by laboratory tests. Approaches to making a clinical diagnosis are provided in annexes III, IV and V.

6. COUNSELLING
a) Prevention of disease transmission
All patients should be informed of the diagnosis, nature of treatment and expected outcome, the need to comply with and complete the treatment, reporting of side effects, and avoidance of sex until cured. In some cases follow-up for tests-of-cure may be necessary.

b) Prevention of further infection
Counselling skills which include respect for privacy, compassion and a non-judgemental attitude are essential for effective delivery of prevention messages.

All patients should be counselled on the methods of reducing their risk of acquiring a STI/ HIV in future, including abstinence, reducing the number of sexual partners (especially concurrency) and avoiding sexual contact with persons who have multiple sexual partners.
They should be instructed on the correct and consistent use of condoms for vaginal, anal and oral sex. The following recommendations ensure the proper use of male condoms:

- Use a new condom with each sex act (e.g., oral, vaginal, and anal).
- Carefully handle the condom to avoid damaging it with fingernails, teeth, or other sharp objects.
- Put the condom on after the penis is erect and before any genital, oral, or anal contact with the partner.
- Use only water-based or silicone based lubricants with latex condoms. Oil-based lubricants (e.g. vaseline, massage oils, body lotions and creams) can weaken latex.
- Ensure adequate lubrication during vaginal and anal sex, which might require the use of exogenous water-based lubricants.
- To prevent the condom from slipping off, hold the condom firmly against the base of the penis during withdrawal, and withdraw while the penis is still erect.

They should be advised to seek medical attention if they feel that they have been exposed to an infection e.g. if the condom broke or slipped off.

They should not self-medicate or seek treatment from unqualified persons. Repeaters (patients with multiple episodes of STI) should receive intensive counselling on strategies to reduce risk.

7. NOTIFICATION OF INFECTIONS

Certain STI are notifiable in Singapore. Reporting of STI and HIV/AIDS allows for accurate monitoring of disease trends; and is needed for monitoring and evaluating the National STI and AIDS control programmes.

Except for HIV/AIDS, there is no need to include the name, identity card number or address of the patient when notifying a STI; only demographic data (age, gender, ethnicity, nationality) for epidemiologic analysis is required. Notification of STIs is not meant for case detection or contact tracing. As such patient privacy and confidentiality is maintained.

Gonorrhoea, Chlamydia infection, syphilis (infectious, non-infectious and congenital), NGU, anogenital herpes (first episode and recurrent) should be notified to the DSC Clinic by fax (6299 4335) using form MD 131 or electronically https://www.cdlens.moh.gov.sg/cdlens/ within 72 hours of diagnosis.

HIV infection and AIDS should be notified to NPHU by fax (6254 1616) using form MD 131 or electronically - https://www.cdlens.moh.gov.sg/cdlens/ within 72 hours of diagnosis.

Viral Hepatitis (A, B, C) infections should be notified to CDD, MOH by fax (6734 8287 or 67319368) using form MD131 or electronically - https://www.cdlens.moh.gov.sg/cdlens/ within 72 hours of diagnosis.
8. PARTNER NOTIFICATION / CONTACT TRACING
The public health objectives of partner notification are – to interrupt the transmission of the STI, identify populations at risk, reduce the incidence of infection; individual’s objectives are – to identify people who may benefit from treatment and counselling, provide individual counselling, and to prevent complications.

Partner notification can be undertaken either by the health care worker (provider referral) using telephone, letter or home visit; by the patient (patient referral); or a combination of the two (conditional referral). Maintaining the confidentiality of the index patient is paramount to successful contact tracing.

Patient delivered partner therapy (PDPT) refers to the practice of providing antibiotic treatment to the index patient to give to their partners is becoming popular in some places, and may become a strategy to control STIs in future.

9. CHEMOPROPHYLAXIS
Blind treatment of a STI in asymptomatic persons must be avoided. There is no universally effective antimicrobial. Furthermore chemoprophylaxis may suppress but not cure a STI. This may lead to complications, promote development of resistant strains of microbes, give a false sense of security to the patient and lead to onward transmission of infection.

10. EPIDEMIOLOGIC TREATMENT
Treatment of sexual contacts of patients (with a confirmed STI) without first obtaining laboratory confirmation may be indicated in situations where the risks of complications are high (e.g. in pregnancy), or when the follow-up of the contact may not be guaranteed or possible. Recommended treatment regimes must be used in these situations.
BACTERIAL VAGINOSIS

DEFINITION
Bacterial vaginosis (BV) is a condition resulting from replacement of the normal $\text{H}_2\text{O}_2$-producing Lactobacillus sp. in the vagina with high concentrations of anaerobic bacteria (e.g. Prevotella species, Mobiluncus species, Gardnerella vaginalis, Ureaplasma and Mycoplasma hominis) leading to an increase in pH from less than 4.5 to as high as 7.0. It can arise and remit spontaneously in sexually active and non-sexually active women. The exact role of sexual transmission in the pathogenesis of BV is unclear.

CLINICAL FEATURES
BV may be asymptomatic or present with a fishy-smelling, thin homogenous vaginal discharge. Risk factors include:
- Vaginal douching
- Receptive cunnilingus
- Recent change of sex partner
- Smoking
- Presence of STI

LABORATORY TESTS
3 out of 4 of the following criteria should be present (Amsel criteria)
- Thin homogenous vaginal discharge that coats the vaginal wall and vestibule
- pH of vaginal fluid > 4.5
- Positive amine (fish-like) odour test (“whiff test”) before or after addition of 10% KOH
- Presence of clue cells on microscopy of vaginal discharge

Note:
- Menses, semen, cervical secretions or douching may affect the pH
- A weakly positive “whiff test” may be produced by menstrual blood or semen
- Exclude trichomoniasis
Culture of G. vaginalis is not recommended because it can be cultured from the vagina of > 50% of uninfected women.

An alternative test involves use of a gram stained vaginal smear evaluated with the Hay/Ison criteria or the Nugent criteria. Commericially available tests which perform adequately when assessed against Amsel and Gram stain criteria include:
- OSOM BVBlue which measures sialidase levels
- A prolineaminopeptidase test card (Pip activity TestCard)
- A DNA probe-based test that detects high concentrations of G. vaginalis (Affirm VP III)
COMPLICATIONS
BV has been associated with adverse pregnancy outcomes (e.g. premature rupture of membranes, chorioamnionitis, preterm labour and preterm birth). BV is also associated with endometritis, PID and vaginal cuff cellulitis after invasive procedures (e.g. uterine curettage, hysterectomy, endometrial biopsy).
There is increasing evidence that the presence of BV (or absence of vaginal lactobacilli) has been shown to increase a woman’s risk of acquiring HIV, *N. gonorrhoeae. C. trachomatis* and HSV-2 via heterosexual intercourse.

TREATMENT
Indications for treatment:
1) All symptomatic women, pregnant or non pregnant [A]
2) Asymptomatic pregnant women with high risk for preterm delivery [A]
3) Asymptomatic women before surgical abortion procedures [A]
4) Women who do not volunteer symptoms may elect to take treatment if offered. They may report a beneficial change in their discharge following treatment

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

Recommended regimens
Metronidazole 400-500mg orally bid x 5-7 days [1a, A]
or
Metronidazole 2g single dose [1b, A]
or
Clindamycin cream 2% one full applicator (5g) intravaginally at bedtime x 7 days [1b, A]
or
Metronidazole gel 0.75% one full applicator (5g) intravaginally once a day x 5 days [1b, A]

Alternative regimens
Clindamycin 300 mg orally bid x 7 days [1b, A]
or
Tinidazole 2g orally single dose [1b, A]

Note:
- Metronidazole 2g single dose therapy may be slightly less effective at 4 week follow up [1b].
- Patients should avoid consuming alcohol during treatment with metronidazole and for 24 hours thereafter.
- Clindamycin cream is oil-based and might weaken latex condoms and diaphragms.
- Non-antibiotic based treatment with probiotic lactobacilli or lactic acid preparations have not yielded consistently reproducible evidence of efficacy as treatments for BV and no recommendation on their use can be made at present.
**BV in Pregnancy**

*Recommended regimens*

Metronidazole 400-500mg orally bid x 7 days [1b, A]

or

Metronidazole 200mg orally tid x 7 days [1b, A]

or

Clindamycin 300 mg bid orally x 7 days [1b, A]

**Note:**
- Intravaginal clindamycin cream administered at 16-32 weeks gestation has been associated with an increase in adverse events (e.g. low birthweight and neonatal infections). Therefore intravaginal clindamycin cream should only be used during the first half of pregnancy.
- Data is conflicting regarding the usefulness of screening and treating low risk asymptomatic pregnant women. Metronidazole use in the first trimester of pregnancy has not been shown to be teratogenic or mutagenic [Ia]
- Metronidazole enters breast milk and may affect its taste. The manufacturers recommend avoiding high doses if breastfeeding. Small amounts of clindamycin enter breast milk, therefore use an intravaginal treatment for lactating women [C]
- Screening for and treating BV in patients undergoing a termination of pregnancy reduces the incidence of subsequent endometritis and PID [Ia]

**BV in HIV infection**

BV tends to recur with a higher frequency in HIV-positive women. These patients should be treated with the same treatment regimens as for HIV-negative women.

**Recurrent BV**

There are few published studies evaluating the optimal approach to women with frequent recurrences of BV. Two studies reported a high incidence of BV in female partners of lesbians with BV [II].

Possible approaches are:
- Suppressive therapy: Metronidazole gel 0.75% twice weekly for 4-6 months [Ia]
- Metronidazole 400mg orally bid for 3 days at the start and end of menstruation (combined with fluconazole 150mg as a single dose if there is a history of candidiasis also) [Ia]
- Maintenance therapy involving acetic acid vaginal gel use at the time of menstruation and following unprotected sexual intercourse [III].
- Small studies using live yoghurt or Lactobacillus acidophilus have not demonstrated benefit [IIa]
FOLLOW-UP
Follow-up is not necessary if symptoms resolve.
For high-risk pregnant women, a one month follow-up visit is recommended to evaluate if
treatment is successful. Alternative regimens can be given for recurrent disease.
Long term maintenance regimens are not recommended.

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

References:
Female Sex Workers in Chiang Mai, Thailand. AIDS, 9:1093.

Vaginal Smears for Use in Genitourinary Medicine Clinics. Sex Transm Infect, 78(6),
413-415.

Treatment for Bacterial Vaginosis: Effects on Preterm Delivery and Low Birth Weight.

Vaginosis is Improved by a Standardized Method of Gram Stain Preparation. J Clin
Microbiol, 29(2), 297-301.


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CANDIDIASIS

DEFINITION
Genital candidiasis is the infection of the vulva, vagina, prepuce and glans penis by *Candida albicans* (80-92%) or occasionally by other *Candida species* (*glabrata, tropicalis, krusei, parapsilosis*), *Torulopsis species*, or other yeasts. It is not generally considered a sexually transmitted infection.

CLINICAL FEATURES
Female patients complain of vulval pruritus and discharge. Non-specific symptoms include soreness, burning, dyspareunia and external dysuria. Male patients may complain of a penile rash. Examination reveals vulval erythema, fissuring, satellite lesions, and thick curdy discharge in females; or white or red patches on the glans penis in males.

Predisposing factors include diabetes mellitus, use of long term oral antibiotics, steroid and oral contraceptives.

LABORATORY TESTS
- Gram-stain or wet mount (saline or 10% KOH) of swabs from the vulva/vaginal wall, or penis/prepuce will reveal budding yeast cells and pseudohyphae (sensitivity 60%)
- Vaginal pH 4 – 4.5
- Culture on Sabouraud media (isolation in the absence of symptoms and negative direct smear is not an indication for treatment)
- Serum antibodies should not be used for diagnosis

DIAGNOSIS
Symptoms and signs of vulvo-vaginitis or balano-posthitis
PLUS
Demonstration of yeasts/pseudohyphae on wet mount or Gram-stain or positive culture

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

*General advice*
Vulval emollients and or topical antifungal/steroid creams may provide symptomatic relief for secondary associated vulval dermatitis. Avoid local irritants (e.g. perfumed products) and tight fitting clothing (IV, C).
Recommended Regimens

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

Alternative Regimens

1. Clotrimazole pessary 100mg or cream (1%) 5g intravaginally daily x 7 days [II, A]
   or
2. Miconazole nitrate vaginal pessary 100mg or cream (2%) 5g intravaginally daily x 7 days [II, A]
   or
3. Tioconazole ointment (6.5%) intravaginally 4.6g in a single application [II, A]
   or
4. Miconazole 1,200mg vaginal pessary x 1 day [II, A]

Note: The topically applied azole drugs are more effective than nystatin.

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

Candidiasis in HIV infection
Candidiasis tends to occur with a higher frequency and persistence in HIV-positive women and colonization rates correlate with the severity of immunosuppression. These patients should be treated with the same treatment regimens as for HIV-negative women.

Recurrent vulvovaginal candidiasis
This is defined as 4 or more episodes of symptomatic vulvovaginal candidiasis annually. Patients must be evaluated for any predisposing factors e.g. uncontrolled diabetes mellitus, immunosuppression, corticosteroid and long-term antibiotic use. Repeated courses of treatment may be required. Infection by less susceptible yeasts e.g. C glabrata may require a longer duration of therapy.
Systemic treatment may be indicated for resistant/recurrent candidiasis:
**Induction Regimens**
1. Itraconazole 100mg orally bid x 1-3 days [II, A]
   or
2. Fluconazole 150mg orally single dose [II, A]

**Maintenance Regimens**
1. Fluconazole 100-200mg orally once a week x 6 months [II, B]
   or
2. Clotrimazole pessary 500mg once a week x 6 months [II, B]
   or
3. Itraconazole 400mg once a month x 6 months [II, B]

Caution: Anecdotal reports of oral contraceptive failure with prolonged oral azole therapy. The creams and suppositories are oil-based and may weaken latex condoms and diaphragms. Risk of idiosyncratic drug-induced hepatitis with itraconazole.

**MANAGEMENT OF SEXUAL CONTACTS**
There is no evidence to support the screening or treatment of asymptomatic male sexual partners. For symptomatic balano-posthitis, topical imidazole creams bid x 7 days will usually eradicate the infection.

**References:**
CHANCROID

DEFINITION
Chancroid is a sexually transmitted infection caused by the bacterium *Haemophilus ducreyi*. This infection is uncommon in Singapore, but still common in parts of India and South East Asia. Patients infected may have a co-infection with syphilis or herpes.

CLINICAL FEATURES
Infection with *H. ducreyi* may present with an erythematous papule that rapidly progresses into a pustule, which erodes into an ulcer. Infected persons may have more than one ulcer, and the lesions are almost always confined to the genital area and its draining lymph nodes.

A typical chancroid ulcer is about 1 to 2 cm in diameter, but the size is variable, especially in HIV-infected patients. The ulcer is painful and has an erythematous base; the borders are clearly demarcated and sometimes undermined. The base of the ulcer is usually covered with a grey or yellow purulent exudate and bleeds when scraped.

The most common sites for chancroid are the prepuce, corona, or glans penis in men, and the labia, vaginal introitus, and perianal areas in women. Some cases of chancroid may go undiagnosed, especially in asymptomatic women with vaginal or cervical lesions.

The involved nodes may undergo liquefaction and present as fluctuant buboes. Most buboes arise one to two weeks after the appearance of the primary ulcer and are often quite painful. Untreated buboes may spontaneously rupture and discharge frank pus. Scarring may result despite successful therapy.

LABORATORY TESTS
- Direct microscopy of a smear from ulcer showing Gram-negative coccobacilli (arranged in “shoals of fish” pattern) (poor sensitivity)
- Culture for *H. ducreyi* of a smear from ulcer or aspirate from buboes (sensitivity <80%)
- Diagnosis is often based on a typical clinical presentation and after exclusion of syphilis and HSV infection
- Multiplex PCR detection (>95%)

TREATMENT

LOCAL TREATMENT
- Saline wash
- Aspiration of fluctuant buboes from adjacent normal skin
SYSTEMIC TREATMENT

Recommended regimens
1. Ceftriaxone 250 mg i/m single dose [lb, B]
   or
2. Azithromycin 1 g orally single dose [lb, A]

Alternative regimens
1. Ciprofloxacin 500 mg orally bid x 3 days [lb, B]
   or
2. Erythromycin base or stearate 500 mg orally qid x 7 days [lb, B]
   or
3. Co-trimoxazole (trimethoprim/sulfamethoxazole) 160/800 mg (2 tabs) orally bid x 7 days

Not recommended
Tetracyclines and Ampicillin

Other Management Considerations
Patients who are uncircumcised and patients with HIV infection do not respond as well to treatment as those who are circumcised or HIV-negative. Patients should be tested for HIV infection at the time chancroid is diagnosed. Patients should be retested for syphilis and HIV 3 months after the diagnosis of chancroid if the initial test results were negative.

FOLLOW-UP
Chancroid ulcers usually begin to heal within 3 days of treatment and should heal completely by 7-14 days. Inguinal lymphadenopathy will take a longer time to resolve. If there is no improvement by 7 days, the patient should be re-evaluated for:

- Compliance with medication
- Co-infection with another STI
- Co-infection with HIV
- Non-STI ulcer disease
- Resistant organism

The response of chancroid-associated lymphadenitis may occur more slowly. In one study, for example, 8 of 35 patients with inguinal lymphadenitis developed fluctuance that required needle aspiration despite successful treatment of the genital ulcer with erythromycin. In advanced cases, scarring may result despite eradication of infection.

MANAGEMENT OF SEXUAL CONTACTS
Sex partners should be screened and treated when indicated if they had sexual contact with the patient 10 days before patient’s onset of symptoms.
Special considerations

Pregnancy
Ciprofloxacin is contraindicated during pregnancy and lactation. No adverse effects of chancroid on pregnancy outcome have been reported so far.

HIV Infection
HIV-infected patients who have chancroid should be monitored closely because, as a group, these patients are more likely to experience treatment failure and to have ulcers that heal more slowly. HIV-infected patients may require longer courses of therapy than those recommended for HIV-negative patients, and treatment failures can occur with any regimen.

References:
CHLAMYDIA TRACHOMATIS INFECTIONS

DEFINITION
*Chlamydia trachomatis* is a bacteria which can cause a variety of genito-urinary infections, depending on the serotypes. Chlamydial genital infections occur frequently among sexually active adolescents and young adults.

CLINICAL FEATURES
Serotypes D to K cause non-gonococcal urethritis, mucopurulent cervicitis, proctitis, epididymitis, pneumonia and conjunctivitis in the newborn. Lymphogranuloma venereum (LGV) is caused by serotypes L1-L3 (see section on LGV). Many adult genital infections and most rectal and pharyngeal infections caused by chlamydia are *asymptomatic*.

Several important complications may result from chlamydial infections, including pelvic inflammatory disease, ectopic pregnancy and tubal infertility in women, epididymo-orchitis in males, and conjunctivitis and reactive arthritis in both sexes. Transmission to neonates during delivery may lead to neonatal conjunctivitis and pneumonia.

LABORATORY TESTS
- *Chlamydia trachomatis* is an intracellular organism, specimens must include epithelial cells and not exudates alone.
- Nucleic acid-based amplification tests (NAAT): most sensitive 90–95%, highly specific, new gold standard; polymerase chain reaction (PCR) can be used to test a range of specimens (urine, urethral, cervical, rectal, pharyngeal).
- Females - cervical or vulvo-vaginal swabs are specimens of choice, followed by first void urine (FVU); males - FVU is as sensitive as urethral swabs; care with inhibitors with urine specimens; storing urine overnight at 40°C or freeze-thawing may enhance sensitivity of urine specimens.
- NAATs may be used for conjunctival, pharyngeal and rectal specimens, although currently *unlicensed* for these sites; rectal swabs should be obtained via proctoscopy.
- Medico legal cases – samples for NAAT should be taken from all the sites where penetration has occurred, a reactive NAAT result must be confirmed using a different NAAT.
- Antigen detection methods – Direct Florescent Antigen (DFA) sensitivity 50–90%; enzyme immunoassay (EIA) poor sensitivity 50–70%, specificity >95%, inexpensive, can be used for large numbers of specimens. FVU or urethral swabs can be used for males, endocervical swabs are preferred for women.
- Cell culture for chlamydia in McCoy cell monolayers, used to be the gold-standard, it is fairly sensitive (70–80%) and 100% specific, requires stringent cold-chain, costly, very expensive, not readily available anymore.
• Giemsa-stained direct smear for the inclusion bodies within infected cells is useful only for ocular infections.

• Serological tests are not useful to diagnose acute chlamydial infections because of cross-reactivity between chlamydial species, high prevalence of chlamydia antibodies in high risk populations, and the unpredictability of serological response and changes in titres of IgM and IgG antibodies in acute uncomplicated infections.

TREATMENT

Recommended regimens
Uncomplicated urethral, endocervical, pharyngeal or rectal infections in adults

1. Doxycycline 100 mg orally bid x 7 days [1a, A]
or
2. Azithromycin 1 g orally single dose [1a, A]

Alternative regimens (A)
1. Erythromycin 500 mg orally qid [1b, A]
or
2. Ofloxacin 200 mg orally bid or 400 mg orally od x 7 days [1b, A]
or
3. Levofloxacin 500 mg orally od x 7 days [1b, A]
or
4. Tetracycline HCl 500 mg orally qid x 7 days [1b, A]

Not recommended
Ampicillin and Trimethoprim-Sulphamethoxazole

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

1. Erythromycin 500 mg orally qid x 7 days [1a, A]
or
2. Azithromycin 1 g orally single dose [1a, A]
or
3. Amoxicillin 500 mg orally tid x 7 days [1a, A]

Contra-Indicated
Tetracyclines and Ofloxacin are contraindicated during pregnancy.
Neonatal *Chlamydia trachomatis* conjunctivitis

The other differential diagnoses of conjunctivitis in infants are - gonococcal ophthalmia neonatorum, pyogenic and enteric Gram-negative conjunctivitis.

Diagnosis is made by culture or non-culture tests on specimens taken from the everted eyelid. Systemic treatment is essential to prevent complications such as chlamydia pneumonitis. Topical therapy alone is *not* adequate and unnecessary when systemic treatment is used. All neonates should be referred to an ophthalmologist.

Syrup Erythromycin - 50 mg/kg/day orally in 4 divided doses x 14 days

*An association between oral erythromycin and infantile hypertrophic pyloric stenosis (IHIS) has been reported in infants aged <6 weeks who were treated with this drug. Infants treated with erythromycin should be followed for signs and symptoms of IHPS.*

Mothers of infected infants and their sex partners should be screened and treated on epidemiological grounds. Follow up to determine resolution is recommended. The efficacy of erythromycin treatment is approximately 80%; a second course of therapy may be required.

*Chlamydia trachomatis* pneumonia in infants

Characteristic signs include a repetitive staccato cough and hyperinflation and bilateral diffuse infiltrates on CXR. Wheezing is rare, and infants are often afebrile. Diagnosis is made by culture or non-culture tests on specimens taken from the nasopharynx or tracheal aspirates.

Syrup Erythromycin - 50 mg/kg/day orally in 4 divided doses x 14 days.

Mothers of infected infants and their sex partners should be screened and treated on epidemiological grounds. Follow up to determine resolution is recommended. The efficacy of erythromycin treatment is approximately 80%; a second course of therapy may be required.

*Chlamydia trachomatis* pelvic inflammatory disease and epididymo-orchitis

1. Doxycycline 100 mg orally bid x 14 days [III, B]
   or
2. Ofloxacin 400 mg orally bid x 14 days [III, B]

**FOLLOW-UP**

A test-of-cure is not necessary when treatment with a tetracycline or azithromycin has been completed, unless symptoms persist or reinfection is suspected.

Test-of-cure is however recommended after 4 weeks for infections in infants, children and pregnant women, or when erythromycin was used.

Non-culture tests (eg NAATs) done within 4 weeks of completing treatment may yield false positive tests due to persistence of chlamydial antigens.
Owing to the increased risk of complications following repeat infection in females, rescreening for reinfection may be indicated especially for high-risk females after 3 to 4 months.

Serologic tests for Syphilis and HIV should be performed; if negative they should be repeated at 3 months for Syphilis and HIV, after the last risky exposure.

**MANAGEMENT OF SEXUAL CONTACTS**

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

**References:**


GONORRHOEA

DEFINITION
Gonorrhoea is caused by the Gram-negative bacterium *Neisseria gonorrhoeae*. The common sites of infection include the urethra, the endocervix, the rectum, the pharynx and the conjunctiva.

CLINICAL FEATURES
Gonorrhoea 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. Contiguous spread of the infection can lead to epididymo-orchitis, prostatitis, endometritis and salpingo-oophritis. Haematogenous spread results in disseminated gonococcal infection (DGI).

LABORATORY TESTS
- Presumptive diagnosis of gonorrhoea is made on finding Gram-negative intracellular diplococci in a smear of the discharge. In men, microscopy of urethral smears is more sensitive in symptomatic (90–95%) than in asymptomatic (50–75%) patients. In women sensitivity of microscopy of Gram-stained endocervical smears is around 50%. Microscopy is not appropriate for pharyngeal and rectal specimens.
- Confirmatory diagnosis is made by identification of the organism on selective culture media.
- NAATs (PCR) are more sensitive than culture and can be used as diagnostic/screening tests on non-invasively collected specimens (urine and self-taken vaginal swabs). The sensitivity of NAATs is >90% for genital sites, whilst the sensitivity of culture may be < than 75% for endocervical swabs.
- There are currently no NAATs licensed for use with rectal or pharyngeal samples, although studies suggest that the sensitivity of NAATs at non-genital sites exceeds 90% whereas the sensitivity of culture can be <60% for rectal swabs and <50% for pharyngeal swabs.
- The DSC clinic currently uses NAATs to detect rectal, urethral and cervical GC, and cultures for pharyngeal GC.
- Some degree of caution is required in interpretation of positive results as the specificity of NAATs is not 100%; especially if the risk profile of the patient is at odds with the result. Confirmation of a NAAT positive result by culture can be considered in cases where there is some doubt. However, generally NAATs are considered reliable for detection.
- As nonculture tests cannot provide antimicrobial susceptibility results, in cases of persistent gonococcal infection after treatment, clinicians should perform both culture and antimicrobial susceptibility testing.
- Gonococcal complement fixation test (GC-CFT) should not be used for diagnosing gonorrhoea.
Specimen collection:

**Males:**
Routinely from the urethra; rectal and/or oropharyngeal tests when indicated by sexual activity. FVU provides an alternative urethral specimen for testing with a NAAT.

**Females:**
Routinely from endocervix if speculum examination performed; and rectal and oropharyngeal tests when indicated by the sexual history. Urine or a self-taken vaginal swab are suitable alternative specimens as screening tests using a NAAT.

**TREATMENT**

*Recommended regimens*
Uncomplicated infection in adults - urethral, endocervical and rectal infection

1. Ceftriaxone 500 mg i/m single dose + azithromycin 1-2g stat or doxycycline 100 bid x 1-2 weeks [IV, C]

*Alternative Regimens (for those with allergy)*
1. Cefotaxime 1g i/m single dose + azithromycin 1-2g stat or doxycycline 100 bid x 1-2 weeks [1b]
   or
2. Spectinomycin 2g i/m single dose + azithromycin 1-2g stat or doxycycline 100 bid x 1-2 weeks [1b, A]
   or
3. Azithromycin 2g stat [II, C] (not as monotherapy)
   or
4. Aztreonam 1g i/m single-dose dose with azithromycin 1-2g stat or doxycycline 100 bid x 1-2 weeks [1b]

(Aztreonam has been used in some patients at DSC when other alternatives were unavailable)

It is important to emphasize that treatment of GC should be accompanied with anti-chlamydia therapy. This not only treats concurrent infection, but there is evidence to suggest that concurrent administration of azithromycin would slow down the possibility of the development of cephalosporin resistant strains of GC.

**Note:** The fluoroquinolones (e.g. ciprofloxacin, ofloxacin, norfloxacin) are contraindicated as > 70% of isolates in Singapore and the region are resistant.
Gonococcal infection in pregnancy

- Cephalosporins [IV, C] in the recommended dosages are safe and effective in pregnancy.
- Spectinomycin [Ib, A] can be administered to women who are unable to tolerate cephalosporins.
- Simultaneous treatment for chlamydial infection with azithromycin 1g stat or erythromycin 500 mg orally qid x 7 – 14 days is advocated.

Pharyngeal infection
1. Ceftriaxone 500 mg i/m single dose with azithromycin 1g stat or doxycycline 100 bid x 1 week [IV, C].

Disseminated gonococcal infection or DGI
Hospitalisation under specialist care is recommended.

1. Ceftriaxone 1g i/m or i/v daily
   or
2. Cefotaxime 1g i/v 8 hourly
   or
3. Spectinomycin 2 g i/m 12 hourly

Therapy should continue for 24-48 hours after improvement begins, and can be converted to an oral cephalosporin therapy for a total of 7 days. Anti-chlamydia therapy should be given at the same time.

Gonococcal acute epididymitis and epididymo-orchitis
Ceftriaxone 500 mg i/m daily x 1 to 3 days with doxycycline 100mg bid x 2 weeks [III, B].

Adult gonococcal ophthalmia
Ceftriaxone 1g i/m single dose with with azithromycin 1g stat or doxycycline 100 bid x 1 week. With lavage of the infected eye with normal saline [IV, C].

Topical antibiotics alone do not eradicate the infection and rigid adherence to topical therapy is not essential. All patients should be referred for ophthalmologic assessment.

Neonatal gonococcal ophthalmia
1. Ceftriaxone 25-50 mg/kg i/m single dose not to exceed 125 mg
   or
2. Cefotaxime 100 mg/kg i/m single dose. With lavage of the infected eye with normal saline.

Topical antibiotics alone do not eradicate the infection. All patients should be referred for ophthalmologic assessment.
Screen the mother and her sexual partners for gonorrhoea and other STIs. The mother should be treated on epidemiological grounds.

Uncomplicated gonococcal infections in older children - urethral, vulvovaginal, cervical, pharyngeal, rectal infections.

Children who weigh > 45 kg or are above 12 years of age should be treated with adult regimens.

Children who weigh < 45 kg or are 12 years of age or younger should be treated as follows:
1. Ceftriaxone 125 mg i/m single dose with azithromycin 1g stat or doxycycline 100 bid x 1 week (if older than 12 years).
   or
2. Cefotaxime 125 mg i/m single dose with azithromycin 1g stat or doxycycline 100 bid x 1 week (if older than 12 years).

Drugs Not Recommended
The following drugs are not recommended for treating gonococcal infection in Singapore as they are either ineffective or have not been adequately evaluated:
- All tetracyclines (they are given as part of anti-chlamydia therapy, not as primary treatment for GC)
- All penicillins
- All fluoroquinolones
- Erythromycin
- Rifampicin
- Kanamycin
- Trimethoprim/sulfamethoxazole

FOLLOW-UP
- Test-of-cure is recommended in all cases, in particular for pharyngeal GC.
- All treatments are less effective at eradicating pharyngeal infection and test-of-cure is recommended following treatment of infection at this site.
- In the DSC Clinic test-of-cure and assessment for post-gonococcal urethritis (PGU) is performed after 14 days.
- Test-of-cure is done using urethral smear. In cases of possible antibiotics resistance, cultures should be performed.
- Patients with gonococcal ophthalmia should have cultures done daily while on therapy and again on the 5th and 14th days after completion of therapy.
- Serologic tests for syphilis and HIV should be performed; if negative they should be repeated at 3 months after the last risky exposure.
MANAGEMENT OF SEXUAL CONTACTS
Sexual contacts of the patients 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.

References:


GRANULOMA INGUINALE (DONOVANOSIS)

DEFINITION
It is a sexually transmitted infection caused by the gram-negative bacillus *Klebsiella granulomatis* (formerly known as *Calymmatobacterium granulomatis*). This infection is rarely seen locally but endemic in India, parts of South America and southern Africa.

CLINICAL FEATURES
Presents with painless “beefy” red (highly vascular) granulomatous genital ulcers which bleed easily; without regional lymphadenopathy. Other clinical presentations are - nodular, hypertrophic, necrotic, and sclerotic types. The lesions may develop secondary bacterial infection or may be co-infected with another STI.

LABORATORY TESTS
- Tissue smears from ulcer to reveal intra-cellular Donovan bodies (Giemsa, Wright’s or silver stains) with “safety-pin” bipolar staining, found within histiocytes
- Biopsy of the ulcer to reveal granulomas and Donovan bodies
- Donovan bodies are characterised by:
  i. Location within large (20-90 μm) histiocytes,
  ii. Pleomorphic appearance 1- 2 x 0.5-0.7 μm
  iii. Bipolar densities and a capsule often visible
  iv. Stain Gram negative
- Culture is difficult
- There are currently no FDA approved PCR kits for diagnosis

TREATMENT

LOCAL TREATMENT
Normal saline wash

SYSTEMIC TREATMENT

*Recommended regimens*

1. Doxycycline 100 mg orally bid x minimum of 3 weeks [IV, C] or
2. Azithromycin 1 g orally once a week for 4 to 6 weeks [Ib, B]

*Alternative regimens*

1. Erythromycin 500 mg orally qid x minimum of 3 weeks [IV, C] or
2. Co-trimoxazole (trimethoprin/sulfamethoxazole) 160/800 mg orally (2 tabs) bid x minimum of 3 weeks [IIb, B] or
3. Gentamicin 1 mg/kg i/m tid as adjunct to above agents if not responding [III, C] or
4. Ciprofloxacin: 750 mg orally bid x minimum of 3 weeks [IIb, B]

FOLLOW-UP
If the treatment is effective, clinical response is evident within 7 days. Treatment should be continued till ulcers heal completely. Relapse can occur 6-18 months after apparently effective therapy.

Management of Sex Partners
Persons who have had sexual contact with a patient who has granuloma inguinale within 60 days before onset of the patient’s symptoms should be examined and offered therapy. However, the value of empiric therapy in the absence of clinical signs and symptoms has not been established.

Special Considerations

Pregnancy
Pregnancy is a relative contraindication to the use of sulfonamides. Pregnant and lactating women should be treated with erythromycin, and consideration should be given to the addition of a parenteral aminoglycoside (e.g. gentamicin). Azithromycin may be useful for treating granuloma inguinale in pregnancy. Doxycycline and ciprofloxacin are contraindicated in pregnant women.

HIV Infection
Persons with both granuloma inguinale and HIV infection should receive the same regimens as those who are HIV negative. Consideration should be given to the addition of a parenteral aminoglycoside (e.g. gentamicin).

References:
HEPATITIS A VIRUS INFECTION

DEFINITION
Hepatitis A (HAV) is a picorna (RNA) virus. Transmission occurs via faeco-oral (via food, water, close personal contact) route. Outbreaks have been reported in MSM, linked to oro-anal or digital rectal contact. Outbreaks have also been reported amongst intravenous drug users, in institutions for people with learning difficulties, and in contaminated batches of factor VIII.

Patients are infectious for approximately 2 weeks before and 1 week after the jaundice by the non-parenteral routes but virus can be found in the blood and stool until after the serum amino transferase levels have peaked. In HIV positive patients, HAV viraemia may continue for over 90 days.

In 2010 there were 68 serologically confirmed HAV infections in Singapore.

CLINICAL FEATURES
Incubation Period: 15-45 days.
Most children and up to half of adults are asymptomatic or have mild non-specific symptoms with little or no jaundice.

In the more ‘typical’ case there are 2 phases of symptoms

- The prodromal illness: flu-like symptoms (malaise, myalgia, fatigue), often with right upper abdominal pain. This phase lasts for 3-10 days.
- This is followed by the icteric illness: jaundice (hepatic and cholestatic) associated with anorexia, nausea, fatigue, liver enlargement and tenderness. Usually lasts for 1- 3 weeks. It can persist for 12 or more weeks in a minority of patients who have cholestatic symptoms (itching and deep jaundice).

Fulminant hepatitis complicates approximately 0.4% of cases, more common in patients already infected with chronic hepatitis B or C. Chronic infection (>6 months) has only been reported in a very small number of case-reports; overall mortality is < 0.1%.

DIAGNOSIS
Confirmed by a positive serum Hepatitis A virus specific IgM (HAV-IgM) which remains positive for six months or more.

HAV-IgG does not distinguish between current or past infection and may remain positive for life. Antibody produced in response to HAV infection persists for life and confers protection against reinfection.

Other tests:

- Serum amino-transferases (AST/ALT)
- Bilirubin
Serum alkaline phosphatase (SAP) will usually be < 2x the upper limit of normal, but higher if there is cholestasis. Prothrombin time PT prolongation by >5 seconds suggests developing hepatic decompensation.

MANAGEMENT
Patients should be advised to avoid food handling and unprotected sexual intercourse until they have become non-infectious.

Hepatitis A is a notifiable disease.

Screen for other STIs in cases of sexually-acquired hepatitis or if otherwise appropriate. 
Mild / moderate icteric hepatitis (80%) - manage as an outpatient emphasising rest and oral hydration [III, B].

Severe icteric hepatitis with vomiting, dehydration or signs of hepatic decompensation (change in conscious level or personality) - admit to hospital [III, B].

SEXUAL AND OTHER CONTACTS
Partner notification should be performed for at-risk homosexual contacts (oral/anal, digital/rectal and penetrative anal sex) within the period 2 weeks before to 1 week after the onset of jaundice.

Hepatitis A vaccine may be given up to 7 days after exposure providing exposure was within the infectious period of the source case (during the prodromal illness or first week of jaundice) [IIa, B].

Hepatitis A vaccine schedule: doses at 0 and 6-12 months, 95% protection for at least 5 years [Ib, A].

Current advice is to revaccinate after 10 years [IIb, B], however there is increasing evidence that vaccine-induced immunity may be > 20 years and possibly lifelong, so no further booster doses may be needed after the primary course in immunocompetent patients.

HIV positive patients respond in 46-88% but titres are lower than in HIV negative individuals, and correlates with CD4 count [IIa, B].

A combined Hepatitis A+B vaccine given on the same schedule as the hepatitis B vaccine has similar efficacy to the individual vaccines although early immunity to hepatitis B may be impaired [IIa, B].

PRIMARY PREVENTION
Most MSM are not at increased risk for hepatitis A infection and therefore universal vaccination in this group cannot be firmly recommended [III, B]. However, many outbreaks have been reported amongst homosexual men in large cities and therefore clinics in these areas should offer vaccination, particularly when increased rates of infection have been recognised locally [III, B].
Screening for pre-existing hepatitis A exposure before vaccination has been found to be cost effective [III,B].

Intravenous drug users and patients with chronic hepatitis C infection should be vaccinated [III, B]. Vaccination is also recommended for travellers to developing countries, people with haemophilia or chronic liver disease, those with occupational exposure and for people at risk in an outbreak [Ib, A]. Postvaccination serologic testing is not indicated because most persons respond to the vaccine.

HEPATITIS B VIRUS (HBV)

DEFINITIONS
Hepatitis B virus (HBV) is a DNA Hepadna virus that causes an infection of the liver. Transmission is through blood or body fluids viz. mother-to-child transmission, sexual intercourse, transfusion of contaminated blood, and sharing of needles and syringes.

Sporadic infection occurs in people without apparent risk factors, in institutions for learning difficulties and also in children in countries of high endemicity, but in these cases the means of transmission is poorly understood.

A total of 65 cases of acute hepatitis B infections were reported in 2010. The overall age-standardised prevalence of HBsAg among Singapore residents aged 18 to 69 years decreased significantly from 4.0% in HBSS 1999 to 2.8% in HBSS 2005 (p = 0.002).

CLINICAL FEATURES

Incubation period. 40-160 days

Symptoms

- Virtually all infants and children have asymptomatic acute infection
  Asymptomatic infection is also found in 10-50% of adults in the acute phase and is especially likely in those with HIV coinfection
- Chronic carriers are usually asymptomatic but may have fatigue or loss of appetite
  - The prodromal and icteric phases are very similar to hepatitis A, but may be more severe and prolonged

Signs

- As for Hepatitis A in the acute phase
- If chronic infection occurs there are often no physical signs. After many years of infection, depending on the severity and duration, there may be signs of chronic liver disease

Complications

- Fulminant hepatitis occurs in <1% of symptomatic cases but carries a worse prognosis than that caused by hepatitis A
- Chronic infection (>6 months) occurs in 5-10% of symptomatic cases but the rate is higher in immunocompromised patients with HIV infection, chronic renal failure or those receiving immunosuppressive drugs. Immunosuppressive treatment can also
reactivate hepatitis B. Almost all (>90%) of infants born to infectious (HBeAg +ve) mothers will become chronic carriers unless immunised

- There are 4 phases of chronic carriage:
  1. Immune Tolerant (HBe Ag +ve, normal ALT levels, little or no necroinflammation on liver biopsy)
  2. Immune Active, HBe Ag +ve phase (HBe Ag +ve, raised ALT, progressive necroinflammation and fibrosis)
  3. Inactive hepatitis B carrier (HBsAg+ve, HBeAg -ve, low levels of HBV DNA and normal ALT)
  4. HBeAg –ve chronic active hepatitis (Precore, Corepromotor mutations, HBeAg –ve, detectable HBV DNA, progressive inflammation and fibrosis). Types 2 and 4 may progress to cirrhosis and liver cancer, with type 4 generally progressing fastest

- Concurrent hepatitis C infection can lead to fulminant hepatitis, more aggressive chronic hepatitis and increased risk of liver cancer. Concurrent HIV infection increases the risk of progression to cirrhosis and death. Hepatitis A coinfection can be severe acutely, but may lead to the reduction of longterm HBV replication

- Concurrent Delta virus infection, or delta virus superinfection may lead to progressive fibrosis, cirrhosis and endstage liver disease

- Mortality is <1% for acute cases. Between 10 – 50 % of chronic carriers will develop cirrhosis leading to premature death in approximately 50%. Ten percent or more of cirrhotic patients will progress to liver cancer

- There is an increased rate of miscarriage/premature labour in acute infection. There is a risk of vertical transmission

**LABORATORY TESTS**

*Serologic markers*

The order of appearance of markers in acute infections is - HBsAg, HBeAg, antiHBc IgM, antiHBe, antiHBc IgG, antiHBs (Annex VI).

The significance of HBs antigen and antibody markers is shown below:

<table>
<thead>
<tr>
<th>Marker</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Presence of HBV</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Virus replication, High infectivity</td>
</tr>
<tr>
<td>Anti-HBc IgM</td>
<td>Acute infection</td>
</tr>
<tr>
<td>Anti-HBc IgG</td>
<td>Late acute or chronic infection</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Loss of replication, low infectivity</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Protective antibody</td>
</tr>
</tbody>
</table>
TREATMENT
Patients should be advised to avoid unprotected sexual intercourse until they have become non-infectious or their partners have been successfully vaccinated [III,B]. Hepatitis B is a notifiable disease. Screen for other STIs in cases thought to have been sexually acquired or if otherwise appropriate.

General counselling:
- No donation of blood, sperm, milk, organs
- No sharing of toothbrushes, shavers
- Household contacts, sexual partners to be immunized if negative HBsAg, anti-HBs and anti-HBc
- Pregnant carrier – inform O&G
- Healthy diet, avoid regular alcohol
- Steroids and immunosuppressive agents can aggravate latent infection
- Clean blood spills with bleach/detergents

Note:
Hepatitis B virus transmission is not transmissible through:
- Sharing of utensils, food or kissing as part of social greetings
- Participating in all activities including contact sports and social interaction with others (e.g. in schools, day care centres) [IV, D]

Acute Hepatitis - as for hepatitis A.

Chronic Hepatitis B Infection
Management of patients with chronic hepatitis B should be tailored according to the clinical state of liver disease (compensated versus decompensated liver disease) as well as virologic and biochemical (i.e. the liver function test, in particular the serum transaminase levels) status.

1) For patients with HBsAg positive > 6 months and well compensated liver disease:
   a. HBeAg–positive hepatitis B virus infection and:
      i. ALT < Upper limit of normal (ULN): no pharmacotherapy needed. Monitor ALT at least 6 monthly and HBeAg at least 12 monthly
      ii. ALT 1-2 X ULN: monitor ALT 3 to 6 monthly and HBeAg 6 monthly. Refer to specialist if persistent evidence of early deterioration of liver function or age >40. Consider liver biopsy and treatment if biopsy shows significant liver damage
      iii. ALT > 2X ULN: repeat ALT and HBeAg within 1 to 3 months. Refer to specialist if persistent. Treat immediately upon evidence of hepatic decompensation

   b. HBeAg–negative hepatitis B virus infection and:
i. ALT < ULN: Monitor ALT 3 months later. If still normal, monitor ALT every 6 to 12 monthly

ii. ALT 1-2X ULN: Monitor ALT 3 to 6 monthly. Refer to specialist if persistent, evidence of early deterioration of liver function or age > 40. If HBV DNA is > 2000 IU/ml, consider liver biopsy and treat if biopsy shows significant liver damage

iii. ALT > 2X ULN: repeat ALT within 1 to 3 months. Refer to specialist if persistent. If HBV DNA > 2000 IU/ml, consider treatment if persistent. Note that common conditions, such as fatty liver and commonly consumed drugs may be confounding factors giving rise to mild to moderate elevation of serum transaminases

2) For patients with decompensated hepatitis B virus–related cirrhosis: Refer to gastroenterologist or hepatologist for management [IV, D].

Surveillance of patients with chronic hepatitis B should be carried out regularly; frequency of surveillance will depend on the risk profile, which should be determined before the start of the surveillance programme (see below):

a. Baseline assessment to stratify risk
   i. check serum ALT, AST, bilirubin, albumin, prothrombin time, alpha-fetoprotein, HBsAg, HBeAg, anti HBe and HBV DNA
   ii. liver imaging

b. Periodic reassessment is necessary

Frequency of surveillance is dependent on patients’ risk profile:

i. **Low-risk group** (patients who have seroconverted and have a nonreplicative hepatitis B virus infection): 6 monthly serum ALT and bilirubin – if abnormal, HBV DNA should be checked

ii. **Medium-risk group** (patients with replicative HBV infection who are beyond the immuno-tolerant window; chronic hepatitis B not on treatment; chronic hepatitis B which is resistant to treatment; patients who are expected to tolerate exacerbation of hepatitis B poorly, e.g. patients with liver cirrhosis): 4-6 monthly serum ALT and bilirubin assessment – if abnormal, HBV DNA should be checked

iii. **High-risk group** (patients who are subjected to immunosuppressive treatment either during immunosuppressive treatment or on withdrawal of immunosuppressive treatment with agents such as steroids, cytotoxics, monoclonal antibodies with immunomodulatory activity; patients withdrawn from nucleoside/tide analogue treatment for prior chronic hepatitis B; demonstrating resistance to their ongoing nucleoside/tide analogue treatment for their prior chronic hepatitis B; having reduced liver mass, e.g. post-hepatic resection): 2-4 monthly serum ALT, bilirubin, HBV DNA, appropriate to each set of circumstances. If abnormal the specialist will have to decide on further appropriate management [GPP]
Most patients in medium risk group and all patients in high risk group should be referred for management by a specialist.

Treatment of Chronic Hepatitis B Infection

- Treatment should normally be given in collaboration with a hepatologist or physician experienced in the management of liver disease [IV, C]. The decision to treat depends on pattern of disease, HBV DNA level, and presence or absence of significant necroinflammation and hepatic fibrosis. A HBV DNA level of ≥ 4 log IU/ml is generally considered as significant and treatment should be considered
- Patients should be considered for therapy with lamivudine, adefovir, tenofovir, telbivudine, entecavir (or combinations of nucleos(t)ide analogues) or pegylated interferon [Ib, A]. Additional treatments that may soon be licensed in HBV monoinfection include emtricitabine (FTC) [Ib,A], clevudine [I, B] and valtorcitabine [III, C]. Treatment responders have long term benefits in terms of reduced liver damage and decreased risk of liver cancer
- All patients should have an HIV test prior to starting HBV therapy because of different treatment strategies required and the significant risk of antiretroviral resistant HIV developing if lamivudine, tenofovir or entecavir are used as monotherapy [Ib,A]
- Lamivudine, emtricitabine and tenofovir will suppress hepatitis B viral replication during therapy of HIV, and may delay liver damage if given as part of triple antiretroviral therapy [Ib, A]
- Lamivudine and emtricitabine should only be given to HIV+ patients in combination with tenofovir as part of HAART because of the rapid high rate of resistance that occurs to these drugs if given as the only HBV active agent [Ib,A]
- Entecavir should not be used in HIV+ patients without adequately suppressed HIV as it causes the M184V (lamivudine/emtricitabine) resistant mutation
- Adefovir or telbivudine can be used alone in HIV+ patients [II,B]
- Active surveillance of cirrhotic patients for Hepatocellular carcinoma (HCC) leads to earlier detection and better treatment outcomes

Pregnancy and Breastfeeding

- Vertical transmission of infection occurs in 90% of pregnancies where the mother is HBeAg +ve and in about 10% of HBsAg +ve, HBeAg -ve mothers. More than 90% of infected infants become chronic carriers
- Infants born to infectious mothers are vaccinated from birth, usually in combination with Hepatitis B specific Immunoglobulin 200 i.u. i.m. [Ia, A]. This reduces vertical transmission by 90%
- There is some evidence that treating the mother in the last month of pregnancy with lamivudine may further reduce the transmission rate if she is highly infectious [III, C], but this needs to be further substantiated
- Infected mothers should continue to breast feed as there is no additional risk of transmission [II, B]
SEXUAL AND OTHER CONTACTS
Partner notification should be performed and documented and the outcome documented at subsequent follow-up. Contact tracing to include any sexual contact or needle sharing partners during the period in which the index case is thought to have been infectious.

The infectious period is from 2 weeks before the onset of jaundice until the patient becomes surface antigen negative. In cases of chronic infection trace contacts as far back as any episode of jaundice or to the time when the infection is thought to have been acquired, this may be impractical for periods of longer than 2 or 3 years.

SCREENING AND PRIMARY PREVENTION
Hepatitis B testing in asymptomatic patients should be considered in MSM, sex workers, injecting drug users, HIV-positive patients, sexual assault victims, needle-stick victims and sexual partners of positive or high-risk patients. If non-immune, consider vaccination. If found to be chronic carriers consider referral for therapy.

With the exception of newborns, serological screening provides a basis for vaccination of an individual without giving an infected individual a false sense of security. Prophylactic vaccination is of no benefit to an individual who already has chronic hepatitis B virus infection; he/she should instead be followed up regularly and treated when indicated. Serological screening for HBsAg and Ab should be done within 6 months pre-vaccination for all except newborn babies [IV, D].
Based on the results of an individual’s serological screening for HBs Ag and Ab, clinicians should act according to the table below [II, B].

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Interpretation</th>
<th>Action to take</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non reactive</td>
<td>&lt;10 IU/L</td>
<td>1. If an individual did not have hepatitis B vaccination before,</td>
<td>1. Administer hepatitis B vaccination</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not immune to hepatitis B Virus.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. If an individual had hepatitis B vaccinations before</td>
<td>2. Offer a booster dose of hepatitis B vaccination and check anti-HBs within 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Either:</td>
<td>or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The antibody level has waned to less than 10 IU/L, but the individual is still immune to the hepatitis B virus.</td>
<td>Give them another course of (3 injections) of hepatitis B vaccination &amp; recheck anti-HBs within 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or</td>
<td>(to discuss options with patient)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The individual did not develop immunity against hepatitis B virus after the primary course of hepatitis B vaccination.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NB*</td>
<td></td>
</tr>
<tr>
<td>Non Reactive</td>
<td>&gt; 10 IU/L</td>
<td>Immune to hepatitis B</td>
<td>Immunisation is not required</td>
</tr>
<tr>
<td>Reactive</td>
<td>&lt; 10 IU/L</td>
<td>Presence of hepatitis B virus infection</td>
<td>Clinically assess the patient for liver disease.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>To repeat the HBsAg test 6 months later.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If HBsAg positive 2 times, 6 months apart, chronic hepatitis B infection confirmed.</td>
</tr>
</tbody>
</table>

*Under rare circumstances, the emergence of hepatitis B surface mutant (‘s’ mutant) virus can be associated with the absence of HBsAg and a negative or low titre of anti-HBs antibody. For individuals previously vaccinated and with anti-HBs levels < 10 IU/L, consider repeat booster of HBV vaccination or give a second course of HBV vaccination before rechecking the anti-HBs antibody titre [II, C].
For immuno-competent people:

- With low risk of acquiring HBV and
- Who have completed their HB vaccination and
- Who had previously demonstrated immunity to HBV after vaccination, there is no need to check for immunity again or receive booster injections if their anti-HBs is < 10 IU/L later on [II, C].

Anti-HBc total should be checked if an otherwise immunocompetent individual fails to seroconvert after 2 courses of HBV vaccinations.

1. HBsAg negative, anti-HBs < 10 IU/L, anti-HBc positive - These individuals may have HBV infection with low viral load and an undetectable level of HBsAg. Refer to specialists for further workup.

2. HBsAg negative, anti-HBs < 10 IU/L, anti-HBc negative - Consider repeat vaccination with pre-S vaccine or other 3rd generation vaccine, if available, especially if the individuals belong to the high-risk group. They should be advised against high risk behaviour, which may expose them to Hepatitis B infections, and counselled about PEP with HBIG if they do sustain high risk exposure [III, D].

Algorithm for Hepatitis B screening & vaccination – Refer to Annex I

POST VACCINATION TESTING FOR SEROLOGIC RESPONSE
Serologic testing for immunity is not necessary after routine vaccination of adolescents or adults. Testing after vaccination is recommended for persons whose subsequent clinical management depends on knowledge of their immune status e.g. health-care workers, HIV-infected persons and other immunocompromised persons, to determine the need for revaccination and the type of follow-up testing; and sex and needle-sharing partners of HBsAg positive persons to determine the need for revaccination and for other methods to protect themselves from HBV infection.

Persons determined to have anti-HBs levels of < 10 mIU/mL after the primary vaccine series should be revaccinated with a 3-dose series, followed by anti-HBs testing 1-2 months after the third dose.

POST EXPOSURE PROPHYLAXIS (PEP)

- Specific hepatitis B immunoglobulin 500 i.u. intramuscularly (HBIG) may be administered to a nonimmune contact after a single unprotected sexual exposure or parenteral exposure/needlestick injury if the donor is known to be infectious. This works best within 48 hours and is of no use after more than seven days [Ib, A]

- An accelerated course of recombinant vaccine should be offered to those given HBIG plus all sexual and household contacts (at 0, 7 and 21 days or 0, 1, 2 months with a booster at 12 months in either course) [Ib, A]. Vaccination theoretically will provide some protection from disease when started up to six weeks after exposure

- Avoid sexual contact, especially unprotected penetrative sex, until vaccination has been successful (antiHBs titres >10i.u./l.)
HEPATITIS C VIRUS INFECTION (HCV)

DEFINITION
Hepatitis C is a RNA virus in the flaviviridae family. Parenteral spread accounts for the majority of cases through shared needles/syringes in IDUs, transfusion of blood or blood products (pre-1990s), renal dialysis, needle-stick injury or sharing a razor with an infected individual.

Sexual transmission occurs at a low rate (generally <1% per year of relationship, or about 2% of spouses in long term relationships) but these rates increase if the index patient is also HIV infected. There has been a steadily rising incidence of acute HCV in MSM in some parts of the world which is largely linked to HIV coinfection, the presence of other STIs including syphilis and LGV, traumatic anal sex and use of recreational drugs.

Vertical (mother to infant) spread also occurs at a low rate (about 5% or less), but higher rates (up to 40%) are seen if the woman is both HIV and HCV positive. In all groups transmission risk correlates with the presence of detectable HCV RNA in the mother’s blood.

The prevalence of positive HCV antibody in first time donors in 2010 was 0.136%. The prevalence of HCV in Singapore is estimated at around 0.1% of the general population, and 2% among persons with HIV infection, mostly among IDUs. There were 6 cases of acute hepatitis C reported in 2010.

CLINICAL FEATURES

Incubation period: 4 to 20 weeks.

Symptoms
- > 80% have asymptomatic acute infection
- uncommon cases of acute icteric hepatitis

Signs
- Acute icteric hepatitis - see hepatitis A
- Chronic hepatitis - see hepatitis B

Complications
- Acute fulminant hepatitis is rare (<1% of all hepatitis C infections), but is more common after hepatitis A superinfection of chronic hepatitis C carriers
- Approximately 50-85% of infected patients become chronic carriers, a state which is normally asymptomatic but may cause nonspecific ill health. Type 1 genotype is more likely to clear spontaneously but leads to more severe chronic infection. Once established, the chronic carrier state rarely resolves spontaneously (0.02%/year). Symptoms/signs are worse if there is a high alcohol intake or other liver disease. Significant liver disease can be present in the 35% of carriers who have normal serum ALT levels
• Mortality in acute hepatitis is very low (<1%) but up to 30% of chronic carriers will progress to severe liver disease after 14–30 years infection, with an increased risk of liver cancer (approximately 14% of all patients and up to 33% of those with cirrhosis) HIV coinfection worsens the prognosis although this may be ameliorated to some degree by ART

• Pregnancy Complications of acute icteric hepatitis: as for hepatitis A. For risk of vertical transmission see “transmission”

**DIAGNOSIS**

• Screening ELISA, confirmatory test e.g. recombinant immuno-blot assay (RIBA), third generation immunoassay or HCV-PCR for RNA. In HIV+ patients with a low CD4 count (<200 cells/mm³) the EIA may be negative and an HCV-PCR may be needed for diagnosis

• HCV-RNA will be positive after 2 weeks. HCV serology is usually positive (90%) 3 months after exposure but can take as long as 9 months

• Chronic infection is confirmed if HCV-RNA assay is positive 6 months after the first positive test. All patients being considered for therapy should have a viral RNA test to confirm viraemia and genotype assay

**Other tests**

• Acute infection - as for hepatitis A
• Chronic infection - as for hepatitis B

**TREATMENT**

**General Advice**

• Patients should not donate blood, semen or organs
• Patients should be given a detailed explanation of their condition, reinforced by giving them clear and accurate written information
• Acute hepatitis C infection is a notifiable disease
• Refer all HCV +ve patients to a liver specialist for consideration of treatment

**Acute icteric hepatitis**

• High dose α-interferon or peg-interferon will reduce the rate of chronicity to 10% or less

• Spontaneous resolution of acute hepatitis C is signified by a loss of HCVRNA within the first 2 months. Only those HCVRNA positive for more than 2 months need to be treated. Genotype 1 infections require 24 weeks therapy whereas other genotypes need only 12 weeks treatment

• Otherwise manage as for hepatitis A
**Chronic infection**

- Pegylated α-interferon with ribavirin will abolish chronic infection in 50% of patients [Ia, A]
- Treatment for 12 to 48 weeks depending on genotypes. HCV viral load monitored to assess response

Treatment should be for 14-24 weeks for patients with genotypes 2 or 3. Other genotypes should be treated for 12 weeks and treatment only continued if there has been a reduction in HCV viral load to 1% of the level at the start of treatment. Patients achieving this 2 log10 reduction should be treated for 24-72 weeks depending on how quickly the viral load becomes undetectable.

Patients are more likely to respond if they have less severe liver disease (low fibrosis index on liver biopsy), low serum HCVRNA levels (<2million RNA copies/ml), if they are infected with certain HCV subtypes (types 2 and 3) or if they become HCVRNA negative in the serum within 12 weeks [Ib, A].

HIV positive patients respond to treatment, although not as well as HIV negative patients, and should be considered for therapy [Ib, A].

Patients with hepatitis C should be vaccinated against hepatitis A and B [III,B], given the high rate of fulminant hepatitis in co-infection hepatitis A & C and the worse prognosis of hepatitis B & C co-infection.

**Pregnancy and Breast feeding**

- Routine testing for HCV infection is not recommended for all pregnant women. Pregnant women with a known risk factor for HCV infection should be offered counselling and testing
- There is at present no known way of reducing the risk of vertical transmission. Women should be informed of the potential risk of transmission in pregnancy (see transmission) [II, B]
- Breast feeding: there is no firm evidence of additional risk of transmission except, perhaps in women who are symptomatic with a high viral load [III, B]

**Sexual and Other Contacts**

- Partner notification should be performed. Contact tracing to include any sexual contact (penetrative vaginal or anal sex) or needle sharing partners during the period in which the index case is thought to have been infectious. The infectious period is from 2 weeks before the onset of jaundice in acute infection, or trace back to the likely time of infection (eg blood transfusion, first needle sharing) although this may be impractical for periods longer than 2 or 3 years. Consider testing children born to infectious women [IV, C]
- There is currently no available vaccine or immunoglobulin preparation that will prevent transmission
• Sexual transmission should be discussed. It seems likely that if condoms are used consistently then sexual transmission will be avoided

**Follow-up**

• As for hepatitis B [IV, C]
• Immunity is probably subtype specific only there are at least seven subtypes and reinfection/ dual infection is well documented

**SCREENING AND PRIMARY PREVENTION**

Consider testing for hepatitis C in all IDUs, especially if equipment has been shared, in people sustaining a needle-stick injury if the donor HCV status is positive or unknown, sexual partners of HCV positive individuals, MSM, all HIV-positive patients, female sex workers, tattoo recipients, alcoholics and ex-prisoners.

Since 1993 all donated blood in Singapore has been screened for HCV.

**References:**


DEFINITION
Genital herpes is a chronic, life-long viral infection. Genital herpes is caused by the DNA Herpes simplex virus (HSV), usually HSV type 2, but type 1 infections are also possible. Transmission of the virus can occur through genital to genital, mouth to genital, genital to anal and mouth to anal contact.

CLINICAL FEATURES
First episode genital herpes may either be primary or non-primary. Primary genital herpes is defined as infection occurring in persons with no prior exposure to either HSV type 1 or 2. Non-primary genital herpes is defined as first genital episode in persons who have evidence of prior HSV infection at another body site with either 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 take 2 to 4 weeks. Complications may include autonomic neuropathy resulting in urinary retention, autoinoculation to fingers and adjacent skin and aseptic meningitis.

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. Recurrences average 5 to 8 attacks a year and are more frequent during the first 2 years of infection. Genital herpes caused by HSV type 1 generally recurs infrequently.

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

A patient’s prognosis and the type of counselling needed depends on the type of genital herpes (HSV-1 or HSV-2) causing the infection; therefore, the clinical diagnosis of genital herpes should be confirmed by laboratory testing.

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.

Type-specific serological tests (TSSTs)
Based on recombinant type-specific glycoproteins gG1 (HSV-1) and gG2 (HSV-2). Good sensitivity and specificity and are useful in certain clinical situations e.g. confirming a diagnosis of genital herpes, counselling of sexual partners of infected persons, detection
of unrecognised infection and for seroepidemiological studies. TSSTs are also useful in high risk populations such as MSM, individuals with multiple sex partners and HIV positive individuals. Screening for HSV-1 and HSV-2 in the general population is not indicated. Examples of these tests are HerpeSelect 1 and 2 ELISA (Focus Technologies, USA) and Immunoblot test kits.

As nearly all HSV-2 infections are sexually acquired, the presence of type-specific HSV-2 antibody implies anogenital infection. Most persons with HSV-1 antibodies have oral HSV infection acquired during childhood, which might be asymptomatic. The presence of HSV-1 antibody does not distinguish anogenital from orolabial infection.

### HSV antigen detection
By Direct Immunofluorescence techniques. Results may be available in 1 to 2 days. HSV type is reported if the test is positive.

### PCR detection of viral nucleic acid
Highest sensitivity viral typing possible; but expensive and not widely available. Test of choice for detecting HSV in spinal fluid.

### Serology
Many commercial tests for HSV antibodies are not type specific and are of NO value in the management of genital herpes.

## TREATMENT
### GENERAL MEASURES
- Cleaning of the affected areas with normal saline
- Analgesia
- Treatment of any secondary bacterial infection

### SPECIFIC THERAPY
Systemic antiviral drugs can partially control the signs and symptoms of herpes episodes when used to treat first clinical and recurrent episodes, or when used as daily suppressive therapy. However, these drugs neither eradicate latent virus nor affect the risk, frequency, or severity of recurrences after the drug is discontinued.

Topical therapy is of limited value for genital herpes and is not indicated if systemic therapy is administered.

### Recommended regimens

#### First episode genital herpes
- **Acyclovir 400mg orally tid x 7 - 10 days** [Ib, A]
- or
- **Valacyclovir 1g orally bid x 7 - 10 days** [Ib, A]
- or
- **Famciclovir 250mg orally tid x 7 - 10 days** [Ib, A]
For optimal benefit, the treatment should be started within 48 to 72 hours of onset of lesions, when new lesions continue to form or when symptoms and signs are severe. Treatment can be extended if healing is incomplete after 10 days of therapy.

**Recurrent genital herpes**
Most recurrent attacks are mild and can be managed with general measures only. Routine use of specific treatment is not necessary. Management should be decided together with the patient.

Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks. The patient should be provided with a supply of drug or a prescription for the medication with instructions to initiate treatment immediately when symptoms begin.

**Episodic treatment**

Acyclovir 400mg orally tid x 5 days [Ib, A]
or
Acyclovir 800mg orally bid x 5 days [Ib, A]
or
Acyclovir 800mg tid x 2 days [Ib, A]
or
Valacyclovir 500mg orally bid x 3 days [Ib, A]
or
Valacyclovir 1g orally once a day x 5 days [Ib, A]
or
Famciclovir 125mg orally bid x 5 days [Ib, A]
or
Famciclovir 1g bid x 1 day [Ib, A]

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).

Suppressive therapy has the additional advantage of decreasing the risk for genital HSV-2 transmission to susceptible partners.

**Suppressive treatment**

Acyclovir 400mg orally bid [Ib, A]
or
Valacyclovir 500mg orally od [Ib, A]
or
Valacyclovir 1000mg orally od (for ≥10 recurrences in 1 year) [Ib, A]
or
Famciclovir 250mg orally bid [Ib, A]
Physicians should stop treatment after 9 to 12 months to see if the recurrence rate warrants continued prophylaxis.

**Treatment of genital herpes in HIV-infected patients**

Genital herpes is common in HIV infected individuals. Acyclovir-resistant strains, which usually lack the thymidine kinase enzyme, have been reported in patients with concurrent HIV infection. Acyclovir-resistant strains will also be resistant to valacyclovir and famciclovir. IV foscarnet, topical cidofovir or trifluridine may be used to treat resistant strains.

**Recurrent treatment**

Acyclovir 400mg orally tid for 7 - 10 days [IV, C]

or

Valacyclovir 1g orally bid for 7 - 10 days [IV, C]

or

Famciclovir 500mg orally bid for 7 - 10 days [IV, C]

**Suppressive treatment**

Acyclovir 400 - 800mg orally bid or tid or qid [IV, C]

or

Valacyclovir 500mg orally bid [IV, C]

or

Famciclovir 500mg orally bid [IV, C]

**FOLLOW-UP**

Counselling of infected persons and their sex partners is critical to the management of genital herpes. The goals of counselling are to help patients cope with the infection and prevent sexual and perinatal transmission.

The following should be discussed:

- Information on the natural history of the 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 the first 12 months after the first attack
- Sexual relationships and transmission to partners
- Information on anti-viral treatment available
- Ability to bear healthy children
- Risk of neonatal infection: women with a history of genital herpes or whose partners have a history of genital herpes should inform their obstetrician early in pregnancy
- The misconception that HSV causes cancer should be dispelled.
Management of genital herpes in pregnancy
Transmission of genital herpes to neonates is most likely to occur when the mother has an attack of symptomatic herpes at the time of delivery. The risk of transmission to the neonate is highest (30-50%) from a mother with primary genital herpes at the time of delivery; it is much lower (<1%) for mothers with recurrent herpes or asymptomatic viral shedding.

The safety of systemic acyclovir, valacyclovir and famciclovir during pregnancy is not yet established (all US FDA class B). Current findings do not show an increased risk for major birth defects after acyclovir treatment in the first trimester. First episode or severe recurrent genital herpes in pregnancy may be treated with oral acyclovir. In the presence of life-threatening maternal HSV infection, IV acyclovir is indicated.

The use of acyclovir near term may reduce the rate of Caesarean sections amongst women who have frequently recurring or newly acquired genital herpes by decreasing the rate of active lesions. Based on decision analysis, oral acyclovir prophylaxis is more cost effective than Caesarean section for women with recurrent genital herpes. However, routine administration of acyclovir to pregnant women is not recommended.

First episode genital herpes - 1st and 2nd trimester acquisition
Management should be in line with the clinical condition with the use of either oral or intravenous acyclovir [IV, 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 [IV, C].

First episode genital herpes – 3rd trimester acquisition
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 [IV, C].

Recurrent genital herpes in pregnancy
If there are no genital lesions at the onset of labour, Caesarean section to prevent neonatal herpes is not indicated [IV, C].

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 [Ia, A].

MANAGEMENT OF SEXUAL CONTACTS
Sexual partners of patients with genital herpes are likely to benefit from evaluation and counselling. They should be questioned on a history of typical and atypical genital lesions, encouraged to examine themselves for lesions and seek medical attention early if lesions appear. TSSTs may be useful in counselling couples.
References:


HIV INFECTION

DEFINITION
Human immunodeficiency virus (HIV) is a blood-borne, sexually transmissible virus. The virus is typically transmitted via sexual intercourse, shared intravenous drug instruments, and mother-to-child transmission (MTCT), which can occur during the birth process or during breastfeeding. Two distinct species of HIV (HIV-1 and HIV-2) have been identified, and each is composed of multiple subtypes, or clades. All clades of HIV-1 tend to cause similar disease, but the global distribution of the clades differs. The majority of HIV infections in Singapore are caused by HIV-1.

HIV-1 and HIV-2 are retroviruses in the Retroviridae family, Lentivirus genus. HIV produces cellular immune deficiency characterized by the depletion of helper T lymphocytes (CD4+ cells). The loss of CD4+ cells results in the development of opportunistic infections and neoplastic processes.

CLINICAL FEATURES
Clinical HIV infection undergoes 3 distinct phases:
1. Acute seroconversion
2. Asymptomatic infection and
3. AIDS

Acute Seroconversion
During this phase, the infection is established and a proviral reservoir is created. Seroconversion may take a few weeks, up to several months. Symptoms during this time may include fever, flu-like illness, lymphadenopathy, and rash. These manifestations develop in approximately half of all people infected with HIV.

Asymptomatic infection
At this stage in the infection, persons infected with HIV exhibit few or no signs or symptoms for a few years to a decade or more. Viral replication is clearly ongoing during this time, and the immune response against the virus is effective and vigorous.

AIDS
When the immune system is damaged enough that significant opportunistic infections begin to develop, the person is considered to have AIDS. A CD4+ T-cell count less than 200/μL is also used as a measure to diagnose AIDS, although some opportunistic infections develop when CD4+ T-cell counts are higher than 200/μL, and some people with CD4 counts under 200/μL may remain relatively healthy.
Opportunistic infections and conditions include the following (* added in the 1993 AIDS surveillance case definition):

<table>
<thead>
<tr>
<th>Opportunistic Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Candidiasis of bronchi, trachea, or lungs</td>
</tr>
<tr>
<td>• Candidiasis, esophageal</td>
</tr>
<tr>
<td>• Cervical cancer, invasive*</td>
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<tr>
<td>• Coccidioidomycosis, disseminated or extrapulmonary</td>
</tr>
<tr>
<td>• Cryptococcosis, extrapulmonary</td>
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<tr>
<td>• Cryptosporidiosis, chronic intestinal (duration &gt;1 month)</td>
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<tr>
<td>• Cytomegalovirus disease (other than liver, spleen, or nodes)</td>
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<tr>
<td>• Cytomegalovirus retinitis (with vision loss)</td>
</tr>
<tr>
<td>• Encephalopathy, HIV-related</td>
</tr>
<tr>
<td>• Herpes simplex: chronic ulcer or ulcers (duration &gt;1 month) or bronchitis, pneumonitis, or oesophagitis</td>
</tr>
<tr>
<td>• Histoplasmosis, disseminated or extrapulmonary</td>
</tr>
<tr>
<td>• Isosporiasis, chronic intestinal (duration &gt;1 month)</td>
</tr>
<tr>
<td>• Kaposi sarcoma</td>
</tr>
<tr>
<td>• Lymphoma, Burkitt (or equivalent term)</td>
</tr>
<tr>
<td>• Lymphoma, immunoblastic (or equivalent term)</td>
</tr>
<tr>
<td>• Lymphoma, primary, of the brain</td>
</tr>
<tr>
<td>• <em>Mycobacterium avium</em> complex or <em>Mycobacterium kansasii</em> infection, disseminated or extrapulmonary</td>
</tr>
<tr>
<td>• <em>M. tuberculosis</em> infection, any site (pulmonary* or extrapulmonary)</td>
</tr>
<tr>
<td>• <em>Mycobacterium</em> infection with other species or unidentified species, disseminated or extrapulmonary</td>
</tr>
<tr>
<td>• <em>Pneumocystis</em> pneumonia</td>
</tr>
<tr>
<td>• Pneumonia, recurrent*</td>
</tr>
<tr>
<td>• Progressive multifocal leukoencephalopathy</td>
</tr>
<tr>
<td>• <em>Salmonella</em> septicemia, recurrent</td>
</tr>
<tr>
<td>• Toxoplasmosis of the brain</td>
</tr>
<tr>
<td>• Wasting syndrome due to HIV infection</td>
</tr>
</tbody>
</table>

**LABORATORY TESTS**

The Centers for Disease Control and Prevention (CDC) recommends HIV screening for patients in all health-care settings, after the patient is notified that testing will be performed unless the patient declines (opt-out screening); the CDC recommends that persons at high risk for HIV infection be screened for HIV at least annually.

The diagnosis of HIV infection is made by the detection of circulating antibodies to HIV. Antibodies are identified by the use of a screening test, usually an enzyme-linked immunosorbent assay (ELISA), followed by definitive diagnosis using a Western Blot assay. HIV antibody is detectable in at least 95% of patients within 3 months after infection.

In some situations such as pre-seroconversion or neonatal infection, measurement of HIV antibodies may be unreliable. In these instances, diagnosis of infection may use direct detection of HIV itself such as quantification of plasma HIV RNA, HIV viral DNA, or HIV antigen or by detection and amplification of virus in a tissue culture.
Screening Antibody tests
The ELISA or EIA test is the standard screening test for HIV infection. Recombinant or native HIV antigens, fixed in a solid phase, are exposed to and bound by HIV antibodies in test serum. The presence of these antibodies is then detected by a second anti-human antibody, with a sensitivity of >99.5%. Most commercially available ELISA kits contain antigens from both HIV-1 and HIV-2 and are able to detect infection with either of these viruses. A positive ELISA test is usually observed within 3-6 weeks following infection. The weeks between infection and seropositivity are termed the “window period” and are associated with high levels of circulating HIV, and potentially more efficient transmission. Commercial fourth-generation screening assays, which combine antigen and antibody screening, may reduce this window period to 6 days. False-positive test results are rare and the specificity of the ELISA is >99.8%.

Confirmatory Antibody Tests
The Western Blot is the definitive diagnostic test for HIV infection. The Western Blot (WB) assay detects antibodies in patient sera that react with a number of different viral proteins. A positive WB is defined by the detection of antibodies to all of the 3 main groups of HIV proteins – envelope (gp160, gp120 or gp41), gag (p24) and polymerase (p66 or p51). An indeterminate WB assay is most commonly caused by the presence of unrelated antibodies that are cross-reactive with HIV proteins. It is possible that an indeterminate result is due to early HIV infection and incomplete evolution of the anti-HIV immune response. An indeterminate test result should be repeated at 1, 2 and 3 months to exclude an evolving pattern.

Using both EIA and WB tests, the sensitivity and specificity exceed 99.9%. Antibody testing can be performed on individuals approximately 1 month after a high-risk sexual exposure. If negative, the test should be repeated again 3 months (window period) after the exposure.

Rapid Tests
Rapid tests are screening tests where results are available in 10-20 minutes. If performed correctly, they detect HIV antibodies with sensitivities similar to currently available EIAs. A negative rapid HIV test result requires no further confirmatory testing. A positive test requires confirmation by both EIA and WB testing.

Four rapid HIV tests have been approved by the US Food and Drug Administration (FDA):
- OraQuick® (and its newer version OraQuick® Advance) Rapid HIV-1/2 Antibody Test (OraSure Technologies, Inc., Bethlehem, PA);
- Reveal™ (and its newer version Reveal™ G2) Rapid HIV-1 Antibody Test (MedMira, Halifax, Nova Scotia);
- Uni-Gold Recombigen® HIV Test (Trinity BioTech, Bray, Ireland);
- Multispot HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories, Redmond, WA).

The Determine HIV-1/HIV-2 (Abbott) rapid test kit is used at the DSC clinic (approved by USAID).
HIV p24 antigen detection
The first marker to appear following infection is free viral p24 antigen. This can be detected using an EIA test. Fourth generation HIV serology tests incorporate testing for both antibodies as well as for the p24 antigen, therefore reducing the window period further.

Polymerase chain reaction (PCR) test
PCR for HIV DNA is available in special circumstances e.g. for infants of mothers with HIV infection to distinguish active infection of the infant from passive transfer of maternal antibodies, and in cases where the WB test is indeterminate in a patient with high-risk behaviour. PCR technology is also employed for quantitative measurement of plasma HIV RNA, this is used to guide and monitor ARV treatment.

HIV TESTING
HIV infection and AIDS are notifiable conditions. HIV testing should be voluntary, persons should be informed orally or in writing that HIV testing will be performed unless they decline. Individuals must not be tested without their knowledge. Confidentiality of the result must be observed, failure to do so may result in prosecution. HIV screening after notifying the patient that an HIV test will be performed (unless the patient declines) is recommended in all health-care settings.

HIV testing is specifically recommended in the following situations:
- for all individuals who seek evaluation and treatment for STIs
- individuals with signs and symptoms suggestive of HIV-related illnesses
- individuals whose behaviour puts them at risk for HIV infection
- individuals who consider themselves at risk or request the test
- pregnant women
- individuals with active TB
- donors of blood, semen, and organs
- health care workers who perform exposure-prone invasive procedures

Post-test Counselling – Negative test
- Reinforce information on safer sex practices to reduce the risk of acquiring HIV
- The significance of “the window period” and the necessity and timing of a repeat test should be discussed with the patient

Post-test Counselling – Positive test
- Providers should expect individuals to be distressed when first informed of a positive HIV test result
- Individuals who test positive for HIV antibody should be counselled concerning the behavioral, psychosocial, and medical implications of HIV infection
• Prevention counseling must be given before leaving the testing site
• A referral letter should be written and an appointment made at the CDC, TTSH
• AIDS helpline numbers should be given for any future needs (Tel: 6295 2944)

Anonymous HIV Counselling and Testing
This is operated by Action for AIDS on Tuesday and Wednesday evenings from 6.30 pm to 8 pm and Saturdays from 1 to 4 pm, at the DSC Clinic, 31 Kelantan Lane, Singapore 200031.

TREATMENT
Each HIV-infected patient entering into care should have a complete medical history, physical examination, and laboratory evaluation and should be counselled regarding the implications of HIV infection. The goals of the initial evaluation are to confirm the presence of HIV infection, obtain appropriate baseline historical and laboratory data, ensure patient understanding about HIV infection and its transmission, and initiate care as recommended by established guidelines. Baseline information can then be used to define management goals and plans.

The following laboratory tests performed during initial patient visits can be used to stage HIV disease and to assist in the selection of antiretroviral (ARV) drug regimens:

• HIV antibody testing
• CD4 T-cell count
• Plasma HIV RNA (viral load)
• FBC, LFTS, renal function tests, thyroid function tests
• Urinalysis
• Serologies for hepatitis A, B, and C viruses
• Syphilis serology
• Toxoplasma and CMV antibody tests
• Fasting blood glucose and serum lipids
• CXR
• Genotypic resistance testing at entry into care, regardless of whether ART will be initiated immediately

Newly diagnosed HIV-infected persons should receive psychosocial evaluation including ascertainment of behavioral factors indicating risk for transmitting HIV. They may require referral for specific behavioural intervention (e.g; a substance abuse program), mental health disorders (e.g; depression), or emotional distress. They might require assistance with securing and maintaining employment and housing as well as medical insurance status and adequacy of coverage. Women should be counselled or appropriately referred regarding reproductive choices and contraceptive options.
Starting ART
More than 20 approved ARV drugs in 6 mechanistic classes are available to design combination regimens. These 6 classes include the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors (FIs), CCR5 antagonists, and integrase strand transfer inhibitors (INSTIs).

A combination ART regimen generally consists of two NRTIs + one active drug from one of the following classes: NNRTI, PI (generally boosted with RTV), INSTI, or a CCR5 antagonist. Selection of a regimen should be individualized based on virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, and the patient’s comorbid conditions.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>Efavirenz*</td>
<td>Tenofovir*^</td>
<td>Lamivudine+**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abacavir**</td>
<td>Emtricitabine*^</td>
</tr>
<tr>
<td>Alternative</td>
<td>Lopinavir/r</td>
<td>Didanosine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fosamprenavir/r</td>
<td>Zidovudine+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atazanavir/r</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saquinavir/r</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specific groups</td>
<td>Nevirapine^^</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atazanavir++</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Choose one drug from columns A, B and C.
* Coformulated as Atripla (licensed for virologically suppressed patients only).
^ Coformulated as Truvada.
+ Coformulated as Combivir
** Coformulated as Kivexa
^^ Only when CD4<250 cells/µL in female patients and <400 cells/µL in male patients
++ Where there are established cardiovascular disease risk factors and a PI is required.

Initiating Antiretroviral Therapy in Treatment-Naive Patients
There have been recent changes to recommendations on initiation of ART in treatment-naive patients. This is due to increasing evidence showing the harmful impact of ongoing HIV replication on AIDS and non-AIDS disease progression. In addition, the updated recommendations reflect emerging data showing the benefit of effective ART in preventing
secondary transmission of HIV. The following recommendations have been accessed from: http://www.aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. as of September 2012.

ART is recommended for all HIV-infected individuals. The strength of this recommendation varies on the basis of pretreatment CD4 cell count:

- **CD4 count <350 cells/mm3 [A]**
- **CD4 count 350 to 500 cells/mm3 [AII]**
- **CD4 count >500 cells/mm3 [BIII]**

Regardless of CD4 count, initiation of ART is strongly recommended for individuals with the following conditions:

- Pregnancy [AI]
- History of an AIDS-defining illness [AI]
- HIV-associated nephropathy (HIVAN) [AI]
- HIV/hepatitis B virus (HBV) coinfection [AI]

Please refer to the latest treatment guidelines before initiating treatment.

Proper management of HIV infection requires medical therapy, which for many patients should be coupled with behavioural and psychosocial services. Comprehensive HIV treatment services are available at the CDC, TTSH and patients should be referred there upon diagnosis of HIV infection.

**PREVENTION**

**Safe sex activities:**
There are activities that avoid contact and exchange of body fluids and include hugging, stroking, mutual masturbation and kissing.

**Low risk activities:**
Vaginal and anal intercourse with condoms, oral sex with a condom.

**High risk activities:**
Vaginal and anal intercourse without a condom, oral sex without a condom.

**PARTNER NOTIFICATION**
HIV-infected patients should be encouraged to notify their partners and to refer them for counselling and testing. If the patient is unwilling to notify his/her partner, the first step should be for the doctor to make the notification. The doctor is empowered to do so under the Infectious Diseases Act (see section 25a). If the doctor is unable or unwilling to make the notification, then the case can be referred to the Ministry of Health.
POST-EXPOSURE PROPHYLAXIS (PEP) FOR SEXUAL CONTACT
There is no firm evidence to recommend for or against prophylaxis post-sexual or i/v exposure.

Please refer to chapter on HIV Post-Exposure Prophylaxis (PEP) for sexual contact.

References:


HIV POST-EXPOSURE PROPHYLAXIS (PEP) FOR SEXUAL CONTACT

The physician should assess the likelihood that HIV may be transmitted as a consequence of sexual exposure and advise the patient about the risks and benefits of treatment.

Appropriate counselling must be given, and if the decision is made to treat, follow up care for potential side effects of medication, repeat HIV testing and reinforcement of counselling messages must be done.

INTRODUCTION

Antiretroviral therapy (ART) offered as PEP has become the standard of care for healthcare workers who have had occupational exposure to HIV. A case-control study has demonstrated that PEP with zidovudine was associated with an 81% decrease in the odds of HIV transmission with a percutaneous exposure in the occupational setting. Although there is no data to show that ART is effective at preventing transmission from non-occupational exposures, the principles of managing patients with recent HIV exposure are similar whether the exposure occurs in an occupational or non-occupational setting. The data supporting ART NO-PEP is limited to animal studies and observational studies (with small sample sizes).

HIV Exposure Risk Assessment

A detailed and careful history of the exposure event is the first step in evaluating a patient.

Table 1 shows the risk of HIV transmission following a single percutaneous occupational, sexual, or injection drug exposure. Patients should be told that these are estimates, and in reality, the odds of infection with a specific exposure are hard to estimate because the risk of HIV transmission is affected by many factors such as the viral load of the infected person, presence of other sexually transmitted infections/genital ulcers, the size of the inoculum, and so forth. Certain sexual practices (receptive anal intercourse) carry much higher risk than others (insertive oral sex).

Generally, exposures to saliva, urine, tears and sweat are not thought to be infectious, and the risk of HIV transmission from splashes of contaminated fluids to mucosal surface or non-intact skin has not been accurately quantified, although it is likely to below.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Estimated Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle stick injury</td>
<td>1/300</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>1/100</td>
</tr>
<tr>
<td>Receptive vaginal intercourse</td>
<td>1/1000</td>
</tr>
<tr>
<td>Insertive vaginal intercourse</td>
<td>1/2000</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>1/2500</td>
</tr>
<tr>
<td>Receptive fellatio with ejaculation</td>
<td>1/2500</td>
</tr>
<tr>
<td>Sharing needles</td>
<td>1/150</td>
</tr>
</tbody>
</table>

Table 1. Estimated risks of HIV transmission per type of exposure
INDICATIONS FOR NO-PEP
The following criteria should be used:

- There is high-risk exposure (any unprotected anal or vaginal intercourse, receptive fellatio with ejaculation) with: (1) a partner known to be HIV-infected, or (2) in HIV-risk group (commercial sex workers, IV drug users, men who have sex with men/bisexual men), or (3) sexual assault
- Patient must be counselled and make a commitment to safer sex
- Patient must make an informed decision regarding potential risks and benefits of the treatment offered
- Exposure must have taken place within the last 72 hours, as initiating PEP after 72 hours is not advised

REGIMEN
The DSC clinic uses a drug combination of Combivir® (zidovudine 300mg/lamivudine 150mg) 1 tablet BID orally + Kaletra® (lopinavir 200mg/rtionavir 50mg) 2 tablets BID orally, both for a duration of 28 days. The cost to the patient is approximately $650 (at time of print).

SIDE EFFECTS
The drugs used can all cause GIT side effects i.e. nausea, diarrhoea, anorexia.

**Zidovudine:** most side effects are dose-related; major side effect is haematological - anaemia, granulocytopenia; pigmentation of nails reported.

**Lamivudine:** well-tolerated; rash, hair loss, vasculitis, photophobia, paraesthesia.

**Kaletra:** diarrhoea, nausea, headache, asthenia, rash, insomnia.

BASELINE TESTS AND FOLLOW UP
- Baseline HIV test is performed.
- Full blood count, liver and renal function tests; these will detect any pre-existing abnormality prior to treatment and can be repeated at 2 weeks.
- Patients should be seen after 4 weeks to document compliance and side effects of medication, as well as to reinforce prevention messages.

COUNSELLING PATIENTS
It is important to counsel patients that:

- There is no absolute proof that ART PEP decreases risk of HIV, although there is supportive evidence based on biologic plausibility, animal studies, observational studies and in a single study on HCW.
- The treatment is not 100% effective, as there have been documented cases of seroconversion after occupational exposures despite PEP.
- Side effects will be encountered with medication.
Most importantly, issues of safer sex and how to prevent future exposures must be addressed.

HIV testing should be performed at 1, 3, 6 months post-exposure.

References:


HUMAN PAPILLOMAVIRUS INFECTION

DEFINITION
Papillomaviruses are a group of small DNA viruses that have been detected in a large number of vertebrates; they induce epithelial cell proliferation and infections that are highly species-specific.

The human papillomavirus (HPV) causes cutaneous disease, genital warts, pre-cancerous lesions and ano-genital malignancies. Utilising nucleic acid hybridisation studies, > 100 HPV types are known, of which more than 30-40 infect the ano-genital area.

CLINICAL FEATURES
HPV infection occurs as:

1. Clinical lesions - condylomata acuminata, papular and flat warts
   • condyloma acuminata – exophytic, filiform, cauliflower-shaped warts, HPV types 6 and 11 in >90% of cases
   • multifocal - usually 5 to 15, in areas of trauma during sex, 1-10 mm diameter, may coalesce especially in immunosuppressed and in the presence of diabetes mellitus
   • may be coinfected with oncogenic “high-risk” HPV e.g. types 16 and 18
   • oncogenic HPV - mostly give rise to subclinical lesions, intraepithelial neoplasia (IN) and anogenital cancer

2. Subclinical lesions - only visible after application of acetic acid and magnification

3. Latent HPV infection defined when HPV DNA can be demonstrated in absence of clinical or histological evidence of infection.

LABORATORY TESTS
1. Subclinical mucosal warts can be identified by turning white (acetowhite) after application of 5% acetic acid for 3 minutes
2. This can be applied onto discrete as well as suspected sub-clinical lesions; the mechanism for this aceto-whitening effect is not clear. One hypothesis is that acetic acid causes a reversible coagulation of some epithelial and stromal proteins
3. Note that this whitening effect may also occur in areas of abrasions or non-specific inflammation, and may also be seen in other infections such as candidiasis, and thus is not specific for HPV infection
4. Skin biopsy - for atypical cases, cases where the benign nature of papular or macular lesions is unclear, cases not responding to treatment or worsening during treatment
5. HPV-DNA detection (according to CDC Atlanta: HPV tests are available for women aged >30 years undergoing cervical cancer screening. These tests should not be used for men, for women <20 years of age, or as a general test for STIs. These HPV tests detect viral nucleic acid (i.e., DNA or RNA) or capsid protein.)
TREATMENT
Anogenital warts display marked variability in their response to any mode of therapy; no treatment modality is completely satisfactory in eliminating HPV. The goal of treatment is to remove visible exophytic warts, not the eradication of HPV.
It is important to perform meatoscopy for meatal warts, proctoscopy for anal warts, and speculum examination with cervical cytology/colposcopy for female genital warts.

Recommended Regimens
Penile, Vulval and Perianal Warts

Home therapy

1. Podophyllotoxin (0.15% cream) [Ib, A]
   - purified non-mutagenic extract of podophyllum plant
   - binds to cell microtubules, inhibits mitosis, induces necrosis, maximal 3–5 days after application
   - b.i.d. x 3 days a week, rest 4–7 days
   - 60-80% clear after 1–4 courses, less successful for circumcised men
   - Recurrence rate ranges from 7–38%
   - S/E - transient burning, erythema, tenderness, erosions, usually after first course only, starting on day 3
   - Contraindicated in pregnancy; women of childbearing age must use contraception
   - It is recommended that the physician or nurse applies the first treatment to demonstrate the proper technique of application and to identify the warts to be treated

2. Imiquimod (5% cream) [Ib, A]
   - Imiquimod is an immune response modifier that induces a cytokine response, including the production of interferon-α, tumour necrosis factor-α, as well as interleukins 1, 6, and 8, when applied to skin infected with HPV. In animal models imiquimod has demonstrated antiviral, anti-tumour, and adjuvant activity
   - 3x a week at bedtime, washed-off next morning
   - Duration: until clearance or 16 weeks maximum
   - Therapeutic response may be delayed / slower than other modalities – (mean 7–8 weeks)
   - Clearance in 56% - women 77%, men 40% (better results in uncircumcised men)
   - Clinical trials show an encouragingly low recurrence rate - 10-15%
   - S/E - erythema, burning, erosions after 3–4 weeks
   - Not approved for use in pregnant women or internally
3. **Podophyllin 0.25% or 0.5% in ethanol [lb, A]**
   - Effective and inexpensive
   - Applied b.i.d x 3 days, rest 4 days and repeat cycle
   - Not to be used in pregnancy or internally

**Office therapy**

1. **Cryotherapy - Liquid nitrogen [lb, A]**
   - Epidermal and dermal necrosis, thrombosis of vessels
   - Weekly to fortnightly intervals, freeze-thaw-freeze cycle (-196°C)
   - Open application by spray or cotton swab
   - Simple, relatively inexpensive
   - Safe during pregnancy
   - S/E – oedema, blister formation, scarring, pigmentary changes
   - Initial response rate 63-89%

2. **Trichloroacetic acid (50%-80%) [lb, A]**
   - Caustic agent - causes cellular necrosis
   - For acuminate warts – anal, meatal, vaginal
   - Applied at weekly intervals
   - Safe during pregnancy
   - A small amount of the chemical is applied to the warts, taking care to avoid contact with clinically normal skin
   - As the product is allowed to dry, a white “frosting” develops
   - Application of TCA usually causes several minutes of mild to moderate discomfort at the site
   - Excessive amounts of unreacted acid should be washed off with liquid soap
   - Acid can be prevented from causing further damage if the entire treated area is quickly dusted with talc or sodium bicarbonate
   - Not effective for keratinized warts, not for large lesions, multiple sessions are not well tolerated
   - S/E - burning sensation for up to 10 minutes after application, ulceration and scarring (rare)
   - Initial response rate – 70-81%, recurrence rate – 36%

3. **Electrosurgery [lb, A]** with mask and smoke evacuator
   - Removal of warts under LA particularly useful for pedunculated warts, and small amounts of keratinized ones at anatomically accessible sites
4. **CO2 laser (10600 nm)** [Ila, B] with mask and smoke evacuator
   - Heats water to 100°C, evaporation of the cell, steam formation
   - Effective, precise, minimal tissue damage, good healing
   - Preferred treatment for lesions on the cervix and vagina
   - Expensive, healing 2–4 weeks

5. **Scissor or scalpel excision** [Ib, A]
   - Suturing not required
   [For surgical treatment modalities - 3, 4, 5, local infiltration anaesthesia, up to 5 ml of 2% lignocaine; proceeded by EMLA. Separation and elevation of lesions facilitates accurate removal, sparing of uninvolved skin. Adrenaline contraindicated on penis and clitoris. Usually eliminates warts at a single visit, recurrence 20-30%].

6. **Podophyllin 10% to 25% in compound tincture of benzoin** [Ib, A]
   - Paint on warts after protecting surrounding skin with vaseline, allow to dry;
   - Dust bismuth subnitrate powder on painted lesion to prevent contamination of surrounding skin
   - Wash off after 4-6 hours, repeat procedure 2x/week for 6 weeks
   - Consider alternative therapy if warts persist after 6 weeks
   - Crude extract, moderate efficacy, mutagenic properties unknown significance.
   - Reported systemic toxicity when used in large volumes (bone marrow suppression, CNS and CVS effects)
   - Limit to <0.5ml or <10 cm² per session
   - Avoid on cervix, anal canal, and in pregnancy [IV, C]

7. **5-Fluorouracil (5% cream)**
   - Use limited by high frequency and severity of local reactions (may appear 2-3 days later)
   - Possible use on intrameatal and intravaginal warts, and as an adjunct to laser therapy [II, B]
   - For urethral warts - apply after each micturition
   - Potentially teratogenic; advise contraception and avoidance in pregnancy
   - Presently not approved by US FDA as a treatment for warts (off-label indication)
   - Applied 1–3 times weekly for several weeks
   - Surrounding normal skin should be protected with a barrier ointment
   - Consult an expert before use

**Vaginal Warts**
CO2 laser or Electrosurgery or Trichloroacetic acid (TCA) or Cryotherapy
Cervical Warts
- Dysplasia must be excluded before starting treatment, cervical cytology and colposcopy (if necessary) are advised
- CO2 laser or Electrocautery or Cryotherapy
- Podophyllin and podophyllotoxin are not recommended for treating cervical warts

Meatal Warts
- Cryotherapy or Electrocautery or Podophyllotoxin 0.5% or podophyllin 0.25% in ethanol or 5-Fluorouracil 5% cream
- Refer to urologist for management in refractory or extensive cases which extend beyond the meatoscope.

Anal Canal Warts
- Cryotherapy or Trichloroacetic acid or Electrocautery or Surgical excision

Genital warts in pregnancy
- Imiquimod, podophyllin and podophyllotoxin should not be used in pregnancy
- Genital warts should be removed in pregnancy because they can proliferate and become friable
- There is also a risk (1 in 400) of transmission to the infant leading to laryngeal papillomatosis

Genital warts in the immunosuppressed
- Immunosuppressed patients with warts do not respond as well to treatment, and may have more frequent recurrences after treatment. Squamous cell carcinomas arising in warts may occur more frequently, requiring biopsy for confirmation of diagnosis

Vaccine
- A quadrivalent HPV L1 virus-like particle vaccine has been approved by the FDA for the prevention of cervical cancer in women. Gardasil® (Merck) has been shown in trials to be effective in protecting against acquisition of HPV infection by HPV 6 and 11 (which causes the majority of genital warts) as well as HPV 16 and 18 (which are associated with 70% of cervical cancers)
- 3 intramuscular injections are required; the second dose is administered 2 months later and the third dose after 6 months
- Universal HPV vaccination may be most effective when implemented in pre-coitarche children, who are likely to be HPV negative

FOLLOW-UP
- Provide clear information - cause, treatment, outcomes, possible complications.
- Reassure - complete clearance will occur sooner or later
- Advise smoking cessation for recalcitrant warts
- Regular cervical cytology (PAP smears) for females
- Condoms - with new partners till clearance is achieved; regular partner already exposed
• Long latency periods mean that only one partner in a relationship may manifest warts.
• Current partners and recent (6 month) partners should be assessed for HPV and other STI

**MANAGEMENT OF SEXUAL CONTACTS**

All regular contacts should be examined and clinical warts treated.

**References:**


LYMPHOGRANULOMA VENEREUM (LGV)

DEFINITION
LGV is a sexually-transmitted infection caused by the L1, L2 and L3 serovars of *Chlamydia trachomatis*.

CLINICAL FEATURES
It presents with a transient genital ulcer and inguinal lymphadenitis (bubo) which is usually unilateral and becomes fluctuant. The genito-anorectal syndrome presents with lower abdominal pain and dyspareunia in females and in MSM. The most common clinical manifestation of LGV among heterosexuals is tender inguinal and/or femoral lymphadenopathy that is typically unilateral. A self limited genital ulcer or papule sometimes occurs at the site of inoculation. However, by the time patients seek care, the lesions have often disappeared. Rectal exposure in women or MSM can result in proctocolitis, including mucoid and/or haemorrhagic rectal discharge, anal pain, constipation, fever, and/or tenesmus.

LABORATORY TESTS
- Serological tests – LGV CFT: single titre of 1:64 or more is significant or a rising titre over 2 weeks with the appropriate clinical presentation
- Culture of the chlamydial organism from lymph node aspiration
- NAATs for Chlamydia trachomatis should also be done from the appropriate clinical sites as well as urine.

TREATMENT
LOCAL TREATMENT
Aspirate the fluctuant buboes. Insert needle through the normal skin to prevent chronic sinus formation.

SYSTEMIC TREATMENT
*Recommended regimens*
1. Doxycycline 100 mg orally bid x 3 weeks [III, B]
   or
2. Erythromycin 500 mg orally qid x 3 weeks [III, B]

*Alternative regimens*
1. Tetracycline HCl 500 mg orally qid x 3 weeks
   or
2. Azithromycin 1 g orally weekly x 3 weeks

FOLLOW-UP
Treatment should be continued till clinical signs improve.
MANAGEMENT OF SEXUAL CONTACTS
Persons who have had sexual contact with a patient within 30 days before onset of patient’s symptoms should be examined and treated when indicated.

Special Considerations

Pregnancy
Pregnant and lactating women should be treated with erythromycin. Azithromycin may prove useful for treatment of LGV in pregnancy. Tetracycline and doxycycline are contraindicated in pregnant women.

HIV Infection
Persons with both LGV and HIV infection should receive the same regimens as those who are HIV-negative. Prolonged therapy may be required, and delay in resolution of symptoms may occur.

References:
MALE GENITAL SYNDROMES

ACUTE EPIDIDYMO-ORCHITIS

DEFINITION
Acute epididymo-orchitis is a clinical syndrome consisting of pain, swelling and inflammation of the epididymis +/- testes. The most common route of infection is local extension and is mainly due to infections spreading from the urethra (sexually transmitted pathogens) or the bladder (urinary pathogens).

Sexually acquired pathogens
- *N. gonorrhoeae*
- *C. trachomatis*

Non-sexually acquired pathogens
- *E. coli*
- *P. aeruginosa*
- Mumps – ask for history of mumps vaccination (MMR)
- Others including *M. tuberculosis*

Non infectious causes of testicular pain
- Trauma
- Testicular torsion - sudden onset of severe pain, absence of urethritis or urine abnormalities, younger patients

DIAGNOSIS
Acute epididymo-orchitis due to sexually acquired pathogens is suspected in the following situations:
- Characteristically unilateral scrotal pain and swelling of relatively acute onset
- Palpable tender swelling of the epididymis starting with the tail at the lower pole of the testis and spreading towards the head at the upper pole of the testis +/- involvement of the testicle
- Sexually active male below 35 years of age
- Recent sexual exposure (within 4 to 6 weeks)
- Multiple sex partners
- Recent treatment for urethritis
- Presence of symptoms or signs or microscopic evidence of urethritis
- No recent history of urinary tract infection, urogenital surgery, catheterisation or instrumentation
- No past history of urogenital abnormalities or pathology
- Torsion of the spermatic cord (testicular torsion) is the most important differential diagnosis
DIFFERENTIAL DIAGNOSES OF TESTICULAR ENLARGEMENT AND SCROTAL SWELLING

- Testicular torsion
  - This is a surgical emergency. It should be considered in all patients and should be excluded first as testicular salvage **IS REQUIRED WITHIN 6 HOURS** and becomes decreasingly likely with time.
  - The testis may be swollen, tender, high-riding with a horizontal lie. The cremasteric reflex is also absent.
  - If testicular torsion cannot be excluded, refer the patient to A&E immediately.
- Spermatocele
- Hydrocele
- Testicular trauma
- Indirect inguinal hernia
- Testicular cancer

The following tests should be performed:
- Urethral Gram-stained smear and culture for *N. gonorrhoeae*
- First void urine (FVU) or urethral smear for NAAT for *C. trachomatis* and *N. gonorrhoeae*
- Mid-stream urine (MSU) - microscopic examination and culture

All patients with sexually transmitted epididymo-orchitis should be screened for other STIs.

All patients with urinary tract pathogen confirmed epididymo-orchitis should be investigated for structural abnormalities and urinary tract obstruction by an urologist.

**TREATMENT**

As identification and isolation of causative agents may not always be easy and immediate, all patients with acute epididymo-orchitis suspected to be sexually-acquired should be treated with drugs that are effective against both gonococcal and chlamydial infections as they may occur concurrently. Empiric therapy is indicated before laboratory test results are available.

**Recommended regimens**

*Infections due to sexually-transmitted pathogens*

Ceftriaxone 500 mg i/m x 1-3 days **[III, B]**

plus:
1. Doxycycline 100 mg orally bid x 10 -14 days **[III, B]**
   or
2. Erythromycin 500 mg orally qid x 10 - 14 days
Infections due to non-sexually-transmitted pathogens

1. Ofloxacin 200 mg orally bid x 10-14 days [IIb, B]
   or
2. Ciprofloxacin 500 mg orally bid x 10 - 14 days [Ib, A]

(If enteric organisms are suspected, or if the patient is allergic to cephalosporins or tetracyclines)

Adjunctive therapy includes bed rest, scrotal elevation and analgesia e.g. NSAIDS. Corticosteroids have not been shown to be useful.

FOLLOW-UP
If there is no improvement in the patient’s condition after 3 days, the diagnosis should be reassessed and therapy re-evaluated. Further follow-up is recommended at 2 weeks to assess compliance with treatment, partner notification and improvement of symptoms. Where there is little improvement further investigations such as an ultrasound scan or surgical assessment should be considered.

MANAGEMENT OF SEXUAL PARTNERS
All sex partners of patients with sexually-transmitted epididymo-orchitis within the preceding 60 days should be referred for examination and treated where indicated.

References:


NON-GONOCOCCAL URETHRITIS (NGU)

DEFINITION
Nongonococcal urethritis (NGU), which is diagnosed when examination findings or microscopy indicate inflammation without Gram-negative intracellular diplococci, is caused by *C. trachomatis* in 15–40% of cases. *M. genitalium* accounts for 15–25% of NGU cases with *T. vaginalis*, HSV, and adenovirus being less common pathogens. Enteric bacteria have been identified as an uncommon cause of NGU and might be associated with insertive anal intercourse. Recent studies have shown that no pathogens can be isolated in up to 60% of the cases.

CLINICAL FEATURES
- Symptoms: Urethral discharge, dysuria, penile irritation or none
- Signs: Urethral discharge. This may not have been noticed by the patient or may only be present on urethral massage. Examination may be normal
- Complications: Epididymo-orchitis and sexually acquired reactive arthritis / Reiter’s syndrome. These are infrequent, occurring in fewer than 1% of cases

DIAGNOSIS
The diagnosis of urethritis must be confirmed by demonstrating Peripheral Blood Mononuclear Leukocytes (PMNLs) in the anterior urethra.

- This can be by means of:
  (i) A Gram stained urethral smear containing ≥5 PMNL per high-power (x1000) microscopic field (averaged over five fields with greatest concentration of PMNLs) The specimen should be taken at 4 hours after the last micturation
  (ii) A Gram stained preparation from a centrifuged sample of a first passed urine (FPU) specimen, containing ≥10 PMNL per high-power (x1000) microscopic field (averaged over five fields with greatest concentration of PMNLs)

- There is little justification in performing urethral microscopy in asymptomatic men [IIb]

- NAAT for *C. trachomatis* should be done

- A negative test for *N. gonorrhoeae* with either culture or NAAT

- The traditional two-glass test adds little to the diagnosis and should be abandoned [IV]
MANAGEMENT

General Advice

The following should be discussed and clear written information provided:

- An explanation of the causes of NGU, including non-infective causes, and possible short term and long-term implications for the health of the patient and his partner
- The side-effects of treatment and the importance of complying fully with it
- The importance of their sex partner(s) being evaluated and treated
- Advice to abstain from sexual intercourse, or if that is not acceptable, the consistent use of condoms, until he has completed therapy and his partner(s) have been treated. [IV]
- Advice on safer sex
- The importance of complying with any follow-up arrangements made
- It is important to note that the inflammatory exudate may persist for an unknown length of time even when the putative organism has been eliminated

Recommended Regimens

- Doxycycline 100 mg twice daily orally for 7 days [A, Ib]
  or
- Azithromycin 1g orally in a single dose [A, Ib]
  or
- Erythromycin 500mg twice daily for 14 days [A, Ib]
  or
- Ofloxacin 200mg twice daily or 400mg once a day for 7 days [A, Ib]

Single dose therapy has the advantage of improved compliance although azithromycin has not been shown to be more effective in clinical studies than doxycycline.

FOLLOW-UP

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

Sexual contacts/partners

All sexual partners at risk within the last 60 days should be assessed and offered epidemiological treatment whilst maintaining patient confidentiality. These partners should also be examined to exclude other associated STI. At least 30% of consorts of men with NGU have chlamydial infections of the cervix 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.

Persistent/Recurrent NGU

This is empirically defined as persistent or recurrent symptomatic urethritis occurring 30-90 days following treatment of acute NGU and occurs in 10-20% of patients.

Its aetiology is probably multifactorial. M. genitalium may be implicated in 20-40%. A role for U. urealyticum in chronic NGU has also been suggested.
Any treatment of chronic NGU should cover *M. genitalium* and *T. vaginalis* which are not covered by standard therapy [IV].

**Diagnosis of Persistent/Recurrent NGU**
The patient must have definite symptoms of urethritis, or physical signs on examination. There must be objective evidence of urethritis e.g. presence of urethral discharge or pus cells on urethral smear. Reassure asymptomatic patients that no further test or treatment is necessary.

Exclude drug adherence failure or re-infection from untreated partner or a new partner

Azithromycin 1g in a single dose [C, IIIb] plus Metronidazole 400 mg orally BID for 7 days [C, IV]  
*or*  
Erythromycin 500 mg orally QID for 2 weeks [C, Ib] plus Metronidazole 400mg orally BID for 7 days [C, IV]  
*or*  
Moxifloxacin 400mg orally OD daily for 10 days [C, IIIb] plus Metronidazole 400mg orally BID for 7 days [C, IV]

Not cured

Azithromycin 500mg stat then 250mg for the next 4 days [C, IIIb]

Not cured

Doxycycline 100 mg orally BID for 4 to 6 weeks [C]  
*or*  
Erythromycin 500 mg orally QID for 4 to 6 weeks [C]

Not cured

Exclude prostatitis, urethral stricture and intraurethral lesions (consider referral to a urologist)

Normal findings

No further antimicrobial treatment, observe and reassure  
Avoid repeated courses of antimicrobials and overinvestigation.  
Urological investigation is usually normal unless the patient has urinary flow problems.
Explain and reassure the patient that:

- the physical sequelae of persistent NGU such as infertility are slight
- the risk of transmission is low because repeated courses of antibiotics would have eliminated infective causes
- even without treatment symptoms will usually resolve with time
- most of the recurrences arise independent of resumption of sexual activity

References:

PROSTATITIS

ACUTE PROSTATITIS
Acute prostatitis is caused by urinary tract pathogens. These include gram-negative organisms: most commonly Escherichia coli, Proteus spp, Klebsiella spp and Pseudomonas spp; Enterococci; Staphylococcus aureus; rarely anaerobes such as Bacteroides spp. Acute prostatitis is an uncommon complication of Urinary Tract Infection (UTI).

CLINICAL FEATURES
Acute prostatitis is an acute severe systemic illness.

Symptoms include:
- symptoms of a UTI: dysuria, frequency and urgency
- symptoms of prostatitis: low back pain, perineal, penile and sometimes rectal pain
- symptoms of bacteraemia: fever and rigors; arthralgia and myalgia may occur

Signs include:
- signs localised to the prostate: an extremely tender, swollen and tense, smooth textured prostate gland which is warm to the touch
- signs of bacteraemia: pyrexia and tachycardia

Complications: acute retention of urine (ARU) secondary to prostatic oedema, prostatic abscess, bacteraemia, epididymitis and pyelonephritis.

DIAGNOSIS
- Mid-stream urine sample for dipstick testing, culture for bacteria and antibiotic sensitivity
- Blood cultures for bacteria and antibiotic sensitivity
- Prostatic massage should not be performed. It is extremely painful may possibly precipitate bacteraemia and is of little benefit as pathogens are almost always isolated from urine

MANAGEMENT

General Advice
Adequate hydration should be maintained, rest encouraged and analgesia prescribed such as NSAIDs.

TREATMENT
- Empirical therapy should be started immediately
- Parenteral or oral treatment should be selected according to the clinical condition of the patient. If there is deterioration or failure to respond to oral therapy, urgent admission and parenteral therapy should be arranged
• Good antibiotic penetration into all areas of the prostate gland is achieved because of the intense inflammation
• Antibiotics should be continued or changed according to sensitivity results
• If ARU occurs, suprapubic catheterisation should be performed to avoid damage to the prostate

**Recommended Regimens**

For patients requiring parenteral therapy, antibiotics covering the likely organisms should be used:

- High-dose cephalosporins – eg cefuroxime, cefotaxime or ceftriaxone plus gentamicin \[\text{IV, C}\]
- When clinically improved, the therapy can be switched to oral treatment according to sensitivities.

For patients suitable for oral therapy, quinolones can be used:

- Ciprofloxacin 500 mg orally bid for 28 days \[\text{IV, C}\]
  - or
- Ofloxacin 200 mg orally bid for 28 days \[\text{IV, C}\]

**Allergy**

For patients intolerant of, or allergic to quinolones, an alternative is:

Co-trimoxazole (trimethoprim/sulfamethoxazole) 160/800mg (2 tabs) orally bid for 28 days.

**MANAGEMENT OF SEXUAL CONTACTS**

Treatment of sexual partners is not required as it is caused by uro-pathogens.

**FOLLOW-UP**

If the patient fails to respond fully to therapy, the diagnosis of a prostatic abscess should be considered. This can be confirmed by a trans-rectal ultrasound scan or computed tomography scan of the prostate gland. Refer the patient to Urology for further evaluation and treatment.

If acute prostatitis is managed correctly, the prognosis is good and a cure is likely. At least 4 weeks of antibiotic therapy is recommended in all patients to prevent chronic bacterial prostatitis.

When the patient has recovered, the urinary tract should be investigated to exclude a structural cause for urinary tract infection. Consider referring the patient to Urology.

**Chronic Prostatitis**

Chronic prostatitis can be differentiated into the following:

**Chronic bacterial prostatitis (CBP)**

**Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)**

- **Inflammatory**
- **Non-inflammatory**
Chronic Bacterial Prostatitis (CBP)
This is chronic bacterial infection of the prostate with or without symptoms of prostatitis, and with a history of recurrent urinary tract infections caused by the same bacterial strain without any structural abnormalities. It is rare in comparison to CP/CPPS.

The usual causative bacteria are those causing urinary tract infection, most commonly Escherichia coli. Some Gram positive organisms such as Staphylococcus aureus and Enterococcus faecalis may cause CBP.

Clinical Features
• Symptoms
  - History of recurrent or relapsing urinary tract infection, urethritis or epididymitis
  - Patients frequently report genitourinary and pelvic pain / discomfort during a flare-up and alleviation of symptoms after antibiotic treatment
  - They may be asymptomatic between acute episodes or have mild pelvic pain or irritative voiding symptoms (frequency, urgency)
• Signs
  - Apyrexial, no systemic signs
  - The patient may have a diffusely tender prostate during acute episodes; otherwise no objective clinical signs

Diagnosis
• This is usually based on history of recurrent urinary tract infections by the same bacterial strain and the exclusion of other causes
• In particular, no structural reason for recurrent urinary tract infection is identified on urinary tract imaging.

Investigations
Consider referral to Urology for evaluation
1. Urine dipstick test (for evidence of urinary tract infection or other abnormality that may require investigation e.g. haematuria).
2. MSU - urine cultures are sterile unless an acute urinary tract infection is present - review past MSU results.
3. Urinary tract imaging (ultrasound or IVU) to exclude structural abnormalities.
4. Urodynamics – may be considered, to exclude other conditions predisposing to recurrent UTI.
MANAGEMENT

GENERAL ADVICE
Patients should be given a detailed explanation of their condition – that the prostate is a focus of infection which causes recurrent urinary tract infection with particular emphasis on the long-term implications for their health and the possibility of further episodes of urinary tract infection unless the focus is eradicated by successful treatment.

TREATMENT
Antibiotic treatment should be chosen according to bacterial cultures and sensitivities. Fluoroquinolones have become the standard of care in CBP [Ib, A] – they have good penetration of the prostate gland and broad spectrum activity against both gram-negative and gram-positive organisms.

RECOMMENDED REGIMENS
For patients with CBP first-line treatment is with a quinolone such as

- Ciprofloxacin 500mg orally bid for 28 days [Ib, A]
- Levoﬂoxacin 500mg orally od for 28 days [Ib,A]
- Ofloxacin 200mg orally bid for 28 days [III, B]
- Norﬂoxacin 400mg orally bid for 28 days [III, B]

For those allergic to quinolones or in patients recommended to avoid quinolones (epilepsy or prone to seizures) treatment should be selected according to antibiotic sensitivities of the bacterial isolate, and an antibiotic with good penetration into the prostate should be chosen.

Options include:

- Minocycline 100mg orally bid for 28 days [III, B] (In practice most experts would use doxycycline 100mg orally bid for 28 days because of more toxicity with minocycline.)
- Trimethoprim 200mg orally bid for 28 days [IV,B]

Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS)
This is a common chronic condition with estimates of between 2 and 14% lifetime prevalence. It cannot be rigidly defined but a suggested definition is the presence of typical symptoms of discomfort or pain in the genital or pelvic region for > 3 months within the past 6 months.
AETIOLOGY
Unknown aetiology; it may be multifactorial.

Proposed mechanisms include:

- Infection (there is no evidence that CPPS is caused by STI)
- Immunological
- Auto-immunity
- Neuromuscular spasm/pelvic floor muscle dysfunction
- Intra-prostatic urine reflux
- Voiding dysfunction leading to increased intra-prostatic pressure
- Neurogenic inflammation
- Functional somatic syndrome
- Chronic pain syndrome

CLINICAL FEATURES

- Symptoms: Perineal pain, lower abdominal pain, penile pain (especially penile tip), testicular pain, rectal and lower back pain and ejaculatory pain
- The constellation of symptoms appears to be relatively similar and consistent in men with CP/CPPS
- Signs: There are few objective clinical signs and the prostate gland may, or may not, be locally or diffusely tender to palpation
- Complications: Significant physical and psychological impact

Exclusion criteria for the diagnosis:
Active urethritis, urogenital cancer, urinary tract disease, functionally significant urethral stricture or neurological disease affecting the bladder.

Diagnosis

- Consider referral to Urology for evaluation and management
- There is no gold standard diagnostic test for this condition; therefore CP/CPPS is a diagnosis of exclusion
- Diagnosis is usually made on a typical history and not on examination or investigation findings
- Initial screening should involve taking a complete history, examination including digital rectal examination, urinalysis and MSU microscopy and culture
- Lower urinary tract localisation study (four-glass test)/Prostatic Massage
  - This is no longer recommended as recent studies have reported that localising leucocytes/bacteria to the prostate cannot accurately differentiate between men with CP/CPPS and men without symptoms, and results of the test do not correlate with duration, frequency and severity of symptoms
Further tests that may be considered:

- Urine cytology
  - If the patient has microscopic haematuria with frequency, urgency and dysuria urine cytology should be performed to help exclude lower urinary tract malignancy
  - Patients with unexplained haematuria should be referred to an urologist
- PSA
  - PSA is recommended if indicated by an abnormal prostate on digital rectal examination. Prostatic tenderness is not an indication
  - PSA can be elevated during active inflammation of the prostate
- Simple urodynamics
  - This may identify bladder neck dysfunction, bladder outflow obstruction and incomplete bladder emptying particularly in those with urinary symptoms
- Transrectal ultrasound (TRUS)
  - This is not useful in differentiating the various forms of chronic prostatitis
  - TRUS may identify prostatic calcification but the significance of this is uncertain. Anecdotal reports indicate that TRUS may rarely identify a treatable prostatic abscess or cyst, seminal vesicle or ejaculatory duct abnormality (which may present with ejaculatory pain), but its routine use in the investigation of suspected CP/CPPS is not justified

MANAGEMENT

GENERAL ADVICE
Patients should be given a detailed explanation of their condition with reassurance, indicating that CP/CPPS is a non-malignant condition and not a sexually transmitted infection that has a tendency to persist.

TREATMENT
There are no reliably effective treatments for CP/CPPS. No large scale, well-designed trials have been conducted. Treatment should be individualised as CP/CPPS is not a standardised disease or specific inflammatory process but rather a clinical syndrome.

- Antibiotics [III,C]
  - There is no convincing evidence that antibiotics are effective in CP/CPPS. Two recent RCTs have shown no benefit of antibiotics versus placebo but both of these studies were in heavily pre-treated patients. The value of antibiotic treatment in treatment naive men has not been assessed.
• Alpha-blockers [Ia, A]
  - There is modest evidence of their efficacy in CP/CPPS and a trial should be considered in patients with troublesome persistent symptoms. The evidence suggests prolonged treatment is needed (14-24 weeks) to show a clinically significant effect and benefits appear greatest in those naïve to alpha-blockers.
  - RCTs where benefit was found included the following drugs and doses:
    • Alfuzosin 5mg bd for 6 months
    • Tamsulosin 0.4mg for 6 weeks
    • Terazosin
      ▪ 1mg for 4 days, 2mg for 10 days then 5mg for 12 weeks (14 weeks total)
      ▪ 5mg for 8 weeks
      ▪ 1-2mg tds for 6 months
    • Doxazosin 4mg daily for 6 months

MANAGEMENT OF SEXUAL CONTACTS
Partner notification and empirical treatment is not required unless a specific sexually transmitted pathogen is found at initial screening. Management should be according to the guidelines for that specific infection.

FOLLOW-UP
Chronic prostatitis is a difficult to manage, relapsing condition and patients are typically followed up for long periods of time. No specific follow-up recommendations can be made.

References:


MOLLUSCUM CONTAGIOSUM

DEFINITION
Molluscum contagiosum is a viral infection caused by a pox virus. Genital molluscum infections in adults are usually sexually-transmitted.

CLINICAL FEATURES
Individual lesions of molluscum contagiosum are discrete, smooth, pearly or flesh-coloured, dome-shaped papules and are often confined to the genital area. Each papule may have a mildly erythematous base and a central punctum beneath which lies a white curdlike core.

In patients with extensive facial lesions, HIV screening should be considered. In immunocompromised patients, lesions may become large, exuberant, and unsightly and secondary infection may be a problem. In immunocompromised patients, cutaneous lesions of infections such as histoplasmosis, penicilliosis or cryptococcosis can also resemble molluscum

LABORATORY TESTS
Giemsa-stained smears of the expressed core from the punctum or a skin biopsy will demonstrate molluscum bodies.

TREATMENT

Recommended Treatment

- Deroof the lesion with a sharp curette, a comedone extractor or a needle
- Destroy the remaining lesion with liquid nitrogen, trichloroacetic acid application or electrocautery [IV, C]
- More than one treatment session may be required

Others
Imiquimod has been used in the treatment of molluscum contagiosum, both on genital and nongenital sites. Presently, this is still considered an ‘off-label’ indication [Ib, A].

MANAGEMENT OF SEXUAL CONTACTS
Regular sex partners should be encouraged to come for examination and treatment, where indicated.

References:
FEMALE GENITAL SYNDROME

MUCOPURULENT CERVICITIS

DEFINITION
Mucopurulent cervicitis (MPC) is defined as the presence of mucopurulent discharge from the endocervix, this appears yellow on a cotton-tipped swab. There is often oedema, erythema and contact bleeding of the cervix. A Gram-stained endocervical smear which shows ≥ 30 cells per high power field (1000X) is significantly correlated with gonococcal or chlamydial infection.

AETIOLOGICAL AGENTS
- Neisseria gonorrhoeae
- Chlamydia trachomatis
- Herpes simplex virus
- Trichomonas vaginalis
- Bacterial vaginosis
- Mycoplasma genitalium

TREATMENT
If *N. gonorrhoeae* is found on Gram-stain or culture
- Treat as for uncomplicated gonorrhoea in adults (see page 25)
  - With co-treatment for chlamydial infection (see page 21)

If *N. gonorrhoeae* is not found
- Treat as that for chlamydial infection with
  - Azithromycin 1g orally single dose
  - or
  - Doxycycline 100mg orally bid x 7 days

If M. genitalium is found
- Treat with Azithromycin 500mg orally single dose on day 1 followed by Azithromycin 250mg orally od x 4 days [C, IIIB]
- Moxifloxacin 400mg OD x 10 days [C,IIIB]

**Note:** Treatment of mucopurulent cervicitis in HIV-infected women is important because cervicitis increases cervical HIV shedding. Treatment of cervicitis in HIV-infected women reduces HIV shedding from the cervix and might reduce HIV transmission to susceptible sex partners.

FOLLOW-UP
Culture for test-of-cure 14 days after treatment for *N. gonorrhoeae*. 
MANAGEMENT OF SEXUAL CONTACTS

Management of sex partners of women treated for MPC should be appropriate for the identified STI. All male sex partners within 60 days should be evaluated and treated for N. gonorrhoeae, C. trachomatis, T. vaginalis and M. genitalium.

References:


PELVIC INFLAMMATORY DISEASE

DEFINITION
Pelvic Inflammatory Disease (PID) is a clinical syndrome comprising of a spectrum of inflammatory disorders of the upper genital tract in women. PID usually results from infection ascending from the cervix causing endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abscess and pelvic peritonitis.

AETIOLOGICAL AGENTS
The aetiology of PID is often polymicrobial.

Sexually-transmitted pathogens
- *N. gonorrhoeae*
- *C. trachomatis*
- *Mycoplasma genitalium*
- *Mycoplasma hominis*
- *Ureaplasma urealyticum*

Non-sexually transmitted pathogens
- Anaerobic bacteria
- *Gardnerella vaginalis*
- Gram-negative rods
- Streptococci

DIAGNOSIS
Individual symptoms alone are of little diagnostic value. Combinations of clinical symptoms and signs are of greater value.

A confirmatory diagnosis of salpingitis is made by laparoscopy. Since laparoscopy is not always available, the diagnosis of PID is often based on imprecise clinical findings and culture, antigen detection tests or NAATs of specimens obtained from the lower genital tract.

Empirical treatment of PID should be started in sexually active women and those at risk of STIs if they are experiencing pelvic or lower abdominal pain (if no cause for the illness other than PID can be identified) and if one or more of the following minimum criteria are present on pelvic examination:

- Abdominal tenderness on palpation with or without rebound tenderness
- Cervical motion tenderness on bimanual vaginal examination
- Uterine/adnexal tenderness on bimanual vaginal examination
Additional criteria that support a diagnosis of PID include the following:
- Cervical infection with *N. gonorrhoeae* or *C. trachomatis*
- Fever > 38°C
- Abnormal cervical or vaginal mucopurulent discharge
- Abnormal vaginal bleeding, including post coital, inter-menstrual bleeding and menorrhagia
- Deep dyspareunia
- Presence of WBCs on saline microscopy of vaginal secretions
- Elevated erythrocyte sedimentation rate
- Elevated C-reactive protein
- Pelvic abscess or inflammatory complex detected by bimanual examination or by ultrasound

The most specific criteria for diagnosing PID include:
- Endometrial biopsy with histological evidence of endometritis
- Transvaginal ultrasound or MRI showing thickened, fluid filled tubes, with or without free pelvic fluid or tubo-ovarian complex
- Laparoscopic abnormalities consistent with PID

**TREATMENT**

The treatment regimens are empiric and should provide broad spectrum cover for *N. gonorrhoeae*, *C. trachomatis*, Gram-negative bacteria, anaerobes, *Group B streptococcus* and the genital mycoplasmas.

**OUTPATIENT TREATMENT** (for patients not requiring hospitalisation)

*General Advice*

1. Rest and analgesia **[IV, C]**
2. Consider removal of IUD (The decision to remove the IUD must be balanced against the risk of pregnancy in those who have had otherwise unprotected intercourse in the preceding 7 days)

*Recommended regimens*

Delaying treatment increases the risk of damage to the reproductive health of women and long term sequelae e.g ectopic pregnancy, infertility and pelvic pain. Therefore a low threshold for empiric treatment of PID is recommended.

1. Ceftriaxone 500mg i/m single injection **[Ib, A]**
   with
   Doxycycline 100mg orally bid x 14 days **[Ib, A]**
   and
   Metronidazole 400mg orally bid x 14 days **[Ib, A]**
2. Ofloxacin 400mg orally bid x 14 days [lb, A] or
   Levofloxacin 500mg orally once daily x 14 days [lb, A] with
   Metronidazole 400 mg orally bid x 14 days [lb, A]

Notes:
Ceftriaxone may be substituted by Cefoxitin 2gm i/m with Probenecid 1gm orally, or Cefotaxime 500mg i/m with Probenecid 1gm orally, or equivalent cephalosporin.

Doxycycline may be substituted by Tetracycline HCl 500mg orally qid x 14 days, or by Erythromycin 500mg qid x 14 days. However, it should be noted that erythromycin is inactive against M hominis.

Ofloxacin should be avoided in patients who are at high risk of gonococcal PID because of increasing quinolone resistance.

Patients who do not respond to oral therapy within 72 hours should be re-evaluated to confirm the diagnosis and given parenteral therapy.

INPATIENT TREATMENT
This is indicated when -
- The diagnosis is uncertain
- Surgical emergencies e.g. appendicitis and ectopic pregnancies, cannot be excluded
- A pelvic abcess is suspected
- The patient is pregnant
- Severe symptoms and signs (including nausea and vomiting) preclude outpatient treatment
- Poor response to previous antibiotics
- Clinical follow-up within 72 hours of starting treatment cannot be arranged
- The patient is immunodeficient

Recommended regimens
1. Cefotetan 2g i/v bid [lb, A] or
   Cefoxitin 2gm i/v qid [lb, A] with
   Doxycycline 100mg orally or i/v bid [lb, A]
2. Clindamycin 900mg i/v tid [lb, A]
   with
   Gentamicin loading dose i/v or i/m 2mg/kg followed by a maintenance dose 1.5mg/kg tid [lb, A]
   with
   Doxycycline 100mg orally or i/v bid [lb, A]

The above regimens are given continuously for 24 hours after the patient improves clinically.

After discharge from hospital, continuation of:
   - Doxycycline 100mg orally bid x total of 14 days [lb, A]
   - or
   - Clindamycin 450mg orally qid x total of 14 days [lb, A]
   - with
   - Metronidazole 400mg orally bid x total of 14 days [lb, A]

**Alternative Regimens**

1. Ofloxacin 400mg i/v bid x 14 days [III, B]
   with
   Metronidazole 500mg i/v tid x 14 days [III, B]

2. Ciprofloxacin 200mg i/v bid x 14 days [III, B]
   with
   Doxycycline 100mg orally or i/v bid x 14 days [III, B]
   and
   Metronidazole 500mg i/v tid for 14 days [III, B].

**Pregnant women with PID** - should be hospitalised and treated with parenteral antibiotics.

**HIV positive women with PID** - should be hospitalised and treated with parenteral antibiotics.

**FOLLOW-UP**

Evaluate daily for inpatients or within 72 hours for outpatients. Failure to respond (defervescence, reduction in direct or rebound tenderness, reduction in adnexal, uterine and cervical tenderness) is an indication for hospitalisation.

Test-of-cure after 5 days and 14 days after the start of treatment for *N. gonorrhoeae*. Repeat testing for *C. trachomatis* may be indicated after 3 weeks.

Removal of IUCD is indicated soon after antimicrobial therapy for gonorrhoea or chlamydial infection.
MANAGEMENT OF SEXUAL CONTACTS
Male partners of women with PID caused by *N. gonorrheae* or *C. trachomatis* are often asymptomatic. Partners who had sexual contact with the patient during the 60 days before the onset of symptoms should be screened for STIs and empirically treated with regimens effective against *N. gonorrheae* and *C. trachomatis*.

References:
VULVOVAGINITIS

The symptoms of vaginitis include vaginal discharge, vulval itch or irritation and vaginal odour. Clinically, there may be an abnormal vaginal discharge, vaginal and vulval erythema and/or oedema.

AETIOLOGICAL AGENTS

- *Trichomonas vaginalis*
- *Candida albicans*
- *Gardnerella vaginalis* and anaerobic organisms

INVESTIGATIONS

1. pH of the vaginal discharge
2. Microscopic examination of a wet mount and Gram-stained specimen of vaginal fluid
3. Whiff test (a fishy odour after the addition of 10% KOH to the vaginal discharge)
4. Culture of the vaginal discharge for *Trichomonas vaginalis* and *Candida albicans*

TREATMENT

See guidelines on management of trichomoniasis (Pg 104), vulvovaginal candidiasis (Pg 15) and bacterial vaginosis (Pg 11)
PEDICULOSIS PUBIS

DEFINITION
This is an infestation of the anogenital region by the crab louse, *Phthirus pubis*. In adults it is usually sexually transmitted.

CLINICAL FEATURES
The infestation is indicated by the presence of brown adult lice on the pubic hair, body hair and rarely, eyebrows and eyelashes. There may also be the presence of eggs (nits) which adhere to the hairs. Small haemorrhagic spots may also be seen on the pubic/genital skin and underwear. Blue macules (maculae caeruleae) may be visible at feeding sites. There may be no symptoms or there may be itch due to hypersensitivity to the feeding lice.

LABORATORY TESTS
The presence of lice or nits recovered from pubic hair confirms the diagnosis.

TREATMENT
*Recommended Regimens*

1. Malathion 0.5% lotion application. Wash off after 12 hours [IV, C]

Permethrin (1%) creme rinse, washed off after 10 minutes, can also be used, but is currently unavailable in Singapore [IV, C]

Permethrin lotion is available at the National Skin Centre pharmacy and may be used as an alternative if malathion cannot be used.

If the eyelashes are affected, apply an occlusive ophthalmic ointment or vaseline to the eyelid margin twice daily for 10 days and/or remove lice with tweezers or forceps [IV, C]

*Treatment in pregnancy*
Pregnant or lactating women should be treated with permethrin.

FOLLOW-UP
Patients should be re-evaluated after 1 week, which is the time taken for any nits to hatch into lice. Re-treat only if the lice are found or eggs are observed. Clothing and bed sheets that have been contaminated should be washed in hot water.

MANAGEMENT OF SEXUAL CONTACTS
Regular sex partners within the last month should be encouraged to attend for examination and treatment.
References:

SCABIES

DEFINITION
Scabies is an infestation by the mite, Sarcoptes scabiei var. hominis.

CLINICAL FEATURES
The clinical features of scabies are pruritic papules on the genitals, finger webs, wrists, axillae and buttocks. There is a nocturnal exacerbation of the itch. Family members and sexual partners may have similar symptoms. The presence of typical symptoms and signs is sufficient to make the diagnosis, even if skin scrapings are negative.

LABORATORY TESTS
The mite can be demonstrated by microscopic examination of scrapings from burrows on the skin.

TREATMENT

Recommended Regimens
1. Malathion 0.5% lotion applied thinly to all areas of the body from the neck down and washed off after 24 hours. Apply nightly for 2 nights [IV, C] or
2. Emulsion benzyl benzoate (EBB) 25% application for adults and 10% for children under 10 years old (but older than 1-year-old). Apply nightly from neck down on all areas of body for 3 nights [IV, C] or
3. Permethrin lotion (only available at NSC pharmacy) – overnight application. Suitable for pregnant women and children less than 1-year-old

Oral medication
Ivermectin [Ib, A]:
Several controlled trials have assessed the efficacy of a single dose of ivermectin 200 mg/kg or 0.2mg/kg for the treatment of scabies. A second dose may be given 1-2 weeks later.

This should not be routinely used as first-line therapy. There has been a previous report of excess risk of death for elderly patients, which has not been confirmed. Several other studies of ivermectin have shown that it is safe in children as well as older patients. Consulting an expert before use is recommended. Not for use in pregnancy.

Pregnancy:
1. EBB 25%
or
2. Permethrin lotion
**Crusted (Norwegian) scabies:**

- Usually in the malnourished, immunodeficient and patients with neurological disturbance
- Intensive topical treatment is required
- Combined topical and oral treatment with ivermectin (0.2 mg/kg) may also be considered
- Occasionally, in-patient treatment may be beneficial

**FOLLOW-UP**

Clothing and bed sheets should be washed with hot water or dry cleaned. Patients must be warned that there might be an initial exacerbation of the pruritus. Antihistamines are required to relieve the itch.

Repeat treatment with a different agent is often necessary - treatment failure may be due to resistance to medication, faulty application techniques, poor penetration through thick scales, mites in difficult to reach areas, and reinfection. Post-scabetic itch can last several weeks and is treated with topical steroids and antihistamines.

**MANAGEMENT OF SEXUAL CONTACTS**

Sex partners and close family contacts and all members of the household should be treated even if asymptomatic.

**Reference:**

SEXUAL ASSAULT AND STI EVALUATION

Recommended Procedures
1. The victim should be evaluated within 24 hours of the assault.
2. Some STIs e.g. gonorrhoea, chlamydial infections and syphilis are almost exclusively transmitted sexually; others e.g. bacterial vaginosis and candidiasis may be transmitted non-sexually.
3. The accurate identification of a sexually-transmitted agent is required for medico-legal action. Certain non-culture tests, serology and smear tests have a lower sensitivity and specificity than culture tests in diagnosing STIs.
4. The presence of STIs after the assault may represent pre-existing infection and may not be the result of the assault.
5. The management of potential pregnancy and psychological and physical injury is not addressed in these guidelines. The patient should be referred to the relevant specialists for management.
6. The victim is examined to provide medical management as well as to obtain forensic evidence. Consider the use of photography for documentation.

For adults:
 a) The following tests should be performed:
   • Gram-stained specimens from sites of penetration
   • cultures or FDA-cleared NAATs for *N. gonorrhoeae* and *C. trachomatis* from sites of penetration
   • blood tests for syphilis, HIV and Hepatitis B infection
   • examination of vaginal secretions for *T. vaginalis*, candidiasis (including culture) and BV
   • pregnancy test
 b) Follow-up examinations for adults:
   • cultures should be repeated after 2 weeks
   • blood tests should be repeated after 3 months (syphilis) and 1 and 3 months (HIV)
 c) Treatment should be based on laboratory findings.

If follow-up cannot be assured, the following regimen of epidemiological treatment can be used:
Ceftriaxone 250 mg i/m
with
Doxycycline 100 mg orally bid x 7 days or Azithromycin 1g stat
with
Metronidazole 2 g orally, single dose
Emergency contraception (within 72 hours of rape)
1. Levonorgestrel 1.5 mg stat [Ia, A] or Ulipristal 30mg stat
   or
2. IUCD insertion

Note:
1. Consider Hep B vaccine and HIV non-occupational post-exposure prophylaxis [IV, C] (refer to relevant section)
2. Examination for STIs should be repeated 1-2 weeks after the assault as infectious agents acquired through assault might not have produced sufficient concentrations of organisms to result in positive test results at the initial examination

For children:
a) The identification of a STI from a child beyond the neonatal period is suggestive of sexual abuse. However, some infections may represent persistence of a neonatally acquired infection e.g. chlamydial infection in the rectum or genitals, genital warts
b) The following tests are recommended for sexually-abused children:
   • Gram-stained specimen from any genital or anal discharge
   • Cultures for *N. gonorrhoeae* and *C. trachomatis* from the pharynx, rectum, vaginal/urethra
   • Examination of vaginal secretions for *T. vaginalis*, candidiasis (including culture) and BV
   • Blood tests for syphilis, HIV and Hepatitis B infections, HSV & TSST
   • Pelvic examinations should not be performed unless indicated, eg. trauma, foreign bodies
c) Cervical specimens are not recommended for prepubertal girls. For boys, a meatal specimen of urethral discharge is an adequate substitute for an intraurethral swab specimen when discharge is present. A urine sample can be used in this situation
d) Follow-up examinations for sexually abused children:
   • Blood tests should be repeated after 3 months (syphilis) and 1 and 3 months (HIV)
   • All other tests should be repeated after 2 weeks
e) Treatment of sexually-abused children should be based on laboratory findings. Presumptive treatment may be administered if follow-up cannot be assured or if the assailant has a confirmed STI

References:
STI SCREENING OF MEN WHO HAVE SEX WITH MEN (MSM)

MSM are at high risk for HIV infection and other viral and bacterial STIs. The frequency of unsafe sexual practices, the rates of bacterial STIs and incidence of HIV infection has been increasing in MSM. More common STIs include syphilis, gonorrhoea and chlamydia. The underlying behavioural changes may be related to effects of improved HIV/AIDS therapy on quality of life and survival, “safer sex burnout”, trends in recreational substance abuse and changes in sex partner networks resulting from new venues for partner acquisition.

Assessment includes routinely enquiring about the sex of patients’ sex partners. MSM, including those with HIV, should routinely undergo straightforward, non-judgmental STI/HIV risk assessment and client-centred prevention counselling to reduce the likelihood of acquisition or transmission of HIV and other STIs. Clinicians should be familiar with local community resources available to assist MSM at high risk, in facilitating behavioural change and contact tracing. In addition, screening for STIs should be performed. The following screening recommendations should be performed at least annually for sexually active MSM.

Screening recommendations for MSM (at least annually):

Serology:

- HIV serology, if HIV-negative or not previously/recently (3-6 months) tested;
- Syphilis serology (should be part of routine HIV monitoring in HIV positive MSM);
- Hepatitis A, if not previously immunised or tested immune*;
- Hepatitis B, if not previously immunised or tested immune/infected*;
- Hepatitis C, if any history of injection drug use or if HIV positive;
- Type-specific serologic test for HSV-2 may be considered but HSV-2 treatment has not been shown to reduce HIV acquisition.

*If not immune, MSM should be vaccinated for hepatitis A and B. Once the primary vaccination schedule has been completed in immunocompetent MSM, further serology and booster doses are not necessary. In HIV positive MSM, hepatitis B surface antibody levels (HBsAb) should be performed annually and a booster dose given if required.

Urine tests and swabs:

- Urine nucleic acid amplification tests (NAAT) such as PCR for urethral gonorrhoea and chlamydia infection in MSM who have had oral-genital exposure or insertive anal intercourse;
- Pharyngeal culture/NAAT for gonorrhoea in MSM who have had receptive oral intercourse; and
- Rectal gonorrhoea culture/NAAT and chlamydia NAAT in men who have had receptive anal intercourse, oral-anal sex, receptive fingering or toy insertion (i.e; all MSM should be offered anal swabs even if they do not report receptive anal intercourse).
Testing intervals:
More frequent STI screening (3 to 6-month intervals) is indicated for MSM who have:

- Engaged in unprotected anal sex;
- Multiple or anonymous sex partners;
- Sex in conjunction with illicit drug use;
- Sex partners who participate in the above activities.

Screening tests usually are indicated regardless of a patient’s history of consistent use of condoms for insertive or receptive anal intercourse.

Vaccinations
Vaccination is the most effective means of preventing sexual transmission of hepatitis A and B. Pre-vaccination serologic testing may be cost-effective in some MSM, among whom the prevalence of hepatitis A and B infection may be high, but it should not delay vaccination.

MSM, and especially those who are infected with HIV, are at an increased risk for HPV infection and anal cancer associated with high-risk HPV types. Quadrivalent HPV vaccination may be beneficial to some MSM particularly those who are young or have just commenced sexual activity.

References:
STI SCREENING OF WOMEN WHO HAVE SEX WITH WOMEN (WSW)

Women who have sex with women are a diverse group with variations in sexual behaviour, identity and risk behaviours. Most WSW report a past history of sex with men and may continue this practice in the future. Some also report higher risk behaviours such as injecting drug use, history of commercial sex work, and higher risk sexual partners. The clinician should be aware that sexual orientation is not synonymous with sexual practice, and WSW should not be presumed to be at low or no risk of STIs and HIV based on sexual orientation alone.

STIs, including HIV, may be transmitted between WSW through the transfer of cervicovaginal fluids during activities involving digital-vaginal or digital-anal contact, shared penetrative sex toys, and via other sexual practices (e.g., oral-genital/oral-anal sex, direct genital-genital contact).

Clinicians should engage in a comprehensive and open discussion about patients’ sexual and behavioural risks, and not only about their sexual identity, to accurately assess STI and HIV risk.

All STIs have been reported with varying prevalence in WSW:

- Bacterial vaginosis (high prevalence, including in WSW in monogamous relationships)
- Trichomonas vaginalis
- Genital herpes
- Genital warts and cervical HPV infection**
- HIV
- Syphilis
- Gonorrhoea and Chlamydia
- Hepatitis B (hepatitis C if a history of injecting drug use)

WSW should be screened regardless of their sexual practices.

Routine screening tests:

1. Cervical or urine NAATs for gonorrhoea and chlamydia
2. Genital swabs for bacterial vaginosis, trichomonas and candida in symptomatic WSW
3. Serology for HIV and syphilis
4. Serology for hepatitis B → offer vaccination if not immune
5. Pap smear** and offer HPV vaccination, both in accordance with current guidelines.

**Low and high grade cervical smear abnormalities have been detected in WSW who reported no previous sex with men, warranting routine cervical cancer screening as per national guidelines.
Advice on safe sex practices:
- Condom use with male sex partners
- Use of dental dams (latex barrier) for oral-genital sex
- Avoid contact with partner's menstrual blood and any visible genital lesions
- Use condoms over penetrating sex toys and a new condom with each new/different partner
- Consider using latex gloves and lubricant for any mutual masturbation that might cause bleeding
- STI and HIV screening, vaccination and contact tracing of partners if diagnosed with an STI

Terminology:
- **WSW**: women who have sex with women (description of sexual behaviour/practice).
- **Lesbian or bisexual**: a woman whose primary sexual and emotional partnerships are with women, or both, respectively (sexual identity as self-identified by the woman).

References:
SYMPHILIS

DEFINITION
Syphilis is a systemic infection caused by *Treponema pallidum*. With the exception of mother-to-child transmission, syphilis is almost exclusively spread by direct contact with infectious lesions.

CLINICAL FEATURES

STAGES OF SYMPHILIS

A. Primary Syphilis
Usually occurs 2-6 weeks following infection. Characterized by a single or less often multiple, painless, indurated ulcer (chancre) at the site of inoculation. Regional lymph nodes are enlarged, feel rubbery and are painless.

B. Secondary Syphilis
Usually occurs 2-6 months following primary syphilis. Characterized by variable mucocutaneous and systemic signs e.g. symmetrical non-itchy rashes, mucous membrane lesions, patchy alopecia, generalised lymphadenopathy.

C. Latent Syphilis
Asymptomatic phase with no clinical signs of organ involvement.
It is categorised into -
- Early latent syphilis (<1 year of infection)
- Late latent syphilis (>1 year of infection)

D. Tertiary Syphilis
Occurs 5 to 10 years after secondary syphilis and includes -
- Benign tertiary syphilis characterized by gumma formation
- Cardiovascular syphilis
- Neurosyphilis

LABORATORY TESTS
The diagnosis of syphilis may be confirmed either by
- Darkfield microscopy to demonstrate *T. pallidum* in secretions from the primary chancre or moist lesions of secondary syphilis.

Serological Tests
i. Non-Treponemal Tests
The Rapid Plasma Reagin (RPR) test and the Venereal Disease Research Laboratory (VDRL) tests are monitored serially to assess the serological response to treatment. RPR titres are slightly higher than VDRL titres. A positive VDRL/RPR test needs to be confirmed by a treponemal test. VDRL/RPR 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
The Treponema Pallidum Haemagglutination Assay (TPHA), Treponema Pallidum Particle Agglutination (TPPA) test, the Line Immunoassay (LIA), the Fluorescent Treponemal Antibody Absorption (FTA-Abs) test, Rapid diagnostic tests (e.g. Abbott Determine Syphilis TP) and the treponemal EIA test are specific and can be used as screening tests. A positive result may need to be confirmed by another specific test, as well as a non treponemal test with a titre (e.g RPR or VDRL).

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.

The FTA-Abs test is the first test to become positive following infection, it is followed by the VDRL/RPR test, and then by the TPHA/TPPA test. In primary syphilis 85-90% of cases will have a reactive FTA-Abs test, but only 60% will have a reactive TPHA/TPPA. The FTA-Abs test is no longer routinely offered by laboratories in Singapore. The syphilis LIA test for both IgM and IgG can be done as an alternative confirmatory test, as well as to detect cases of early syphilis. There is evidence that the syphilis EIA test is also useful for detecting early infections.

Most cases of syphilis in HIV-infected persons will demonstrate typical serological responses. However there may be instances of an altered serological response (abnormally high, low or fluctuating titres).

Neurosyphilis is often difficult to diagnose, as there is no single test that is useful in all types of neurosyphilis.

Tests that are used to diagnose neurosyphilis include:
CSF - WBC count, protein and globulin levels, VDRL, LIA IgM and IgG, and TPHA.
A positive CSF VDRL in the absence of gross blood contamination is confirmatory for neurosyphilis. However there may be false negatives as the test is not very sensitive. The LIA is a more sensitive test. A negative CSF LIA result makes neurosyphilis very unlikely.

TREATMENT
Parenteral penicillin G (aqueous crystalline, aqueous procaine, or benzathine) is the drug of choice for treating all stages of syphilis. If the patient is allergic to penicillin, tetracycline, doxycycline, azithromycin and erythromycin are the alternatives. However, they do not have the established and well-evaluated high rate of success of penicillin.

Early Syphilis
Primary syphilis
Secondary syphilis
Latent syphilis of less than 1 year’s duration
**Recommended Regimens**

1. Benzathine Penicillin G 2.4 million units i/m weekly x single dose  *[III, B]*
   or
2. Aq. Procaine Penicillin G 600,000 units i/m daily x 10 days  *[III, B]*

**Penicillin-allergic patients**

1. Doxycycline 100 mg orally bid x 14 days  *[III, B]*
   or
2. Tetracycline 500 mg orally qid x 14 days  *[III, B]*
   or
3. Erythromycin 500 mg orally qid x 14 days  *[III, B]*
   or
4. Azithromycin 500 mg orally od x 10 days  *[IV, C]*
   or
5. Ceftriaxone 500 mg i/m od x 10 days  *[IV, C]* (limited data only; note low risk of possible cross reaction with penicillin).

For HIV-infected individuals, we recommend the same treatment regimens as those who are HIV negative *see section on infection in HIV infected individuals*  *[IV, C]*

**Late Syphilis (excluding neurosyphilis)**

Latent syphilis of more than 1 year’s duration, or of unknown duration

Late benign syphilis

Cardiovascular syphilis

*Recommended Regimens*

1. Benzathine penicillin G 2.4 million units i/m weekly x 3 doses  *[III, B]* (7.2 million units total)
   or
2. Aq. Procaine penicillin G 600,000 units i/m daily x 17-21 days  *[III, B]*

**Penicillin-allergic patients (close follow-up required)**

1. Doxycycline 100 mg orally bid x 28 days  *[IV, C]*
   or
2. Tetracycline 500 mg orally qid x 28 days  *[IV, C]*
   or
3. Erythromycin 500 mg orally qid x 28 days  *[IV, C]*

**Neurosyphilis, ocular and otologic syphilis**

A high sustained blood level of penicillin is required for adequate penetration of the blood-brain barrier in the treatment of neurosyphilis.

Patients with syphilis and the following should have CSF examination:

- Neurologic, cognitive, auditory or ophthalmic symptoms and signs
- Evidence of active tertiary syphilis (e.g. aortitis, gumma, iritis)
- Treatment failure
Some experts recommend CSF examination in HIV infection with late syphilis or syphilis of unknown duration (some experts would treat all HIV positive syphilis with neurosyphilis regimens) but newer evidence suggests that treatment outcomes are not significantly altered.

The CSF findings in neurosyphilis are:

- Increased mononuclear cell count (>5 cells/mm3)
- Increased total protein (>0.4 g/l)
- Positive CSF VDRL (negative in about 20%)
- Positive CSF LIA

**Recommended Regimens**

1. Aq. Procaine penicillin G 2.4 million units i/m daily x 10 days with Probenecid 500 mg orally qid x 10 days followed by Benzathine penicillin G 2.4 mega units i/m weekly x 3 doses [III, B]
   or
2. Aq. Crystalline Benzyl penicillin 3 to 4 million units i/v every 4 hours (total 18 to 24 million units a day) x 10 days followed by Benzathine Penicillin G 2.4 million units i/m weekly x 3 doses [III, B]

**Penicillin-allergic patients**

RAST tests, skin testing and desensitisation should be performed in consultation with an expert.

Penicillin is the drug of choice unless really contraindicated.

1. Doxycycline 100 mg orally bid x 28 days [IV, C]
   or
2. Tetracycline 500 mg orally qid x 28 days [IV, C]
   or
3. Erythromycin base or stearate 500mg orally qid x 28 days (least effective) [IV, C]

Doxycycline is the preferred oral alternative in view of its more favourable dosing intervals.

**Oral corticosteroid cover**

This is to minimize the effects of the Jarisch-Herxheimer reaction that may occur 4 to 12 hours after the first dose of antibiotic therapy and is indicated in the following situations where the reaction may result in morbidity or even mortality:

- Laryngeal gumma
- Cardiovascular syphilis
- Neurosyphilis

**Recommended Regimen**

Prednisolone orally 20 mg tid (60mg/day) for 24 hours before treatment and continued for 2 days after starting therapy [IV, C].
FOLLOW-UP
Quantitative nontreponemal tests should be repeated for a total period of two years (at 3 months; 6 months; 12 months; 18 months; 24 months).

Following treatment of early syphilis, VDRL/RPR should demonstrate a 4 x (2 dilutions) decrease in titre within 6 months. Failure to do so probably means treatment failure, and is an indication for retreatment with 3 injections of Benzathine penicillin. Some experts recommend CSF examination.

Clinical signs that persist or recur, or a rising VDRL/RPR titre of 4 x or more suggests either reinfection or relapse. In these situations CSF examination is recommended before retreatment. Seroreversion in primary syphilis often occurs within 12 months; it may take a longer time for secondary and early latent syphilis, but usually occurs within 24 months. Following treatment of late syphilis, seroreversion occurs rarely; a stable, low titre, serological scar, is the result in most patients.

All patients treated for neurosyphilis should be followed up for life at 6-month intervals. If CSF pleocytosis was present initially, CSF examinations should be repeated every 6 to 12 months until the cell count returns to normal. Serologic tests for HIV should be performed 3 months after the last risky exposure.

MANAGEMENT OF SEXUAL CONTACTS
At risk partners are those who have been exposed within the following periods – 3 months plus duration of symptoms for primary syphilis, 6 months plus duration of symptoms for secondary syphilis, and 1 year for early latent syphilis.

Epidemiologic treatment should be given to sexual contacts who were exposed 3 months prior to the diagnosis of primary, secondary or early latent syphilis, if follow-up is uncertain. Sexual partners of late syphilis should be screened and evaluated for syphilis, and treated on the basis of these findings.

Epidemiologic treatment can be given as follows
1. Benzathine Penicillin G 2.4 million units i/m weekly x single dose [III, B] or
2. Doxycycline 100 mg orally bid x 14 days [III, B] or
3. Azithromycin 1 g orally stat [III, B]

Syphilis in pregnancy
All pregnant women should have serological tests for syphilis at the first antenatal visit. This should be repeated in women who have high-risk behaviour or have spouses who have high-risk behaviour.
Penicillin should be used in dosage schedules appropriate for the stage of syphilis as recommended for the treatment of non-pregnant patients. A Jarisch-Herxheimer reaction may precipitate premature labour or foetal distress; women should be advised to seek obstetric care if abnormal contractions and decreased foetal movements occur.

For penicillin-allergic patients, give erythromycin in dosage schedules appropriate for the stage of syphilis 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.

Ceftriaxone 500 mg i/m od x 10 days and Azithromycin 500 mg orally od x 10 days (limited data only) have been tried.

Tetracyclines are contraindicated in pregnancy. Pregnant woman treated for early syphilis should have monthly RPR/VDRL for the remainder of the current pregnancy.

**Children with acquired syphilis**
Birth and maternal records should be reviewed to exclude congenital syphilis.

**Primary, Secondary and Early Latent Syphilis**
Benzathine penicillin G 50,000 units/kg i/m, up to adult dose of 2.4 mega units in single dose.

**Late latent syphilis, latent syphilis of unknown duration, late syphilis (not neurosyphilis)**
Benzathine penicillin G 50,000 units/kg i/m, up to adult dose of 2.4 mega units, administered as three doses at 1 week intervals (total 150,000 units/kg up to adult dose of 7.2 million units).

**Neurosyphilis**
Aq. Crystalline Penicillin G 50,000 unit/kg i/v every 4-6 hours (total 200,000 - 300,000 unit/kg/day) for 10 days.

**Congenital Syphilis**
Diagnosis and treatment decisions must be based on

1. Identification of syphilis in the mother.
3. Clinical, laboratory, radiological evidence of syphilis in the infant.
4. Comparison of the infant’s VDRL/RPR result with the mother’s.

**Who should be evaluated?**
Infants should be evaluated if they have been born to seropositive mothers who -

- have untreated syphilis
- were treated for syphilis < 1 month before delivery
- were treated for syphilis during pregnancy with a non-penicillin regimen
• did not have the expected decrease in non-treponemal antibody (RPR or VDRL) titres after treatment for syphilis
• were treated but had insufficient serologic follow-up during pregnancy to assess disease activity

Evaluation is not required if both these criteria are met -
• Mother had well-documented history of treatment in pregnancy with a penicillin regime appropriate for the stage of syphilis
• Mother has sufficient serologic follow-up after treatment to show that she responded to treatment (≥ 4 fold decrease in RPR/VDRL titre in early syphilis; stable or declining titres of ≤ 1:4 in other patients)
• Some experts would treat the infant with a single dose of Benzathine Penicillin 50,000 units/ kg i/m; others would not but instead provide close serologic follow-up. If the infant’s RPR/ VDRL is non-reactive no treatment is needed.

What to evaluate in the infant?
• Thorough physical examination
• Infants blood - RPR/VDRL, LIA IgM or EIA IgM on the serum - if available
• DG or DIF microscopy of suspicious lesions or body fluids
• CSF - FEME, VDRL, LIA IgM
• Other tests as clinically indicated (e.g. long bone and chest X-rays, FBC)

When to treat infants?
• Positive syphilis serology with evidence of active disease (physical examination or X-ray)– rhinitis, mucocutaneous signs, hepatosplenomegaly, osteitis, periostitis, osteochondritis, glomerulonephritis, ascites, stigmata
• A reactive CSF-VDRL
• An abnormal CSF finding (WBC >5/cmm or protein >50mg/ml) regardless of CSF VDRL titre
• A detectable LIA IgM in the infant
• VDRL titre in the infant is fourfold or greater than in the mother
• VDRL titres in the infant show a serial rise
• Treatment of the mother was inadequate or unknown (adequate maternal treatment means full dosage of penicillin at least 1 month before delivery)
• Drugs other than penicillin e.g. erythromycin was used to treat the mother during pregnancy
Recommended Regimens

1. Aq. Crystalline Penicillin G 50,000 units/kg/day i/v daily every 12 hours (total 100,000 to 150,000 units/kg/day) during the first 7 days of life, and every 8 hours thereafter for a total of 10 days [III, B]

or

2. Aq. Procaine Penicillin G 50,000 units/kg i/m daily single dose x 10 days [III, B]

or

3. Benzathine penicillin 50,000 units i/m single dose may be used if the infant’s evaluation is normal and follow-up is certain; however if any part of the evaluation is abnormal, not done or cannot be interpreted, a 10 day course of penicillin is needed [IV, C]

FOLLOW-UP

Seroreactive infants and infants whose mothers were reactive at delivery should be followed up every 2-3 months until the test becomes nonreactive or the titre falls fourfold; the RPR/VDRL should fall by 3 months of age and be nonreactive by 6 months of age if the infant was not infected (passive transfer) or if treatment was adequate. Treatment after the neonatal period may result in a slower decline of titres.

Passively transferred treponemal antibodies may be present in the infant for 15 months, the presence of a reactive treponemal test after 18 months indicates congenital syphilis, and the infant should be (re)evaluated.

Congenital syphilis in older infants and children

- Review maternal serology and records if congenital syphilis is possible
- Full evaluation including CSF examination, eye and auditory examination, X-rays etc.

Recommended Regimens

1. Aq. crystalline penicillin G 200,000-300,000 units/kg/day i/v (administered as 50,000 units/kg every 4-6 hours) for 10 days [IV, C]

or

2. Aq. Procaine Penicillin G 50,000 units/kg i/m daily single dose x 10 days [IV, C]

Treatment of syphilis in a HIV infected person

Serological tests for syphilis are generally reliable in HIV co-infection. Some authorities recommend routine CSF examination and/or treatment for neurosyphilis for all patients, regardless of the stage of syphilis. However, most HIV-infected persons respond appropriately to standard benzathine penicillin for primary and secondary syphilis. CSF abnormalities (e.g. mononuclear pleocytosis and elevated protein levels) are common in HIV-infected persons, even in those without neurologic symptoms, although the clinical and prognostic significance of such CSF abnormalities with primary and secondary syphilis is unknown. Several studies have demonstrated that among persons infected with both HIV and syphilis, clinical and CSF abnormalities consistent with neurosyphilis are associated with a CD4 count of ≤350 cells/mL and/or an RPR titer of ≥1:32; however, unless neurologic symptoms are present, CSF examination in this setting has not been associated with improved clinical outcomes.
A lumbar puncture is recommended for HIV patients with syphilis if there are any neurological abnormalities, or if titres do not decline after penicillin therapy. All HIV patients should be treated wherever possible with penicillin.

**Some experts recommend treatment in the same doses as for HIV-negative patients, while others would treat all HIV-infected patients with the neurosyphilis regimen** [IV, C].

**We recommend that all HIV-infected patients without evidence of neurosyphilis be given doses of benzathine penicillin that are appropriate for the stage of syphilis as in non HIV patients.**

However, it is more important to monitor for treatment failures in these patients. Such patients should be followed-up clinically and with nontreponemal tests at 3, 6, 9, 12 and 24 months after treatment.

**Retreatment**

Best to refer to a specialist.  
Indications -

- Clinical signs and symptoms of syphilis persist or recur (clinical relapse)
- Four-fold or greater rise in VDRL/RPR titre e.g. from R4 to R16 (serological relapse)
- Initial high VDRL/RPR titre e.g. R32 or greater persists for a year (sero-fast)
- Failure of VDRL/RPR titre to decrease four-fold after a year for treated early syphilis
- For pregnant women treated for early syphilis, the failure to show a four-fold decrease in VDRL/RPR titre after 3 months.

**References:**


TRICHOMONIASIS

DEFINITION
Trichomoniasis is an infection of the genital tract by the protozoan *Trichomonas vaginalis*. Women are the main carriers of the disease. Infected men are usually asymptomatic.

CLINICAL FEATURES
Vaginal trichomoniasis may be asymptomatic or present with a purulent foul smelling vaginal discharge that is yellow-green in colour, and vulvar pruritus or irritation. The vagina and cervix (strawberry cervix) are often inflamed. 15 to 50% of men with *T. vaginalis* are asymptomatic and usually present as sexual partners of infected women. Some male patients may present with symptoms of urethritis.

COMPLICATIONS
There is increasing evidence that *T. vaginalis* infection is associated with adverse pregnancy outcomes such as preterm delivery and low birth weight.

LABORATORY TESTS
- Direct microscopy of a wet mount of vaginal secretions mixed with normal saline will show the trichomonads, about the size of white blood cells moving with a jerky motion (sensitivity 60-70%). This is not a sensitive test in men
- Culture on Feinberg-Whittington media (sensitivity >90%)
- FDA-cleared rapid strip tests e.g. OSOM Trichomonas Rapid Test (an immunochromatographic capillary flow dipstick technology), Affirm™ VP III nucleic acid probe test that evaluates for *T. vaginalis*, *G. vaginalis* and *C. albicans* (sensitivity > 83%, specificity >97%). Both these tests are considered point-of-care diagnostics
- Trichomonads are sometimes reported on cervical cytology (sensitivity ~ 60-80%) but there is a false positive rate of about 30%. Use of liquid-based pap smear testing has shown enhanced sensitivity. The diagnosis should still be confirmed by direct microscopy of vaginal secretions or culture
- An FDA-cleared PCR assay for detection of gonorrhoea and chlamydia infection (AmpliCor, manufactured by Roche Diagnostics Corp.) has been modified for *T. vaginalis* detection in vaginal or endocervical swabs and in urine from women and men (sensitivity 88-97%, specificity 98-99%)
- APTIMA *T. vaginalis* Analyte Specific Reagents (ASR; manufactured by Gen-Probe, Inc.) also can detect *T. vaginalis* RNA by transcription-mediated amplification using the same instrumentation platforms available for the APTIMA Combo2 assay for diagnosis of gonorrhoea and chlamydia infection (sensitivity 74-98%, specificity 87-98%)
TREATMENT
Both symptomatic and asymptomatic patients should be treated.

Recommended regimen

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

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

Children
Trichomoniasis may be acquired perinatally and occurs in ~ 5% of babies born to infected mothers. Infection beyond the first year of life should suggest sexual contact and the child should be appropriately evaluated.

Metronidazole 15mg/kg orally tid x 7 days

Treatment in pregnancy
Trichomoniasis has been associated with adverse pregnancy outcomes (premature rupture of membranes, preterm delivery, low birth weight). Metronidazole in pregnancy has not been shown to be teratogenic or mutagenic and can be used during all stages of pregnancy or breastfeeding. Imidazole and metronidazole pessaries may be used to provide symptomatic relief, but systemic metronidazole is needed for eradication of infection.

Note:
Metronidazole and Tinidazole may provoke a disulfiram - like reaction when taken with alcohol. Patients should be advised to abstain from alcohol use for 24 hours after completion of metronidazole and 72 hours after completion of tinidazole.

Allergy to Metronidazole
Clotrimazole pessaries 100mg od intravaginally x 6 days [IV, C]

TV in HIV infection
T. vaginalis infection in HIV-infected women has been shown to enhance HIV transmission by increasing genital shedding of the virus and treatment for T. vaginalis has been shown to reduce HIV shedding. Rescreening at 3 months after completion of therapy should be considered in HIV-positive women. Single dose metronidazole is not as effective as 400-500mg twice daily for 7 days in HIV-positive women.
FOLLOW UP
Follow-up is unnecessary for asymptomatic patients. Patients with persistent symptoms treated with either regimen should be retreated with metronidazole 400mg bid for 7 days. If treatment failure occurs repeatedly, the patient should be treated with a single 2g dose of metronidazole once a day for 3-5 days. Such cases should have determination of susceptibility of *T. vaginalis* to metronidazole.

MANAGEMENT OF SEXUAL CONTACTS
Sex partners should be encouraged to come for examination and be treated on epidemiological grounds. There is evidence to suggest that patient-delivered partner therapy might have a role in partner management for trichomoniasis.

References:
VACCINATIONS

Immunisations are important in the prevention of human papillomavirus, hepatitis A and hepatitis B.

Human papillomavirus — Two human papillomavirus (HPV) vaccines are available for the prevention of HPV infection:

1. A bivalent vaccine (Cervarix), which protects against HPV types 16 and 18 and
2. A quadrivalent vaccine (Gardasil), which protects against HPV types 6, 11, 16 and 18.

Both vaccines offer protection against the HPV types that cause up to 70% of cervical cancers (types 16 and 18) and the quadrivalent HPV vaccine has additional protection against HPV types that are commonly associated with genital warts (types 6 and 11).

Immunisation with HPV vaccine is recommended by the CDC’s Advisory Committee on Immunization Practices (ACIP) in girls and women 9 to 26 years of age. The quadrivalent vaccine can also be used in males aged 9 to 26 years to prevent genital warts. The ACIP does not recommend serologic or HPV DNA testing prior to immunization.

For maximum benefit, HPV vaccine should be administered before onset of sexual activity since neither vaccine treats or accelerates the clearance of pre-existing vaccine-type HPV infections or related disease. However, a history of an abnormal Papanicolaou smear, genital warts, or HPV infection is NOT a contraindication to HPV immunization.

Vaccination schedule: 3 doses are recommended over six months. CDC recommends that the second dose be given one to two months after the first, and the third dose be given six months after the first dose.

Women who have received the HPV vaccine should continue routine cervical cancer screening because 30% of cervical cancers are caused by HPV types other than 16 or 18.

Hepatitis B — Risk factors associated with hepatitis B (HBV) infection are unprotected sex with an infected partner, unprotected sex with more than one partner, and history of other STIs. MSM and IVDU are considered at risk groups for HBV acquisition. HBV is also endemic in South-East Asia therefore vaccination is recommended for the general population.

The Advisory Committee on Immunization Practices (ACIP) recommends universal hepatitis B immunisation for all unvaccinated adults presenting to a STI clinic. Patients with a history of HBV vaccination should have either documentation of immunisation or serologic testing for hepatitis B surface antibody. Please refer to the chapter on viral hepatitis for the appropriate screening tests and the vaccine administration schedule.
All pregnant women receiving STI services should be tested for HBsAg, regardless of whether they have been previously tested or vaccinated.

All HIV-infected patients should receive HBV immunisation. Although the vaccine is safe, efficacy can be affected by the presence of HIV RNA and advanced immunosuppression.

**Hepatitis A** — Vaccination against hepatitis A is recommended by the CDC for MSM, IVDU and patients with chronic liver disease. Post vaccination serologic testing is not recommended because most persons respond to the vaccine.

Hepatitis A virus replicates in the liver and is shed in high concentrations in faeces from 2 weeks before to 1 week after the onset of clinical illness. Since sexual transmission of hepatitis A probably occurs because of faecal-oral contact, barrier measures, such as condoms, are ineffective in preventing acquisition of this disease.

Immunization is also recommended for HIV-infected patients who have chronic liver disease or are at risk for hepatitis A (MSM, IVDU). Hepatitis A vaccine is safe and effective in HIV-infected patients, particularly when administered before onset of advanced immunosuppression.

<table>
<thead>
<tr>
<th>Type of vaccination</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV vaccine</td>
<td>Day 1</td>
<td>Month 2</td>
<td>Month 6</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Day 1</td>
<td>Month 1</td>
<td>Month 6</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Day 1</td>
<td>Month 6</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

**Reference:**

### ANNEX II – SEROLOGICAL RESPONSE IN SYphilis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>RPR/VDRL Result</th>
<th>TPPA/TPHA Titres</th>
<th>EIA IgM</th>
<th>EIA IgG</th>
<th>LIA IgM</th>
<th>LIA IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-primary syphilis (Incubation period)</td>
<td>+/- Rising</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Primary syphilis</td>
<td>+/- Rising</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>+ High</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Early latent syphilis</td>
<td>+ Mod</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Late latent syphilis</td>
<td>+/- Mod/Low</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CVS syphilis</td>
<td>+/- Mod/Low</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>+/- Mod/Low</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Early congenital syphilis</td>
<td>+ Rising</td>
<td>+</td>
<td>+/-*</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Passive transfer of maternal antibodies</td>
<td>+ Same or lower than mother</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Late congenital syphilis</td>
<td>+ Mod/Low</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Biological false positive reaction</td>
<td>+ Low</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Treated early syphilis</td>
<td>- NA</td>
<td>+/-</td>
<td>+/-</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Treated late syphilis</td>
<td>+/- Low</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*LIA-Abs IgM may be negative in feeble or premature infants*
# ANNEX III - 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>DGI</td>
<td>Reiter’s Disease</td>
</tr>
<tr>
<td>Urethral Smear</td>
<td>+/+++</td>
<td>+/++ (&gt;5wbcs/hpf)</td>
</tr>
<tr>
<td>Gram Stain</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Gram negative i/c diplococci</td>
<td>N.gonorrhoeae</td>
<td>C.trachomatis</td>
</tr>
<tr>
<td>Culture/NAAT</td>
<td></td>
<td>U.urealyticum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M.genitalium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M.hominis</td>
</tr>
</tbody>
</table>
## ANNEX IV – APPROACH TO DIAGNOSIS OF VAGINAL DISCHARGES

<table>
<thead>
<tr>
<th>Feature</th>
<th>Normal</th>
<th>Gonorrhoea</th>
<th>Chlamydia</th>
<th>Candidiasis</th>
<th>Trichomoniasis</th>
<th>Bacterial Vaginosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Examination</td>
<td>Mild white, milky discharge</td>
<td>Purulent discharge from cervix</td>
<td>Purulent discharge from cervix</td>
<td>Thick white cheesy plaques, erythema of vulva and perineum</td>
<td>Profuse, frothy grey to yellowish/ green discharge</td>
<td>Profuse grey, smooth, watery discharge May contain bubbles Vaginal walls and vulva</td>
</tr>
<tr>
<td>Vaginal pH</td>
<td>&lt;4.5</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td>&gt;4.5</td>
<td>&gt;4.5</td>
<td>&gt;4.5</td>
</tr>
<tr>
<td>Wet film microscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactobacilli</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Polymorphs</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Trichomonads</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Clue Cells</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Pseudohyphae and budding yeast cells</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
ANNEX V - APPROACH TO DIAGNOSIS OF GENITAL ULCERS

Is pain present?

<table>
<thead>
<tr>
<th>No. of ulcers</th>
<th>Single</th>
<th>Multiple</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NO</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>YES</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Differential Diagnosis**
- Chancroid
  - 1 – 5 days (1 – 30 days)
  - Undermined edges, purulent, soft
  - Tender, matted, unilateral
  - Chancroid culture (high false negative)
  - Darkground, VDRL, TPPA
- Infected Chancroid
  - 1 – 5 days (1 – 30 days)
  - Indurated
  - Rubbery, discrete, bilateral
  - Darkground, VDRL, TPPA
- Lymphogranuloma venereum (LGV)
  - 1 – 5 days (1 – 35 days)
  - Non-indurated, transient
  - Bubo (presenting symptom)
  - LGV CFT, PCR
- Carcinoma (elderly males)
  - Long
  - Fungating infiltrative
  - Firm to hard
  - Biopsy
- Herpes Genitalis
  - 2 – 6 days (< 7 days)
  - Grouped or coalesced, small erosions
  - Tender, bilateral
  - Herpes culture, Tzanck test, PCR

**Incubation Period**
- Chancroid: 2/ days (9 – 90 days)
- Infected Chancroid: 2/ days (9 – 90 days)
- Carcinoma (elderly males): Long
- Lymphogranuloma venereum (LGV): 1 – 5 days (1 – 35 days)

**Ulcer Appearance**
- Chancroid: Undermined edges, purulent, soft
- Infected Chancroid: Indurated
- Carcinoma (elderly males): Fungating infiltrative
- Lymphogranuloma venereum (LGV): Non-indurated, transient

**Lymph Node**
- Chancroid: Tender, matted, unilateral
- Infected Chancroid: Rubbery, discrete, bilateral
- Carcinoma (elderly males): Firm to hard
- Lymphogranuloma venereum (LGV): Bubo (presenting symptom)

**Laboratory Tests**
- Darkground, VDRL, TPPA
- Biopsy
- LGV CFT, PCR
- Herpes culture, Tzanck test, PCR
ANNEX VI – SEROLOGICAL RESPONSES IN HEPATITIS B INFECTION

(a) Acute Infection

(b) Acute Infection leading chronic hepatitis

<table>
<thead>
<tr>
<th>Levels of Evidence</th>
<th>Grades of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia Evidence obtained from meta-analysis of randomised controlled trials.</td>
<td>A (evidence levels Ia, Ib) Requires at least 1 randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation</td>
</tr>
<tr>
<td>Ib Evidence obtained from at least one randomised controlled trial.</td>
<td>B (evidence levels IIa, IIb, III) Requires availability of well-controlled clinical studies but no randomised clinical trials on the topic of recommendation.</td>
</tr>
<tr>
<td>IIa Evidence obtained from at least one well-designed controlled study without randomization.</td>
<td></td>
</tr>
<tr>
<td>IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.</td>
<td>C (evidence level IV) Requires evidence obtained from expert committed reports or opinions and/or clinical experiences of respected authorities.</td>
</tr>
<tr>
<td>III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.</td>
<td></td>
</tr>
<tr>
<td>IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.</td>
<td></td>
</tr>
</tbody>
</table>

Levels of Evidence Grades of Recommendation

A (evidence levels Ia, Ib) Requires at least 1 randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation

B (evidence levels IIa, IIb, III) Requires availability of well-controlled clinical studies but no randomised clinical trials on the topic of recommendation.

C (evidence level IV) Requires evidence obtained from expert committed reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.
ANNEX VII – ID NOTIFICATION FORM

MD 131

INFECTION DISEASES ACT
(CHAPTER 137)

INFECTION DISEASES (NOTIFICATION OF INFECTION DISEASES) REGULATIONS
NOTIFICATION OF INFECTION DISEASES UNDER SECTION 6

PARTICULARS OF PATIENT (Please ✓ appropriate box where applicable)

Name of Patient (BLOCK LETTERS) [
NRIC No./Passport No./Foreign Identification Number (FIN) [

Gender [ Male [ Female
Date of Birth (dd/mm/yyyy) [
Ethnic Group [ Chinese [ Indian [ Malay [ Others
Residential Status [ Resident [ Non-Resident
Occupation [
Residential Address [
Postal Code [
Place of Work/School/Child Care Centre/Kindergarten [
Postal Code [
Telephone No. [
Office/HP/PG [

DISEASE DIAGNOSED (CLINICAL OR LABORATORY DIAGNOSIS)

TO CDD® NOT LATER THAN 24 HOURS FROM TIME OF DIAGNOSIS. FAX NO. 62215528 OR 62215538


* For any diseases not appearing in this form which may be of an infectious nature and result in or epidemic if name of disease is not known, please specify symptoms.

TO CDD® NOT LATER THAN 72 HOURS FROM TIME OF DIAGNOSIS. FAX NO. 62215528 OR 62215538

#27. Measles [ #27. Measles [ #31. Poliomyelitis
# For notifiable diseases marked #, please provide vaccination history [ Yes - if yes, Date of vaccination (dd/mm/yyyy) [
☐ No

TO DCE® NOT LATER THAN 72 HOURS FROM TIME OF DIAGNOSIS. FAX NO. 52561616

☐ 33. AIDS
☐ 34. HIV Infection (non-AIDS)

TO NSC® NOT LATER THAN 72 HOURS FROM TIME OF DIAGNOSIS. FAX NO. 62994335

* 35. Chlamydia Genital Infection [ *36. Non-Infectious Syphilis (latent/tertiary) [ *41. Genital Herpes (first episode)
* 36. Gonorrhea [ *39. Infectious Syphilis (primary/secondary) [ *42. Genital Herpes (recurrent)

* For sexually transmitted infections marked *; full name, NRIC/Passport No./FIN, address and telephone number need not be completed.

Indents, date of birth, ethnic group and residential status of the patient should be given.

For TB Please use Notification of Tuberculosis Form (MD352) to notify TBCU (FAX No. 62523051) not later than 72 hours from the time of diagnosis.

Diagnosis [ Clinical [ Confirmed by laboratory tests
Date present diagnosis was made/ suspected
For laboratory notification, please provide the date of test of positive sample [ (dd/mm/yyyy)

Date of onset of illness [ (dd/mm/yyyy, for laboratory notification, please provide the date of receipt of sample)

Follow-up of patient [ Treated as outpatient [ Referred to Communicable Disease Centre
[ Referred to DSC / TBCU [ Hospitalised
[ Death [ Others (specify) [______________]

Travel history over the last one month From (dd/mm/yyyy) [ to (dd/mm/yyyy) [ Countries visited: [______________]

PARTICULARS OF INFORMANT

Name of Medical Practitioner/Scientist (BLOCK LETTERS) [
Signature and Date [
Physician Code (MCR No.) [

Name and Address of Clinic/Hospital/Institution/Laboratory [
Postal Code [
Telephone Number [

Remarks : [______________]
## ANNEX VIII – COMMON LABORATORY TESTS FOR STI SCREENING

### Common Laboratory Tests for STI Screening

<table>
<thead>
<tr>
<th>Type of STI</th>
<th>Type of tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Epididymo-orchitis</strong></td>
<td>• Urethral Gram-stained smear and culture for N. Gonorrhoea</td>
</tr>
<tr>
<td></td>
<td>• <strong>First Void urine (FVU):</strong> Urethral Smear for NAAT (C Trachomatis &amp; N. Gonorrhoea)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Mid-stream urine:</strong> Microscopic Examination &amp; Culture (MSU)</td>
</tr>
<tr>
<td><strong>Bacterial Vaginosis</strong></td>
<td>• Amine Odour Test (Whiff Test)</td>
</tr>
<tr>
<td></td>
<td>• Gram-stained vaginal smear</td>
</tr>
<tr>
<td></td>
<td>• OSOM BVBlue</td>
</tr>
<tr>
<td></td>
<td>• prolineaminopeptidase test</td>
</tr>
<tr>
<td></td>
<td>• Affirm VP III</td>
</tr>
<tr>
<td><strong>Candidiasis</strong></td>
<td>• Gram-stain or wet mount of swabs</td>
</tr>
<tr>
<td></td>
<td>• Culture (Sabouraud Media)</td>
</tr>
<tr>
<td><strong>Chancroid</strong></td>
<td>• Direct Microscopy of smear</td>
</tr>
<tr>
<td></td>
<td>• Culture for H. ducreyi of smear from ulcer/aspirate from buboes</td>
</tr>
<tr>
<td></td>
<td>• Multiplex PCR detection</td>
</tr>
<tr>
<td><strong>Chlamydia Trachomatis Infections</strong></td>
<td>• Nucleic Acid-Based Amplification Test (NAAT) for conjunctival/pharyngeal/rectal specimens</td>
</tr>
<tr>
<td></td>
<td>• Polymerase Chain Reaction (PCR) for urine/urethra/cervical/rectal/ pharyngeal specimens</td>
</tr>
<tr>
<td></td>
<td>• Cervical/vulvo-vaginal swabs: female</td>
</tr>
<tr>
<td></td>
<td>• <strong>FVU:</strong> males</td>
</tr>
<tr>
<td></td>
<td>• Direct fluorescent antibody (DFA)</td>
</tr>
<tr>
<td><strong>Gonorrhoea</strong></td>
<td>• Gram-negative intracellular diplococci in smear</td>
</tr>
<tr>
<td></td>
<td>• Gram-stained endocervical smear (50% sensitive): Females</td>
</tr>
<tr>
<td></td>
<td>• NAATs for rectal/urethral/cervical/</td>
</tr>
<tr>
<td></td>
<td>• Culture for pharyngeal</td>
</tr>
<tr>
<td><strong>Granuloma Inguinale</strong></td>
<td>• Tissue smears from ulcer</td>
</tr>
<tr>
<td></td>
<td>• Ulcer biopsy</td>
</tr>
<tr>
<td><strong>Hepatitis A</strong></td>
<td>• Positive serum Hepatitis A virus specific IgM (HAV-IgM) for &gt; 6 months</td>
</tr>
<tr>
<td><strong>Hepatitis B</strong></td>
<td>• HBsAg</td>
</tr>
<tr>
<td></td>
<td>• HBeAg</td>
</tr>
<tr>
<td></td>
<td>• antiHBe</td>
</tr>
<tr>
<td></td>
<td>• antiHBC IgM</td>
</tr>
<tr>
<td></td>
<td>• antiHBe</td>
</tr>
<tr>
<td></td>
<td>• antiHBs</td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>• Screening ELISA (for HIV+ patients with low CD4 count: &lt;200 cells/mm3)</td>
</tr>
<tr>
<td></td>
<td>• HCV-RNA (after 2 weeks of exposure)</td>
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<td>• HCV serology (after 3 months of exposure)</td>
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<td></td>
<td>• Positive HCV-RNA (6 months after 1st positive test): Chronic infection</td>
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<td></td>
<td>• Viral RNA (to confirm viraemia &amp; genotype essay)</td>
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<tr>
<td><strong>Herpes Simplex Virus Infection</strong></td>
<td>• Viral Isolation in cell culture (Gold standard)</td>
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<td></td>
<td>• Type-specific serological tests (TSSTs)</td>
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<td></td>
<td>• HSV Antigen Detection</td>
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<td></td>
<td>• PCR detection of viral nucleic acid</td>
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<tr>
<td><strong>HIV Infection</strong></td>
<td>• <strong>Rapid Tests:</strong> OraQuick®, The Determine HIV-1/HIV-2 (Abbott), Reveal™,</td>
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<tr>
<td></td>
<td>• Reveal™ G2, Uni-Gold Recombigen® HIV Test, Multispot HIV-1/HIV-2 Rapid Test</td>
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<tr>
<td></td>
<td>• <strong>Screening antibody test:</strong> ELISA test</td>
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<td>• <strong>Confirmatory antibody tests:</strong> Western Blot</td>
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</tbody>
</table>
## ANNEX VIII – COMMON LABORATORY TESTS FOR STI SCREENING

**Common Laboratory Tests for STI Screening**

<table>
<thead>
<tr>
<th>Type of STI</th>
<th>Type of tests</th>
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</thead>
</table>
| **Human Papillomavirus Infection** | • Acetic acid 5% (Acetowhite results 3 mins after application = positive subclinical warts)  
• Skin biopsy (atypical cases)  
• HPV-DNA (only for women >30 years old undergoing cervical cancer screening) |
| **Lymphogranuloma Venereum** | • LGV CFT (single titre of 1:64 or more)  
• Culture of chlamydial organism from lymph node aspiration  
• NAATs (for appropriate sites & urine) |
| **Non-Gonococcal Urethritis (NGU)** | • Gram-stained urethral smear (≥ 5PMNL per high-power [x1000]) taken 4 hours after last micturation  
• Gram-stained preparation from centrifuged sample of First Pass Urine (FPU)  
• NAAT for C. trachomatis  
• NAAT or Culture for N. Gonorrhoea |
| **Molluscum Contagiosum** | • Giemsa-stained smears of the expressed core from the punctum or a skin biopsy |
| **Mucopurulent Cervicitis (MPC)** | • Presence of mucopurulent discharge from the endocervix |
| **Pediculosis Pubis** | • Presence of lice or nits recovered from pubic hair |
| **Pelvic Inflammatory Disease (PID)** | • Clinical findings and culture, antigen detection tests or NAATs of specimens obtained from the lower genital tract. |
| **Prostatitis** | • Blood culture (bacteria/antibiotic sensitivity)  
• Mid-stream urine dipstick test  
• Mid-stream urine culture (bacteria/antibiotic sensitivity) |
| **Scabies** | • Presence of mite in microscopic examination of scrapings from burrows on skin |
| **Syphilis** | • Darkfield microscopy (+ T. pallidum in secretion of primary chancre/moist lesions of secondary syphilis)  
• Non-treponemal serological test: Rapid Plasma Reagin (RPR) and venereal disease research laboratory (VDRL) tests  
• Treponemal serologic test: Treponema Pallidum haemagglutination Assay (TPHA), Treponema Pallidum Particle Agglutination (TPPA), Line Immunoassay (LIA), Fluorescent Treponomal Antibody Absorption (FTA-Abs), Rapid diagnostic tests e.g. Abbott Determine Syphilis TP, Treponemal EIA test |
| **Trichomoniasis** | • Direct microscopy (wet mount of vaginal secretions)  
• Culture on Feinberg Whittington media (90% sensitivity)  
• Rapid Strip Tests: OSOM Trichomonas Rapid Test, Affirm™ VP III nucleic acid probe test  
• Cervical cytology (60-80% sensitivity)  
• PCR Assay: Amplicor by Roche Diagnostic Corp  
• APTIMA T. vaginalis Analyte Specific Reagents (ASR) by Gen-probe, Inc. (74-98% Sensitivity, 87-98% specificity) |
| **Vulvovaginitis** | • pH of vaginal discharge  
• Microscopic examination (wet mount + Gram-stained specimen of vaginal fluid)  
• Whiff Test  
• Culture of vaginal discharge (Trichomonas Vaginalis & Candida Albicans) |