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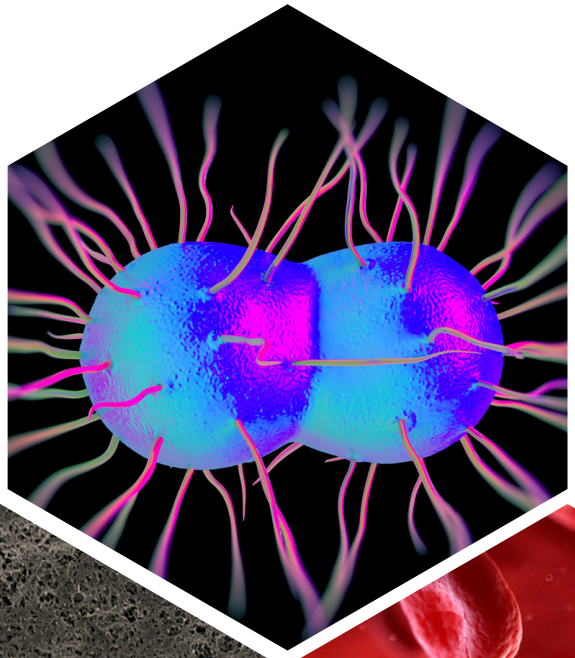
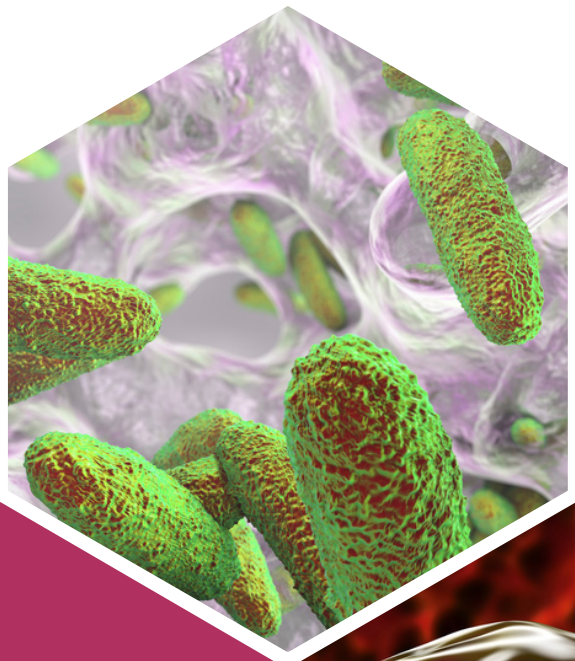
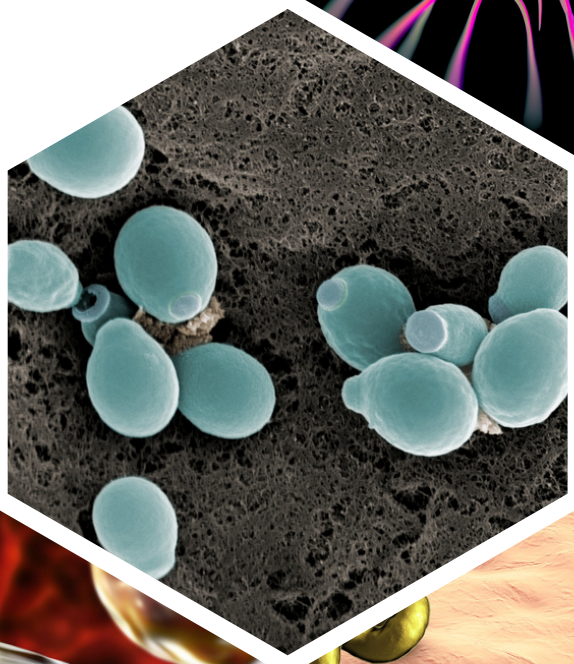
MALAYSIAN GUIDELINES

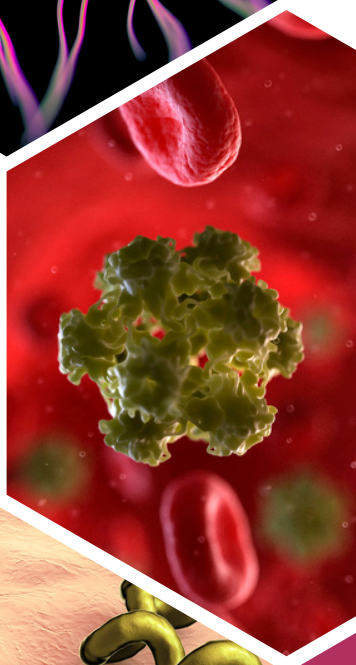
MINISTRY OF HEALTH MALAYSIA

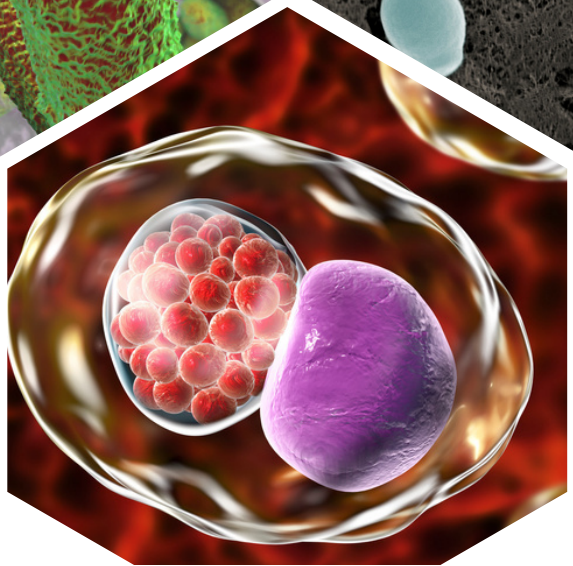
MANAGEMENT OF SEXUALLY TRANSMITTED INFECTIONS

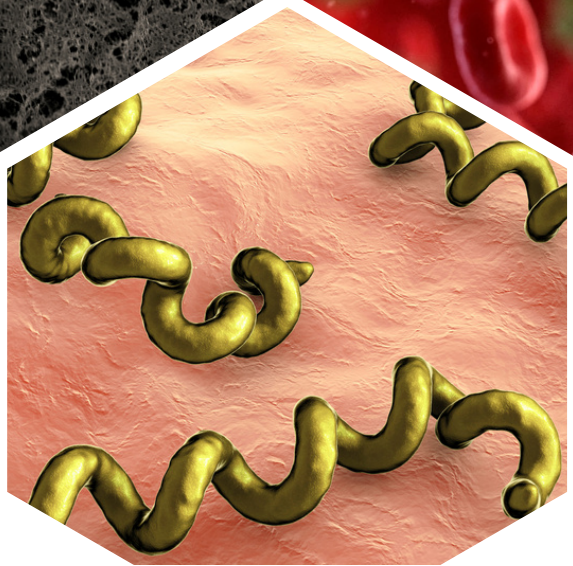












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MESSAGE FROM DIRECTOR GENERAL OF HEALTH

I'm pleased to launch a comprehensive guide on sexually transmitted infections (STIs), specifically designed to assist clinicians in their crucial role of managing and preventing such common and complex conditions.

STIs continue to be a significant global health concern, affecting individuals of all genders, ages and backgrounds. As healthcare providers, it is our responsibility to stay informed about the latest advancements in STI research, diagnosis, treatment and prevention strategies. This guide aims to serve as a reliable reference, enabling clinicians to deliver optimal care to patients and help curb the spread of these infections.

This guide provides a wide range of information on various STIs, including their epidemiology, aetiology, clinical presentation, diagnostic techniques, treatment options and prevention measures. A panel of experts has meticulously curated the content to ensure it is relevant, evidence-based and practical for clinical practice.

As clinicians, our role extends beyond the clinical setting. We also play a pivotal role in promoting sexual health education, STI screening and prevention and reducing the stigma associated with STIs.

Therefore, I would like to express my sincere gratitude to the dedicated healthcare professionals and organizations who have contributed their expertise to produce this guide. Their tireless efforts in advancing the field of STI care are commendable and we are fortunate to benefit from their efforts.

I encourage you to delve into this guide and use the information to enhance your practice. Together, we can make a profound impact on the health and well-being of our patients and communities.

Thank you for your unwavering commitment to excellence in healthcare.

DATUK DR MUHAMMAD RADZI BIN ABU HASSAN

Director General of Health

Ministry of Health Malaysia

MESSAGE FROM DEPUTY DIRECTOR GENERAL OF HEALTH

I would like to congratulate the committee for producing the latest edition of the Sexually Transmitted Infection Guidelines.

I am aware of the challenges posed by STIs and the profound impact they can have on individuals, communities, and society at large.

This document is a testament to our dedication to furnishing evidence-based, current, and readily available guidance to our healthcare professionals. It is a guide to navigate the complexities of STIs, empowering healthcare worker to make decisions that promote prevention, early detection, and compassionate care.

The guidelines encompass a wide spectrum, addressing not only the clinical aspects of STIs but also the socio-cultural factors that contribute to their spread. By taking a holistic approach, we aim not only to treat those affected by STIs but also to create an environment conducive to prevention and destigmatization.

I extend my gratitude to the dedicated professionals who have contributed their expertise to this initiative. Their dedication is evident in the thoroughness and relevance of the guidelines presented herein.

As we commence the implementation of these guidelines, let us bear in mind that our efforts extend beyond the confines of this document. It signifies a dedication to constructing a healthier and more enlightened society.

May these guidelines serve as a knowledge and compassion in our collective journey towards a future where the burden of sexually transmitted infections is significantly reduced, and the well-being of our communities is enhanced.

DATO' INDERA DR NOR AZIMI BINTI YUNUS

Deputy Director General of Health

Ministry of Health Malaysia

MESSAGE FROM THE CHAIRPERSONS

We wish to take this opportunity to thank and congratulate the secretariat and the working committee for their great effort to revise The Malaysian Guidelines in the Treatment of Sexually Transmitted Infections Year 2015.

Accurate and prompt diagnosis, followed by effective treatment, complemented with comprehensive prevention strategies are paramount in the management of patients with sexually transmitted infections (STIs). With that, we believe it is timely that this revision of guidelines is done, in accordance with various international guidelines on STIs to date.

In 2020, World Health Organisation (WHO) estimated 374 million new STIs with population groups who are disproportionately affected, including MSM, adolescents, sex workers and their clients, pregnant women and transgender community. Effective management of STIs is very important for control, as it prevents the development of complications and decreases the spread in the community.

These revised guidelines are intended to assist health care providers to play a crucial role in treating and preventing STIs. Although the guidelines emphasize on treatment, prevention strategies and diagnostic recommendations are also discussed.

Access to treatment and care is vital for a successful STI control programme. Although Malaysia has evolved over the years in the management of STIs, we do struggle at times with situations where individuals at risk are reluctant to seek treatment for fear of stigma and discrimination. Upscaling sexual health services, particularly in primary care, by providing new point-of-care rapid STI tests for screening and provision of treatment without delay in this country is absolutely pivotal. Availability and affordability of STI diagnostics particularly PCR and NAAT testing should be focused on and emphasized in order to achieve correct diagnosis and appropriate treatment.

Finally, allow us to thank again to those who have helped in making this revision of guidelines possible. It is our sincere hope that these revised guidelines will be beneficial to all health care providers who are involved in the management of STIs.

Thank you.

Dr. Suganthi Thevarajah & Dr. Khairil Erwan Bin Khalid

ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
Anti-HCV	Hepatitis C antibodies
ART	Antiretroviral Therapy
BASHH	British Association for Sexual Health and HIV
BCA	Bichloroacetic acid
BVAB	Bacterial Vaginosis-associated bacteria
BV	Bacterial Vaginosis
CDC	Centers for Disease Control and Prevention
CMIA	Chemiluminescence Immunoassay
CMV	*Cytomegalovirus*
CNS	Central nervous system
CO2	Carbon Dioxide
CT	*Chlamydia trachomatis*
DsDNA	Anti–double stranded DNA
DGI	Disseminated Gonococal Infection
DNA	Deoxyribonucleic acid
EIA	Enzyme Immunoassay
ECLIA	Electrochemiluminescence Immunoassay
EMTCT	Elimination of mother to child transmission
FAST score	FibroScan-aspartate Aminotransferase score
FPU	First pass urine
FSW	Female Sex worker
FTA-ABS	Fluorescent Treponemal Antibody Absorption Test
GC NAAT	Gonococcus nucleic acid amplification test
HBsAg	Hepatitis B surface Antigen
Hep B	Hepatitis B
Hep C	Hepatitis C
HIV	*Human immunodeficiency virus*
HPV	*Human Papillomavirus*
HSV-1	*Herpes Simplex Virus Type 1*
HSV-2	*Herpes Simplex Virus Type 2*
ID Physician	Infectious Disease Physician
IgG	Immunoglobulin G
IM	Intramuscular
IUD	Intrauterine device
IVDU	Intravenous drug users
LGV	Lymphogranuloma venereum
LSI	Last sexual intercourse
MAC	Malaysian AIDS Council
MAF	Malaysian AIDS Foundation
MSM	Men who have sex with men

MTCT	Mother to child transmission
NAAT	Nucleic Acid Amplification Tests
NG	*Neisseria gonorrhoeae*
NGO	Non-governmental organization
NGU	Non-Gonococcal Urethritis
NAAT	Nucleic acid amplification tests
PCR	Polymerase Chain Reaction Test
PHC	Primary Health Care
PID	Pelvic inflammatory disease
PLHIV	People living with HIV
PMNs	Polymorphonuclear Neutrophils
PMTCT	Prevention of mother to child transmission
PO	Peroral
POCT	Point-of-Care Test
PrEP	Pre-exposure prophylaxis
PROSTAR	Programme without AIDS for Youth
PSI	Previous sexual intercourse
RDT	Rapid Diagnostic Test
RPR	Rapid plasma reagin
SARA	Sexually acquired reactive arthritis
SRH	Sexual Reproductive Health
STI	Sexual Transmitted Infection
TCA	Trichloroacetic acid
TG	Transgender
TOC	Test-of-Cure
TPHA	*Treponema pallidum* haemagglutination assay
TPPA	*Treponema pallidum* particle agglutination
Urine C&S	Urine culture and sensitivity
Urine FEME	Urine Full Examination and Microscopic Examination
UTI	Urinary Tract Infection
VDRL	Venereal Disease Research Laboratory
VZV	*Varicella zoster virus*
WBC	White blood cell
WCC	White cell count
WHO	World Health Organization

1. INTRODUCTION

1.1 Overview

Sexually Transmitted Infections (STIs) have a profound impact on sexual and reproductive health worldwide. In 2020, World Health Organization (WHO) estimated 374 million new STIs infection with 1 of 4 curable STIs due to chlamydia (129 million), gonorrhoea (82 million), syphilis (7.1 million) and trichomoniasis (156 million). More than 490 million people were estimated to be living with genital herpes in 2016, and an estimated 300 million women have a *Human Papillomavirus* (HPV) infection, the primary cause of cervical cancer and anal cancer among men who have sex with men (MSM). An estimated 296 million people are living with Chronic Hepatitis B globally. There are the population groups who are disproportionately affected by STIs, including MSM, adolescent girls and young women, sex workers and their clients, pregnant women, and transgender people.

STIs can have serious consequences beyond the immediate impact of the infection itself. For example, STIs like herpes, gonorrhoea and syphilis can increase the risk of HIV acquisition, mother-to-child transmission of STIs can result in stillbirth, neonatal death, low-birth weight and prematurity, sepsis, neonatal conjunctivitis and congenital deformities, HPV infection causes cervical and other cancers and Hepatitis B resulted in an estimated 820 000 deaths in 2019, mostly from cirrhosis and hepatocellular carcinoma. STIs such as gonorrhoea and chlamydia are major causes of pelvic inflammatory disease and infertility in women. STI transmission is predominantly through sexual contact either via the vagina, anal, or oral transmission. However, STIs also can spread through nonsexual activities such as by blood or vertical transmission from mother-to-child during pregnancy and birth.

In Malaysia, there are four types of STIs that need to be notified under the Prevention and Control of Infectious Disease Act 1998 (Refer Appendix 2). These are syphilis, gonorrhoea, HIV and chancroid. The first three are the most notified STI diseases. Effective management of STIs is very important for control, as it prevents the development of complications, decreases the spread of these diseases in the community and offers a unique opportunity for screening and targeted education about HIV prevention. There is a strong correlation between the spread of conventional STIs and HIV transmission and both ulcerative and non-ulcerative STIs have been found to increase the risk of sexual transmission of HIV. Appropriate treatment of STI patients at their first encounter with a healthcare provider is therefore an important public health measure.

1.2 The Challenges and Strategies in The Prevention and Control of STIS In Malaysia

Over the past three decades, Malaysia has invested significant time and resources which resulted in a significant reduction in the spread of HIV in the country. In 2012, the HIV incidence rate was 11.72 cases per 100,000 population and it has dropped to 8.5 cases per 100,000 population in 2021. Meanwhile, the trend of the three notifiable STIs (chancroid, gonorrhoea and syphilis) varies. The incidence rate for chancroid remained stable at 0 to 0.02 per 100,000 population between 2012 and 2022. However, there was an increasing trend observed for gonorrhoea and syphilis. The incidence rate for gonorrhoea increased from 5.1 per 100,000 population in 2012 to 5.6 per 100,000 population in 2022, whereas the incidence rate for syphilis increased almost double from 5.7 per 100,000 population in 2012 to 14.3 per 100,000 population in 2022. Nonetheless, the increase in the incidence of syphilis and gonorrhoea might have been contributed by the improvement in the STI surveillance systems in the country and the establishment of STI Friendly Clinics in selected government health clinics starting from the year 2015.

Much need to be done to control the spread of STIs in Malaysia and around the region in order to meet the Global Health Sector Strategy 2022-2030 initiatives on STIs, focusing on the three major global significant infections which are syphilis (*Treponema pallidum*), gonorrhoea (*Neisseria gonorrhoeae*) and HPV (*Human papillomavirus*) infection. The Ministry of Health has to tackle the increasing challenges in the prevention and control of STIs by ensuring the continuation of sustainable programmes and activities linked to the established HIV programmes. Some key challenges faced, and recommendations are discussed below:

(i) The increase in STIs among young people

The increase in reported STI cases is disproportionately higher for males compared to females, with male to female ratio being 3.36 and 3.62 for syphilis and gonorrhoea, respectively. In addition, it is also observed that young people aged 20-39 years accounted for 67% of new syphilis cases and 78% of new gonorrhoea cases in 2022. This is also consistent with the new HIV cases where 77% occurred within the same age distribution. These indirectly indicate that high-risk sexual behaviour may have started as early as secondary school years.

According to the findings from National Health and Morbidity Survey (2017) for risky sexual behaviour among school-going adolescents in Malaysia, the prevalence of ever-had sex was 7.3%, among which mostly are males, 87.3% did not use condoms, 16.6% had multiple sexual partners and 31.7% had sex before the age of 14 years. The other associated factors to sexual activity among young people include ever-smoked and ever-used drugs. Therefore, addressing HIV and STIs in the young population requires young people to have access to the information and tools they need to reduce risk, make healthy decisions, and get treatment and care if needed. Abstinence from sexual intercourse and delayed initiation of sexual behaviour are among the central aims of HIV prevention efforts for young people. Decreasing the number of sexual partners and increasing access to, and utilization of comprehensive

prevention services, including prevention education and increasing access to condoms are essential for young people who are sexually active.

The school-based Sexual Reproductive Health (SRH) is also imperative to instil a better understanding of safe sex and the consequences of unintended health outcomes from premarital sex. Inculcating knowledge and awareness on SRH have been proven to reduce unintended pregnancies and also mitigate sexually transmitted infection among adolescents.

One of the main initiatives is the Healthy Programme without AIDS for Youth (PROSTAR). This programme was introduced by the Ministry of Health in 1996 in its effort towards solving the AIDS problem among youths. The programme, which has the theme 'Action by Youth, for Youth and Through Youth' uses peer education to disseminate messages as well as to directly involve youths in HIV/AIDS awareness campaigns. Recently the programme has been rebranded to PROSTAR 2.0 which includes awareness about STIs as well as stigma and discrimination issues.

In addition, Malaysia also has the National Adolescent Health Plan of Action 2021-2030 that is in development to streamline the efforts of various Government agencies and other stakeholders in promoting and supporting adolescents toward optimum health in adulthood. This includes focusing on specific morbidities and mortalities related to risk behaviours and sexual reproductive health such as teen pregnancy, unsafe abortion, sexually transmitted infection, HIV/AIDS, smoking, alcohol consumption, mental illness and suicide.

(ii) Interventions for high-risk populations

Achieving appropriate targets and a high percentage of coverage are often the key challenges of interventions in high-risk populations. Sexual transmission of HIV among key populations i.e., MSM, FSW and TG and their sexual partners have been increasing. The HIV prevalence among MSM, FSW and TG have increased significantly between 2012 and 2017 from 7.1% to 21.6% for MSM, 4.2% to 6.3% for FSW and 4.8% to 10.7% for TG. This is comparable with our surveillance data which show the share of new infections attributed to sexual transmission has increased to more than 90% of the annual total. Recent reports have suggested that the use of alcohol or drugs related to sexual behaviour, such as unprotected intercourse, is known to place an individual at higher risk for HIV infection.

The Ministry of Health has played a major role in targeted interventions for key populations through various programmes and activities for many years. Some of the programmes and activities were implemented through networking with Non-Governmental Organizations (NGOs), principally the Malaysian AIDS Council (MAC) and Malaysian AIDS Foundation (MAF). Along with their other partner organizations, both MAC and MAF have supported MOH to coordinate the HIV response among key populations, through harm reduction programme, HIV continuum of care, community-based testing, outreach activities, pre-exposure prophylaxis or PrEP demonstration study and expansion of differentiated health services for key populations through client-friendly government health clinic set up (KK model 2.0). Through this model, MOH allows NGOs to operate in certain health clinics to help strengthen prevention programmes and also reduce social stigma and discrimination among people living

with HIV (PLHIV). In addition, the way forward for providers of sexual services is to reach the key populations by using digital platforms i.e., mobile phones and social media to link them to treatment, care and support.

(iii) Sustaining elimination of congenital syphilis

Syphilis continues to affect a large number of pregnant women, causing substantial perinatal morbidity and mortality. As one of the adverse pregnancy outcomes of mother-to-child transmission (MTCT) of syphilis, congenital syphilis can be prevented by screening and treatment of infected pregnant women. In 2018, Malaysia became the first country in the Western Pacific Region to be certified as having eliminated mother-to-child transmission of HIV and syphilis. The current version of the global initiative for the elimination of MTCT (EMTCT) of syphilis emphasizes the coverage of intervention services targeting pregnant women, i.e, ≥95% antenatal care (at least one visit), ≥95% syphilis testing and ≥95% treatment coverage (at least one dose of intramuscular benzathine benzylpenicillin) for at least 30 days prior to delivery in order to achieve the goal of having a congenital syphilis rate ≤50 cases per 100,000 live births. The annual rate of congenital syphilis per 100,000 live births was 2.39 (2018), 4.66 (2019), 6.37 (2020) and 5.16 (2021).

In order to sustain the elimination status, several weaknesses need to be addressed immediately such as an increase in cases of unbooked or late booker syphilis positive pregnant mothers, screening of high-risk mothers are not repeated at 28 to 32 weeks of pregnancy, infants exposed to syphilis infection are not monitored closely to ensure the drop in RPR titre, epidemiological treatment is not being given to the spouse of syphilis positive mother, treatment for syphilis positive mother was not given according to the recommended regime and RPR serology test was not carried out for mother and infant immediately after birth for purpose of comparison.

Based on these weaknesses, all government and private health facilities should refer to the *Guidelines for Strengthening of Prevention of Mother-to-Child Transmission of HIV and Syphilis, second edition 2021* issued by the Ministry of Health Malaysia. This is to ensure that the correct management and treatment are given not only to pregnant mothers and their babies but also to their spouses or partners.

(iv) Availability of screening and diagnostic tests for various STIs

In cases where STIs are suspected, a good history and thorough clinical examination coupled with either a screening or diagnostic test would aid in the final diagnosis. There are multiple screenings and diagnostic tests available using blood, swabs or biopsies taken from the lesions.

Therefore, there is an urgent need for other newer tests for various STIs to be made available either in hospitals or primary health clinics i.e., PCR test for chlamydia, immunofluorescent test for HSV, culture and PCR test for gonorrhoea and better point of care tests (POCT) using the rapid test with increased sensitivity and specificity.

(v) STI case management

Early diagnosis and effective treatment of STIs is an essential component of STI control programmes. The traditional method for STI diagnosis has been through laboratory diagnosis of the aetiological agent. Whilst this is still the method of choice, this approach is expensive in terms of diagnostics, infrastructure, and maintenance. In addition, some primary health centres in Malaysia have limited laboratory capacity resulting in delays in diagnosis and treatment.

Therefore, in resource-limited settings, syndromic management is still relevant and has become the standard of care where laboratory diagnosis is not available or is hard to access. Management is simplified using clinical flowcharts and allows time in the consultation to provide simple education messages, discuss partner notification and promote condoms. Antimicrobial therapy is provided at once to cover the majority of pathogens presumed responsible for that syndrome, in that specific geographical area. Syndromic management is simple and lends itself to use in a variety of outlets such as STI clinics, primary healthcare (PHC) facilities, family planning/maternal and child health services and private practitioners' clinics. However, there are two main limitations to syndromic management that should be addressed. First, the sensitivity and specificity of the approach for the diagnosis and management of urethral discharge syndrome and genital ulcer syndrome in various settings have been very satisfactory. However, it has poor sensitivity and specificity or the detection of cervical infections in women, even in settings with higher STI prevalence. Another limitation is the cost of over-diagnosis and treatment of patients with no or only one infection.

(vi) Partner notification

Partner notification is a strategy consisting of contacting the sexual partners of STI patients to offer them screening and treatment. Partner notification aims to help interrupt the transmission of infections, prevent potential re-infection and prevent complications. Currently, there is strong evidence that referral from an index patient ('patient referral') can be effective, and less labour intensive and costly than 'provider referral'. However, the acceptability of partner notification depends upon confidentiality and potential negative impacts such as violence against the index case (especially women).

(vii) Promotion of treatment-seeking behaviour and the role of the private healthcare sector

Studies have shown that there is a substantial proportion of people with symptomatic STI seek treatment informally from traditional healers, unqualified practitioners, or self-medication. Patients will only attend formal health services after alternative treatments have failed. STI patients also seek care in the private health facilities for many reasons, especially with convenient opening times. Private healthcare facilities are often seen as providing more personalised and confidential services with less social stigma between client and provider. In general, the private healthcare sector should be viewed as a complement to effective and accessible STI management services. Attempts should be made to stimulate effective collaboration between public and public sectors.

(viii) The changing epidemiology of STI

Additional challenges to STI control include the capacity of pathogens to develop resistance to antimicrobials, and the emergence of some pathogens (HSV-2) or conditions (bacterial vaginosis) as novel significant causes of morbidity, including the facilitation of HIV transmission.
Surveillance programmes to detect antimicrobial resistance should be made available locally. There is also an urgent need for research into more interventions such as behaviour change and development of new vaccines.

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2. SEXUAL HISTORY TAKING & STI SCREENING

2.1 Sexual History Taking

1. General principles

- Ensure privacy and confidentiality
- Welcoming, comfortable, private physical environment is likely to encourage openness when discussing sensitive issues
- Emphasize the non-judgemental nature of assessment
- It is recommended that all patients receive a chaperone during intimate examinations. If necessary, requests from patients for a particular gender of clinicians based on their culture, religion, or personal preferences should be accommodated.
- Open questions followed by exploration of initial concerns and more closed questions as the consultation continues
- Be explicit when asking about sexual behaviour and clarify if you are unsure of what the patient says
- Avoid unclear terminology unless the patient initiates and clarify what they mean
- Be aware of the patient's signs of anxiety and distress
- Recognise non-verbal cues from patients
- Clinical record is confidential

2. The importance of sexual history

- To guide proper examination and investigation
- To ascertain contraception use and risk of pregnancy
- To assess other sexual health issues (also allowing a discussion of psychosexual problems)
- To assess HIV, Hepatitis B, Hepatitis C and syphilis risk for both testing and prevention
- To assess risk behaviours, which will then facilitate health promotion activity including partner notification and sexual health promotion

3. Proposed sexual health consultation template (symptomatic male)

Reason for attendance	☐
Sexual history (*refer components of a sexual history**)	☐
Past medical history	☐
Medication history	☐
Allergies	☐
Occupation	☐
Travel history	☐
Last HIV test	☐
HIV risk factors: • HIV + partner? • MSM partner? • IVDU partner? • Previous blood transfusion?	☐
Hepatitis B status (vaccinated, natural immunity, unsure?)	☐
Hepatitis C status (known/unknown)	☐
Syphilis status (known/unknown)	☐
Alcohol (If yes, FAST score)	☐
Smoking	☐
Did you use drugs/recreational substance last 6 months? If yes: • Which drugs did you use? (Ketamine, crystal meth, GHB/ GBL, mephedrone, cocaine, others) • Did you inject?	☐
Examination findings – in diagram if possible (hernia, lymph nodes, penis, testes/scrotum, perineum, rectum/proctoscopy, others)	☐
Last passed urine? (Ideally > 2 hours)	☐
Name of chaperone if available	☐
Types of specimens (blood, pharyngeal swab, urethral swab, rectal swab, ulcer swab, urine, others)	☐
Urethral/rectal microscopy (gram stain smear: pus cells, gonorrhoea?)	☐
Urinalysis (if indicated)	☐

Diagnosis	☐
Management	☐

4. Proposed sexual health consultation template (symptomatic female)

Reason for attendance	☐
Sexual history (*refer components of a sexual history**)	☐
Past medical history	☐
Medication history	☐
Allergies	☐
Occupation	☐
Travel history	☐
Contraception? (If yes, which type?)	☐
Obstetrics/gynaecology history (previous pregnancy, termination of pregnancy, emergency contraception, post-coital bleeding)	☐
Last menstrual period	☐
Last cervical cytology/pap smear	☐
Last HIV test	☐
HIV risk factors: • HIV + partner? • Bisexual partner? • IVDU partner? • Previous blood transfusion?	☐
Hepatitis B status (vaccinated, natural immunity, unsure?)	☐
Hepatitis C status (known/unknown)	☐
Syphilis status (known/unknown)	☐
Alcohol (If yes, FAST score)	☐
Smoking	☐
Did you use drugs/recreational substance last 6 months? If yes: • Which drugs did you use? (Ketamine, crystal meth, GHB/GBL, mephedrone, cocaine, others) • Did you inject?	☐

Examination findings – in diagram if possible (bimanual, cervix, lymph nodes, perineum, vagina, vulva, rectum/proctoscopy, others)	☐
Name of chaperone if available	
Types of specimens (blood, pharyngeal swab, vulvo-vaginal swab, rectal swab, ulcer swab, urine, others)	☐
Microscopic examination of vaginal smear (gram stain smear for bacterial vaginosis and candidiasis)	☐
Vaginal wet mount microscopy (for trichomoniasis)	☐
Endocervical smear microscopy and culture (for gonorrhoea)	☐
Rectal microscopy and culture (for gonorrhoea) if indicated	☐
Urinalysis (if indicated)	☐
Diagnosis	☐
Management	☐

5. *Components of a sexual history (The 6Ps)

i. Partners:

- Gender of sexual partner/s
- Number of partners in the last 3 months - not necessary to ask for the specific details (if > 5 partners)

ii. Practices:

- Last sexual intercourse (LSI):
    - How long ago?
    - Spouse, regular non-spouse, casual?
    - If regular, duration of relationship?
    - Type of sex and use of condoms (oral, vaginal, anal)
    - In MSM, are they insertive or receptive for anal sex?

- How did you meet your partner/s?
- Any drug use (self/partner)?
- Have you or your sex partner/s ever exchanged sex for life needs? (money, housing, safety, drugs)

iii. Protection:

- Use of condoms/barrier methods – “How often would you say you use condoms? All of the time? 50% of the time?”
- If all sexual contact was protected (i.e., condoms used), when was the last unprotected vaginal/anal sex?
- If not using protection, what are the reasons?

iv. Past history:

- Known STI/symptoms (diagnosis, when and whether was treated)
- Known STI/symptoms in the partner/s (diagnosis, when and whether was treated)
- Previous sexual intercourse (PSI) with different partner (for the last 3 months) – to obtain same information as LSI

v. Pregnancy planning:

- Any plans/desires to have children/more children?
- Assess timing, importance of prevention, conduct preconception education

vi. Plus (Pleasure, Problems and Pride):

- How is your sex life?
- What difficulties are you having with your sex life or during sex?
- What support do you have about your gender identity and/or sexual orientation?

6. Symptom review

- Ask about specific genital symptoms, in case this reveals overlooked or ignored problems

Male	Female
Urethral discharge Dysuria Genital skin problems Testicular pain/swelling Ejaculatory problems Peri-anal/anal symptoms (in MSM)	Unusual vaginal discharge Vulval skin problems Lower abdominal pain/deep dyspareunia Dysuria Unusual vaginal bleeding (intermenstrual bleeding/post coital bleeding)

7. Ending consultation

- Summarise the consultation and inform which tests need to be done
- Discuss how results will be reviewed and confirm contact details
- Ask if any questions or concerns (including psychosocial, disclosure, safety in relationships, information on STI transmission)
- Offer condoms

2.2 STI Screening

1. Heterosexual male (symptomatic/asymptomatic)
   - Blood test:
     - HIV Ag/Ab
     - Syphilis serology (RPR/VDRL + TPPA/TPHA/CMIA/ECLIA)
     - HBsAg*
     - Anti HCV*

- Urine:
    - Chlamydia/Gonorrhoea (CT/NG) NAAT

2. Heterosexual female (symptomatic/asymptomatic)

- Blood test:
    - HIV Ag/Ab *
    - Syphilis serology (RPR/ VDRL+TPPA/TPHA/EIA/CIA)
    - HBsAg*
    - Anti HCV*

- Vulvo-vaginal swab:
    - Chlamydia/Gonorrhoea (CT/NG) NAAT

- Consider pharyngeal swab for CT/NG NAAT (receptive oral sex) and rectal swab for CT/NG NAAT (receptive anal sex). May need pool samples for testing

3. MSM (symptomatic/ asymptomatic)
- Blood test:
    - HIV Ag/Ab*
    - Syphilis serology (RPR/VDRL+TPPA/TPHA/CMIA/ECLIA)
    - HBsAg*
    - Anti HCV*

- Urine:
    - Chlamydia/Gonorrhoea (CT/NG) NAAT

- Consider pharyngeal swab for CT/NG NAAT (receptive oral sex) and rectal swab for CT/NG NAAT (receptive anal sex). May pool samples for testing

4. Women who have sex with women (WSW)
- Do not require routine testing, unless they are symptomatic or report sexual contact with men
- Manage as per heterosexual female
- Ask explicitly about sex with men and discuss contraception only if applicable

5. Transgender individuals
- Should be assessed and screened based on their sexual behaviour, similarly to cisgender individuals
- Transmen with a vagina should provide a vaginal swab rather than a urine sample, if having vaginal sex
- Transwomen with neovagina, urine sample is preferred rather than a vaginal swab
- All transgender individual should provide a rectal swab if having receptive anal sex

*Blood Borne Virus (BBV) Risk:

- Unprotected sex with HIV+ individual
- Unprotected sex with MSM
- Engaging in chemsex/group sex
- Injecting drug use or sexual partner who injects drugs
- Sharing of paper rolls/straws for snorting drugs
- Paid for or been paid for sex
- Medical treatment/tattooing where sterility cannot be guaranteed

6. Window periods
    - Window periods should be noted and patients should be offered re-testing if appropriate
    - The window period is the length of time it takes for a test to detect an infection following transmission
    - If a person is known contact of an infection and is within the window period, treatment should be considered

Infection	Window Period
Chlamydia (NAAT)	2 weeks
Gonorrhoea (NAAT)	2 weeks
HIV Ag/Ab	4 weeks
Syphilis (serology)	6 weeks – 12 weeks
Hepatitis B	3 months – 6 months
Hepatitis C	Up to 6 months

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3. MODIFIED SYNDROMIC APPROACH TO STI MANAGEMENT

STIs which have similar signs and symptoms are grouped into syndromes. STI management uses this syndromic approach to ensure a quick and effective treatment could be initiated for the patient on the same day. This syndromic approach includes types of STIs that could be fully treated such as syphilis, gonorrhoea, chlamydia, trichomoniasis and candidiasis.

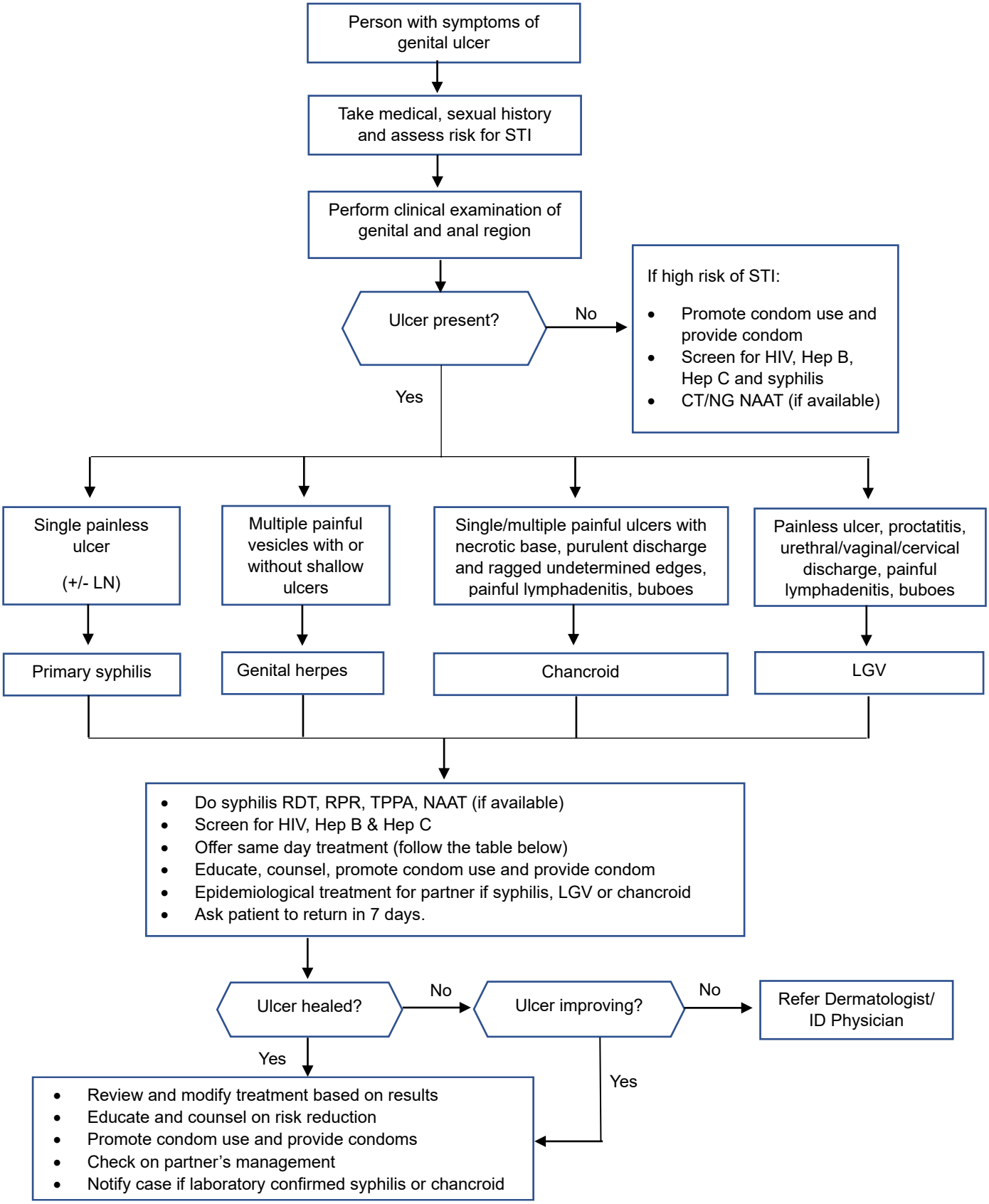
The syndromes which are currently used for the approach are:

1. Anogenital ulcer disease syndrome
2. Urethral discharge syndrome
3. Vaginal discharge syndrome
4. Lower abdominal pain syndrome
5. Anorectal discharge syndrome

By using the Modified Syndromic Approach (MSA), diagnosis is made based on the possible pathogen. The difference between MSA and aetiological management is that in MSA, treatment is given empirically during patient's first visit to the clinic. During follow-up, the lab test results are traced to confirm the diagnosis according to the causing pathogen, change treatment according to the lab test result, and evaluate patient's response to the treatment given during the first visit.

3.1 Anogenital ulcer disease syndrome

Flowchart for the syndromic approach to management of anogenital ulcers

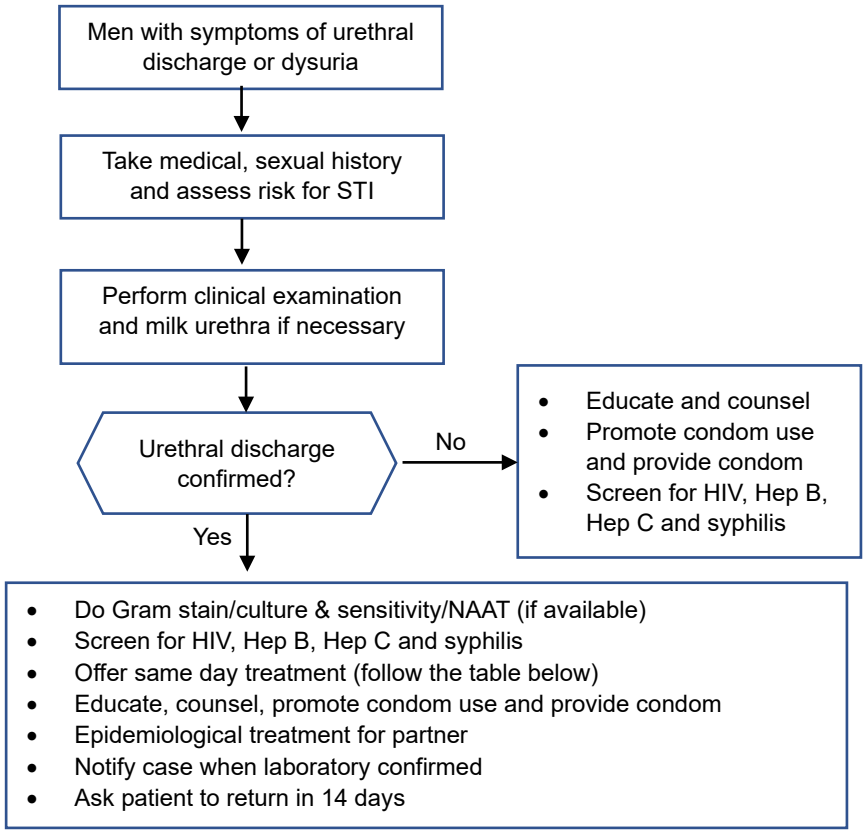


Recommended treatment options for anogenital ulcer disease syndrome

Type of infection	Preferred	Alternative	Pregnancy
Herpes	Acyclovir 400mg PO q8h for 7-10 days	Valaciclovir 1g PO q12h for 7-10 days	Acyclovir 400mg PO q8h for 7-10 days *For acquisition from 36 weeks onwards, continue treatment till delivery
Primary syphilis	Benzathine penicillin 2.4MU IM STAT **OR** Procaine penicillin 600,000units IM q24h for 10 days	For penicillin allergy: Doxycycline 100mg PO q12h for 14 days	Benzathine penicillin 2.4MU IM STAT **OR** Procaine penicillin 600,000units IM q24h for 10 days For penicillin allergy: *Desensitise and treat with penicillin as there are no proven alternatives. If failed desensitisation: Ceftriaxone 500mg IM q24h for 10 days **OR** Azithromycin 2g PO STAT
LGV	Doxycycline 100mg PO q12h for 21 days	Azithromycin 1g PO weekly for 3 weeks **OR** Erythromycin ethylsuccinate 800mg PO q6h for 21 days	Azithromycin 1g PO weekly for 3 weeks
Chancroid	Azithromycin 1g PO STAT	Ceftriaxone 250mg IM STAT **OR** Ciprofloxacin 500mg PO q12h for 3 days **OR** Erythromycin ethylsuccinate 800mg PO q8h for 7 days	Azithromycin 1g PO STAT

3.2 Urethral discharge syndrome

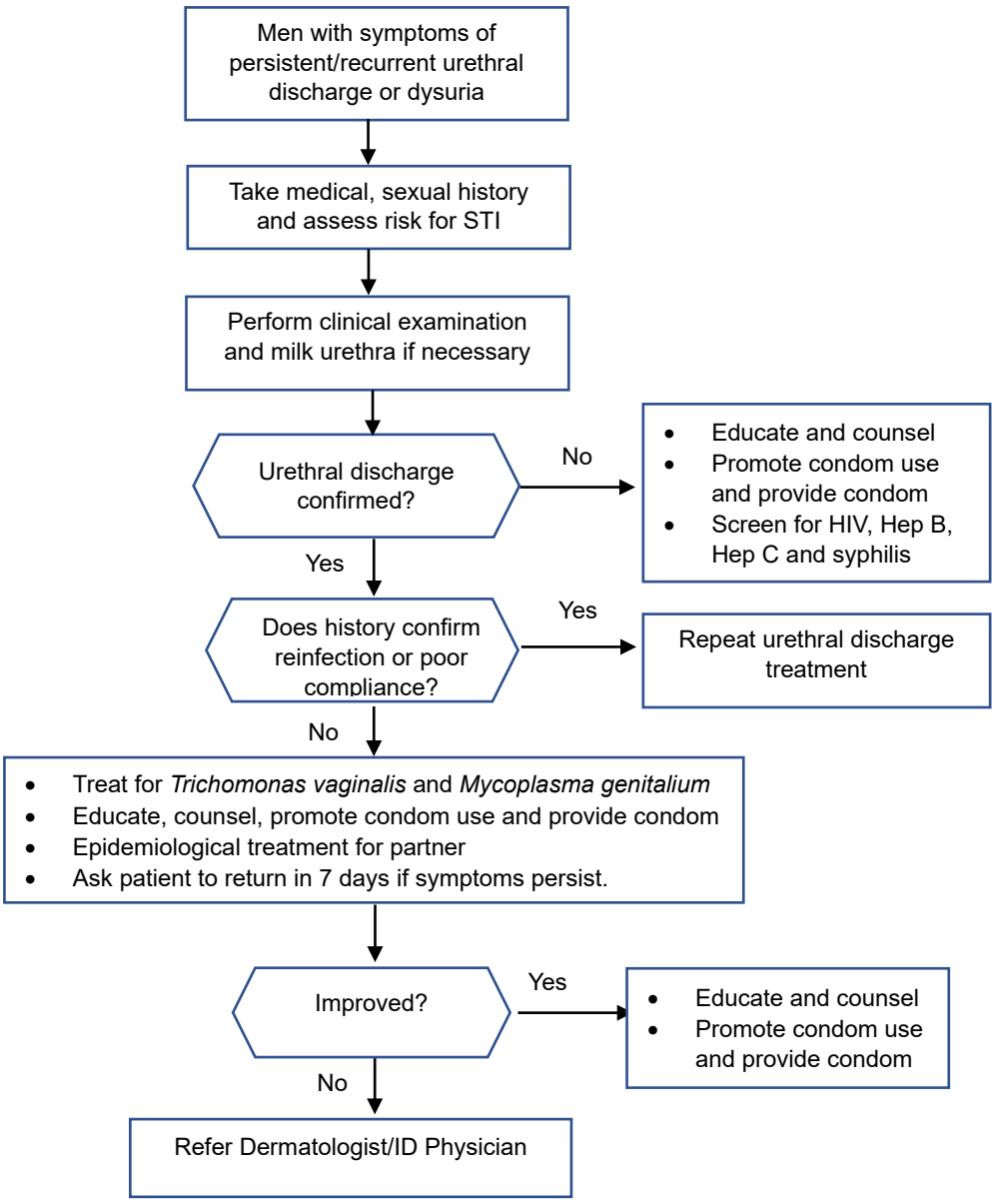
Flowchart for the syndromic approach to management of men presenting with urethral discharge



Recommended treatment options for urethral discharge syndrome

Type of infection	Preferred	Alternative	Pregnancy
Uncomplicated *Neisseria gonorrhoeae*	Ceftriaxone 500mg IM STAT (BW > 150kg, use 1g) **PLUS**	Gentamicin 240mg IM STAT **PLUS**	Ceftriaxone 500mg IM STAT (BW > 150kg, use 1g) **PLUS**
Chlamydia trachomatis	Doxycycline 100mg PO q12h for 7 days	Azithromycin 2g PO STAT	Azithromycin 1g PO STAT

Flowchart for the syndromic approach to management of men presenting with resistant or persistent urethral discharge



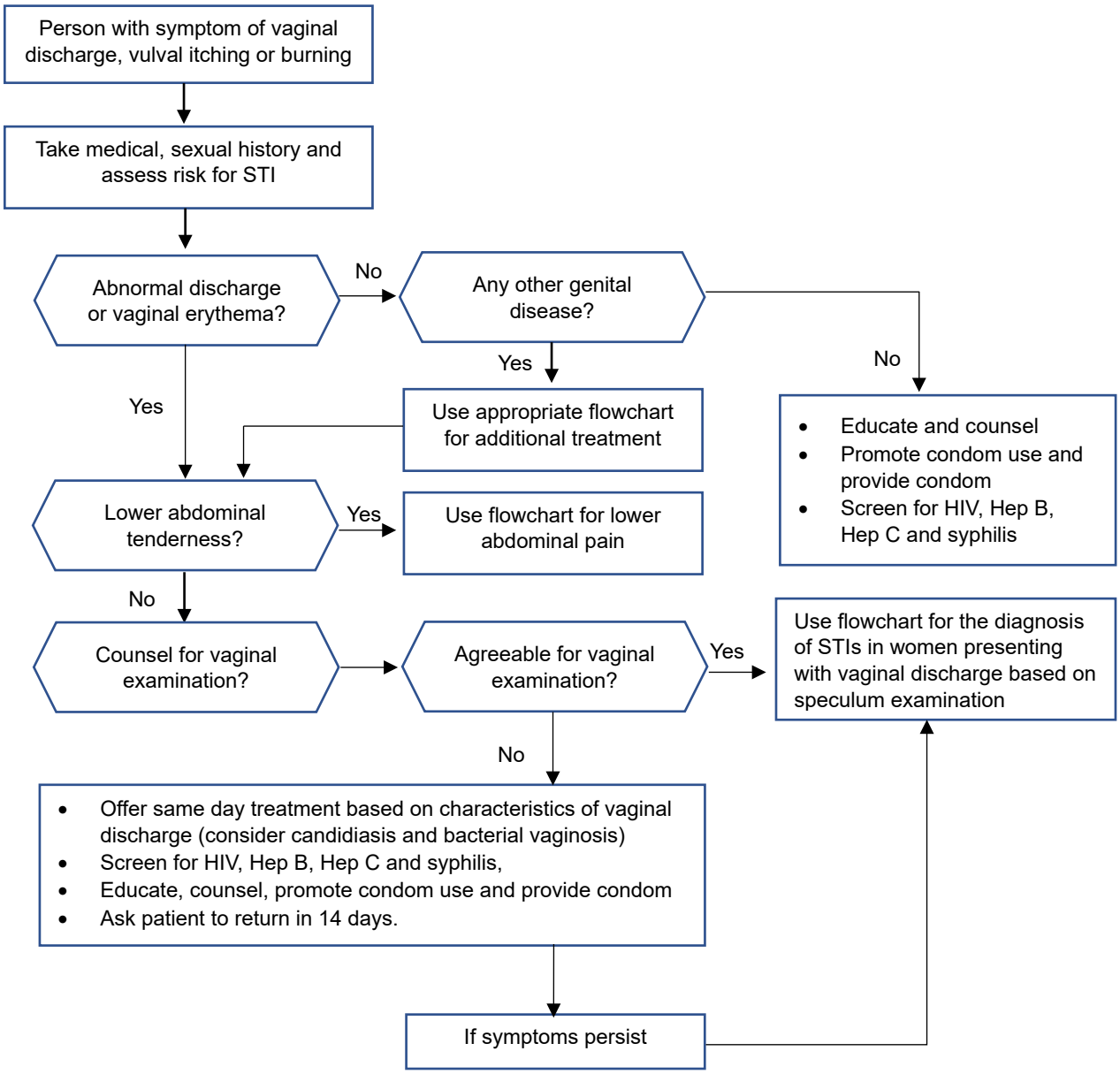
Recommended treatment options for resistant or persistent urethral discharge

Type of infection	Preferred
Trichomonas vaginalis	Metronidazole 400mg PO q12h for 5 days **PLUS** **If treated with Doxycycline first line:** Azithromycin 500mg PO STAT, then 250 mg q24h for 4 days **If treated with Azithromycin first line:** Moxifloxacin 400mg PO q24h for 10-14 days
Mycoplasma genitalium	

3.3 Vaginal discharge syndrome

- MSA has low sensitivity and specificity for cervical gonococcal and chlamydial infection in women

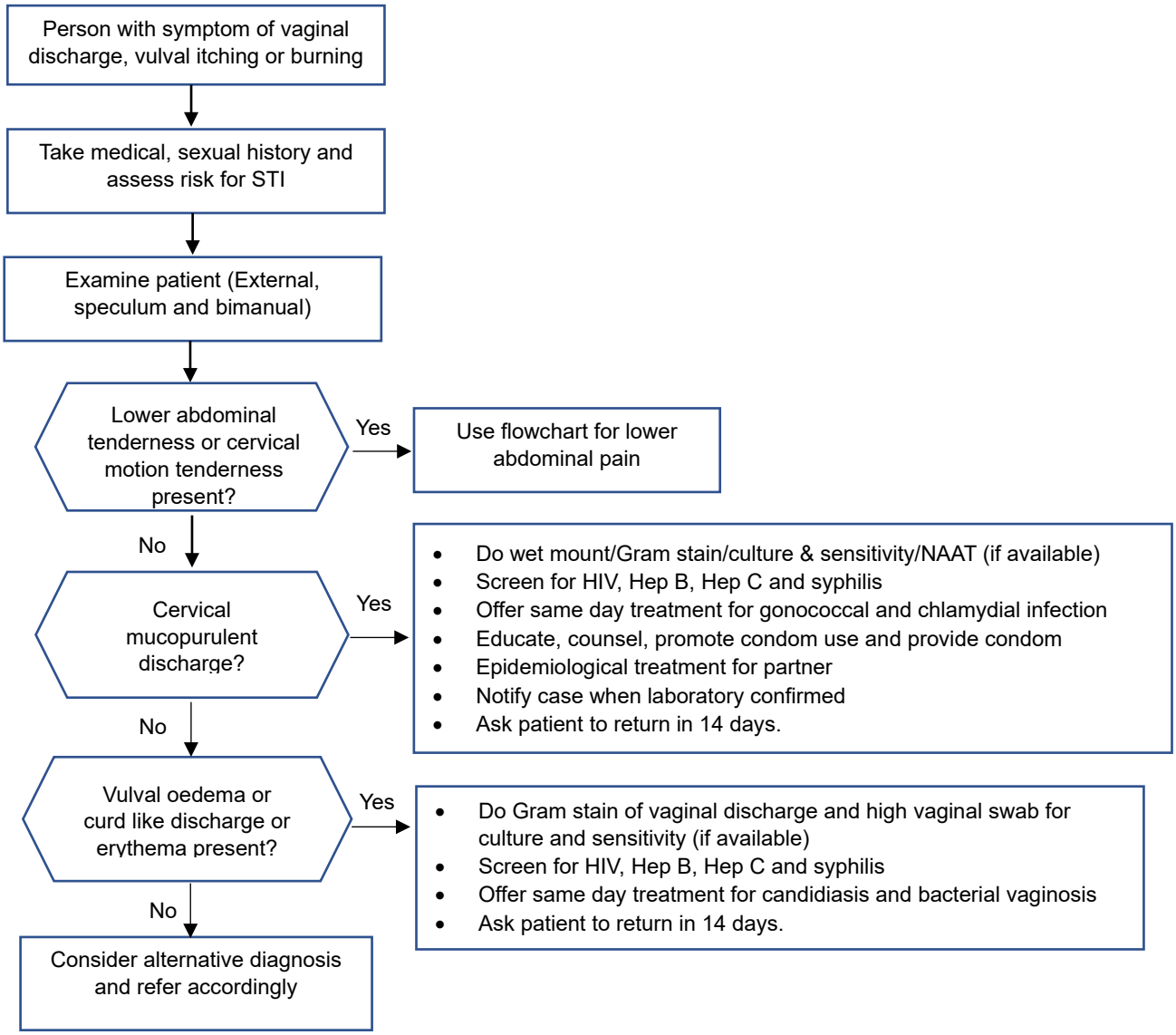
Flowchart for the syndromic approach to management of women presenting with vaginal discharge based on risk assessment.



Recommended treatment options for vaginal discharge based on risk assessment:

Type of infection	Preferred	Alternative	Pregnancy
Candidiasis	Clotrimazole 500mg as a single vaginal pessary STAT **PLUS**	Fluconazole 150-200mg PO STAT **PLUS**	Clotrimazole 500mg as a single vaginal pessary STAT **PLUS**
Bacterial vaginosis	Metronidazole 400mg PO q12h for 5-7 days **OR** Metronidazole 2g PO STAT*	Clindamycin 300mg PO q12h for 7 days	Metronidazole 400mg PO q12h for 5-7 days No evidence of teratogenicity from the use of metronidazole during the first trimester. Increased risk of second trimester miscarriage

Flowchart for the syndromic approach to management of women presenting with vaginal discharge based on speculum examination

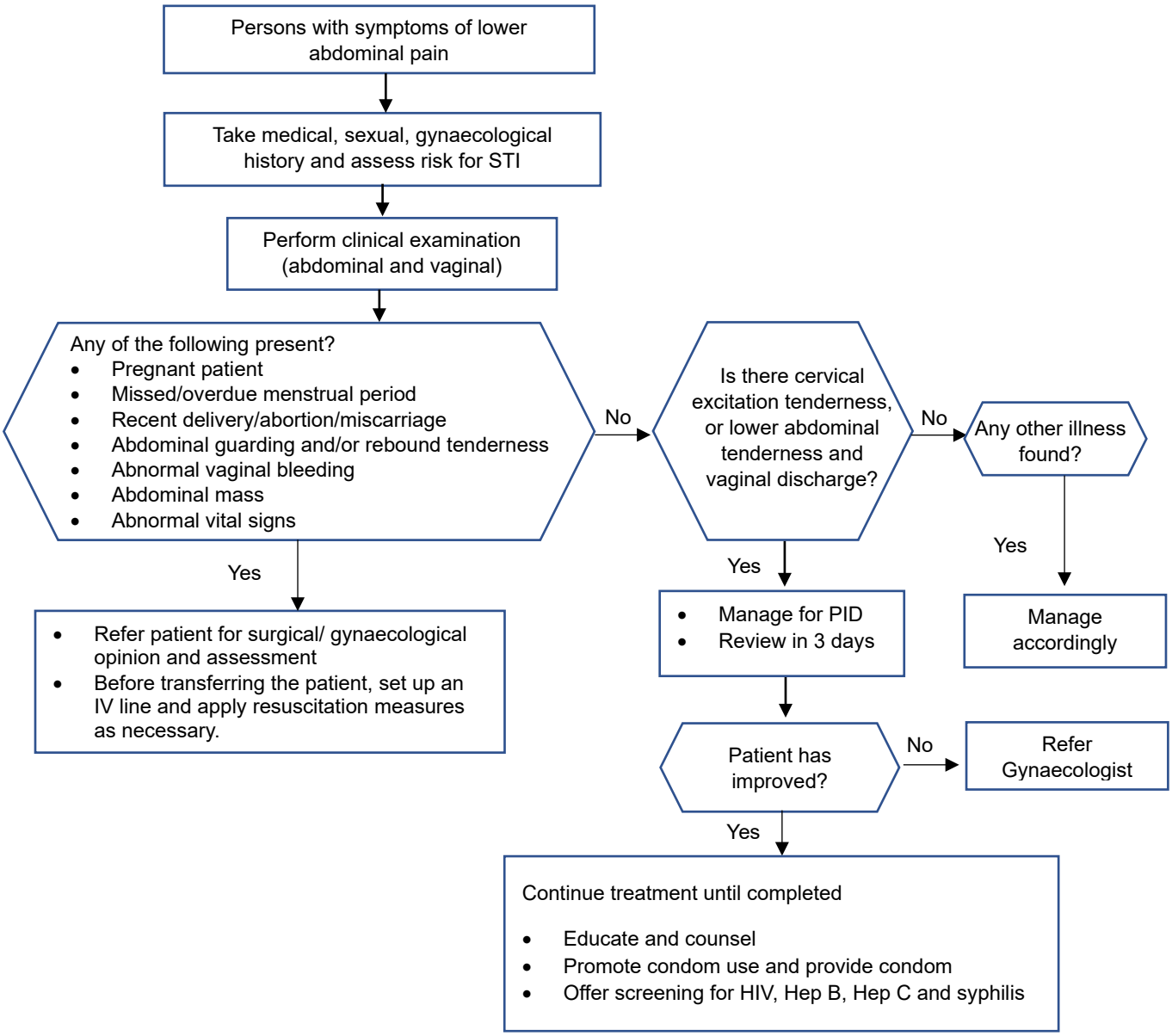


Recommended treatment options for cervical mucopurulent discharge:

Type of infection	Preferred	Alternative	Pregnancy
Uncomplicated *Neisseria gonorrhoeae*	Ceftriaxone 500mg IM STAT (BW > 150kg, use 1g) **PLUS** Doxycycline 100mg PO q12h for 7 days	Gentamicin 240mg IM STAT **PLUS** Azithromycin 2g PO STAT	Ceftriaxone 500mg IM STAT (BW > 150kg, use 1g) **PLUS** Azithromycin 1g PO STAT
Chlamydia trachomatis			

3.4 Lower abdominal pain syndrome

Flowchart for the syndromic approach to management of lower abdominal pain

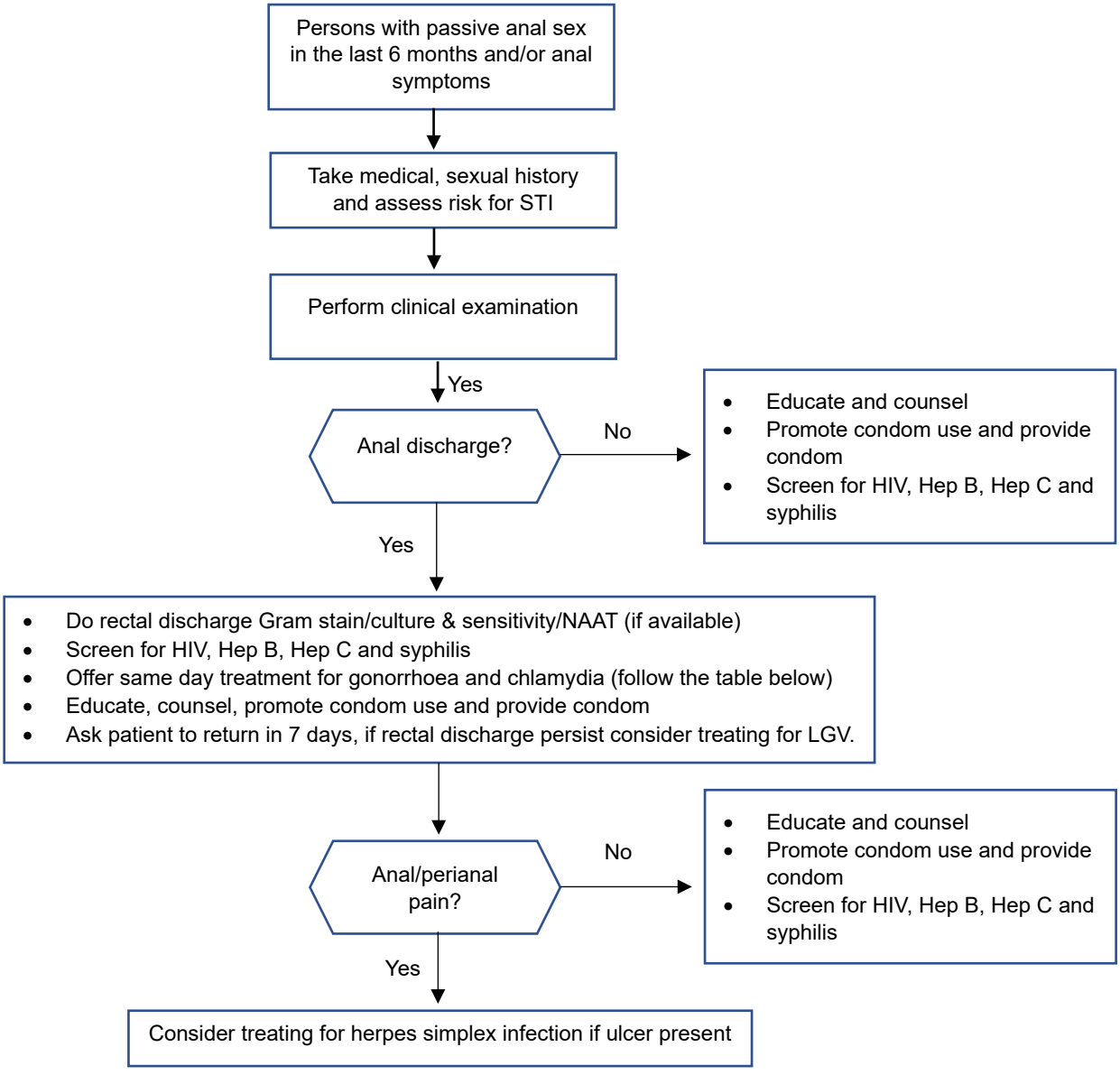


Recommended treatment options for pelvic inflammatory disease:

Preferred	Alternative
Ceftriaxone 500mg IM STAT **PLUS** Doxycycline 100mg PO q12h for 14 days **PLUS** Metronidazole 400mg PO q12h for 14 days	Ceftriaxone 500mg IM STAT **PLUS** Azithromycin 1g PO weekly for 2 weeks **PLUS** Metronidazole 400mg PO q12h for 14 days

3.5 Anorectal discharge syndrome

Flowchart for the syndromic approach to management of anorectal discharge syndrome



Recommended treatment options for anorectal discharge:

Type of infection	Preferred	Alternative	Pregnancy
Uncomplicated *Neisseria gonorrhoeae*	Ceftriaxone 500mg IM STAT (BW>150kg, use 1g) **PLUS**	Gentamicin 240 mg IM STAT **PLUS**	Ceftriaxone 500mg IM STAT (BW>150kg, use 1g) **PLUS**
Chlamydia trachomatis	Doxycycline 100mg PO q12h for 7 days	Azithromycin 2g PO STAT	Azithromycin 1g PO STAT
LGV	Doxycycline 100mg PO q12h for 21 days	Azithromycin 1g PO weekly for 3 weeks **OR** Erythromycin ethylsuccinate 800mg PO q6h for 21 days	Azithromycin 1g PO weekly for 3 weeks

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4. SPECIFIC DISEASE MANAGEMENT

4.1 SYPHILIS

Aetiology

Treponema pallidum, subspecies *pallidum*

Clinical classification

Acquired	

Early syphilis (< 2 years)
• Primary syphilis
• Secondary syphilis
• Early latent syphilis
	Late syphilis (> 2 years) or unknown duration
	• Late latent syphilis
	• Tertiary syphilis:
	  ○ Gumma
	  ○ Cardiovascular syphilis
	  ○ Neurosyphilis

Congenital	
Early (< 2 years old)	Late (> 2 years old)

Investigations:

1. Serological tests
2. Demonstration of *Treponema pallidum*

1. Serological tests:

A diagnosis of syphilis requires two serologic tests namely:

1. Non-treponemal tests - RPR/VDRL, and
2. Treponemal tests - TPPA/CMIA/ECLIA/RDT

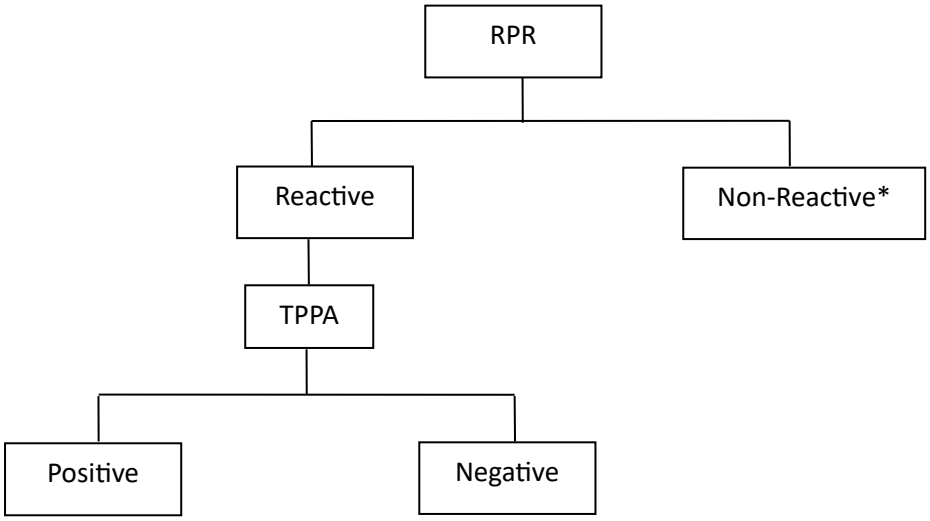
Screening for syphilis can be performed using three algorithms, with the preferred algorithm being determined by institutional/ local resources, including staffing, costs, laboratory space, test volume and patient population.

Antenatal screening with non-treponemal tests RPR should be routinely performed at resource limited clinics:

1. on first visit and at 28 weeks of gestation
2. confirm positive results with treponemal tests (TPHA/TPPA)

A quantitative RPR should be performed for positive treponemal tests to classify/stage the disease, determine the need for treatment and monitor response to treatment.

Algorithm 1 : Syphilis Screening Using 'Traditional Algorithm'



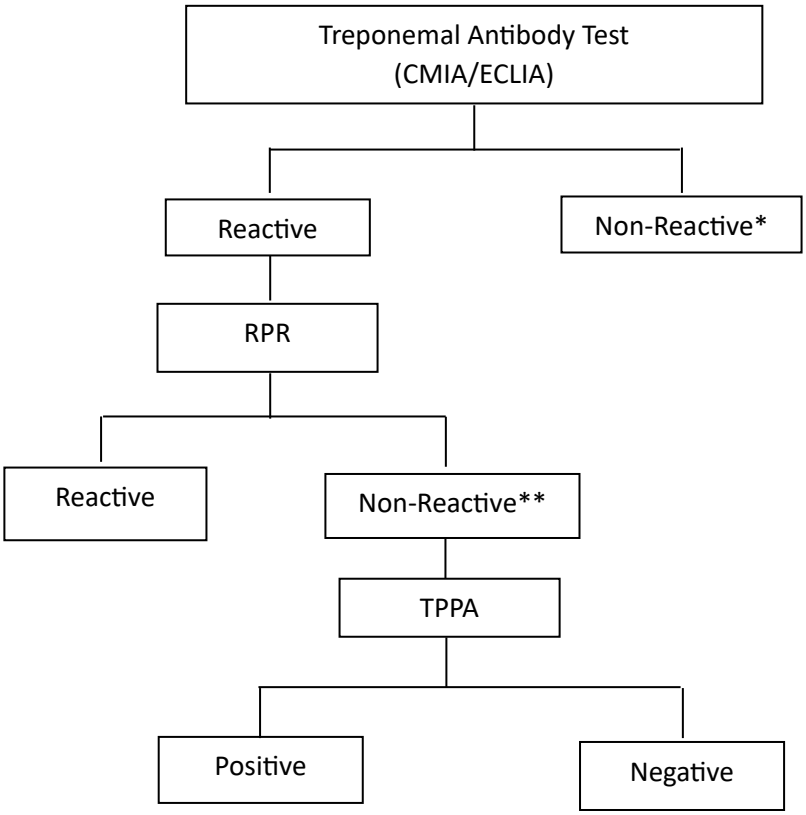
Note:
RPR = Rapid Plasma Reagin
TPPA = *Treponema pallidum* Particle Agglutination

Laboratory interpretation

RPR	TPPA	INTERPRETATION
Non-Reactive	N/A	In the absence of high risk behaviour/exposure, syphilis is unlikely. Please correlate with clinical findings. Suggest to repeat testing after 2-4 weeks if clinically indicated.
Reactive	Positive	Suggestive of syphilis infection (previously treated or untreated syphilis).
Reactive	Negative	Syphilis infection unlikely; possible biological false positive. If at risk for syphilis, repeat test in 2-4 weeks.

N/A = Not applicable

Algorithm 2 : Syphilis Screening Using 'Reverse Algorithm'



Note:
CMIA = Chemiluminescence Immunoassay
ECLIA = Electrochemiluminescence Immunoassay

*In the absence of high-risk behaviour/exposure, syphilis is unlikely.
Please correlate with clinical findings.

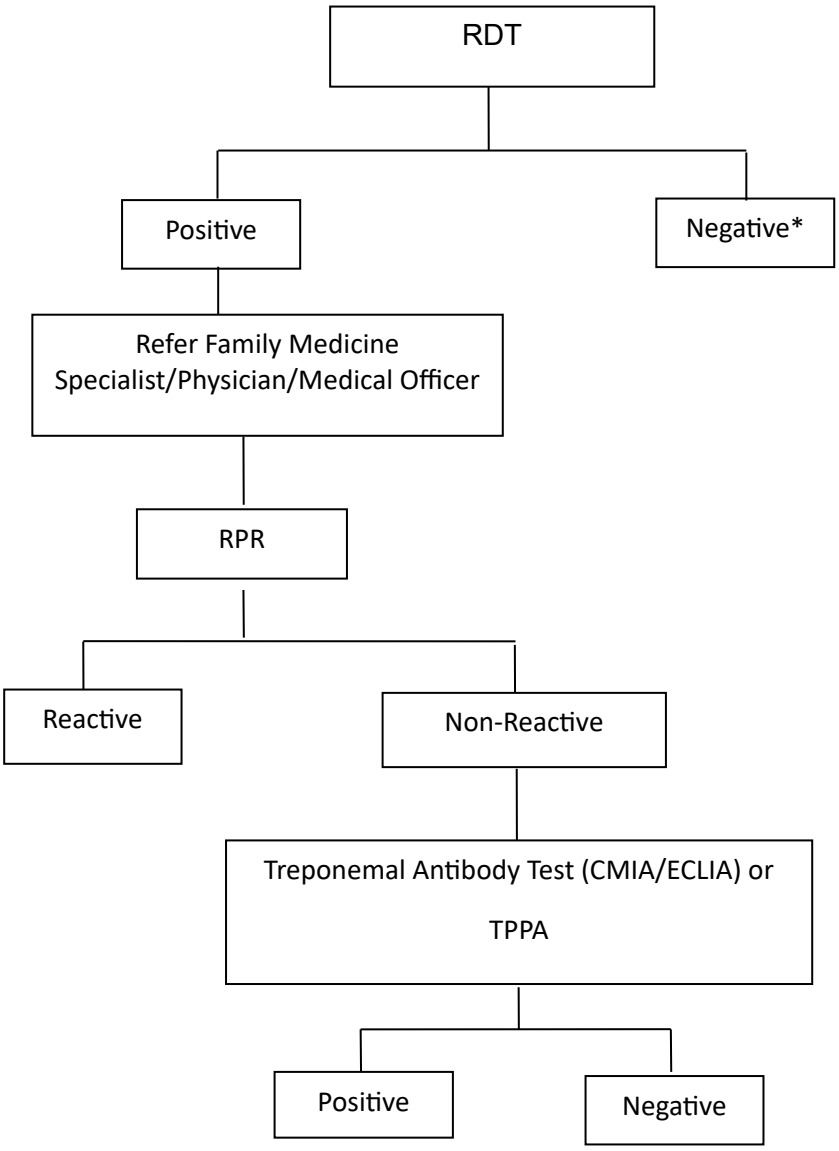
** Check for previous TPPA result. If TPPA is positive, no need to proceed.

Laboratory interpretation

Treponemal Antibody Test	RPR	TPPA	INTERPRETATION
Non-Reactive	N/A	N/A	In the absence of high risk behaviour/exposure, syphilis is unlikely. Please correlate with clinical findings. Suggest to repeat testing after 2-4 weeks if clinically indicated.
Reactive	Reactive	N/A	Consistent with syphilis (past or current).
Reactive	Non-Reactive	Positive	Suggestive of syphilis infection (previously treated or untreated syphilis).
Reactive	Non-Reactive	Negative	Syphilis unlikely. If at risk for syphilis, repeat test in 2-4 weeks.

N/A = Not applicable

Algorithm 3 : Syphilis Screening Using Rapid Diagnostic Test (RDT)



Note:
RDT = Rapid Diagnostic Test
RPR = Rapid Plasma Reagin
CMIA = Chemiluminescence Immunoassay
ECLIA = Electrochemiluminescence Immunoassay
TPPA = *Treponema pallidum* Particle Agglutination

*In the absence of high-risk behaviour/exposure, syphilis is unlikely.

Please correlate with clinical findings.

Laboratory interpretation

RDT	RPR	Treponemal Antibody test/TPPA	INTERPRETATION
Negative	N/A	N/A	In the absence of high risk behaviour/exposure, syphilis is unlikely. Please correlate with clinical findings. Suggest to repeat testing after 2-4 weeks if clinically indicated.
Positive	Reactive	N/A	Consistent with syphilis (past or current).
Positive	Non-Reactive	Positive	Suggestive of syphilis infection (previously treated or untreated syphilis).
Positive	Non-Reactive	Negative	Syphilis unlikely. If at risk for syphilis, repeat test in 2-4 weeks.

N/A = Not applicable

2. Demonstration Of T. Pallidum *Polymerase Chain Reaction Test* (PCR)

In certain circumstances, PCR may be helpful in diagnosis by demonstrating *T. pallidum* in tissue samples, vitreous fluid and CSF.

4.1.1 Early Syphilis

Early syphilis is defined as infection during the first 2 years and includes primary, secondary and early latent syphilis.

4.1.1.1 Primary Syphilis

Incubation period

9-90 days

Clinical presentation

Primary syphilis presents classically as a solitary, non-tender, indurated and well- circumscribed ulcer (chancre) with regional lymphadenopathy. The chancre is commonly located in the anogenital region. However, chancres may be multiple, painful, purulent and extragenital (most frequently oral). It may present as syphilitic balanitis of Follman. Chances may go unnoticed if present

as anal, oral or cervical lesions. Syphilis should be considered in any anogenital ulcer unless proven otherwise.

Investigation

Diagnosis is made by a combination of history, examination and investigation. If there is a clinical suspicion of primary syphilis but serology is negative, repeat serology after 2 weeks following presumptive treatment and consider doing a PCR swab.

4.1.1.2 Secondary Syphilis

Incubation period
6 weeks - 6 months

Clinical presentation

The commonest presentation is a generalised non-irritating skin lesion involving the palms and soles with or without generalised lymphadenopathy. Condylomata lata, mucocutaneous lesions and patchy alopecia are seen less commonly. The rash is classically non-itchy but may be itchy, particularly in dark-skinned patients.

Secondary syphilis is a stage of bacteraemia and hence, patients can present with symptoms and/or signs referable to any system in the body for example anterior uveitis, meningitis, cranial nerve palsies, hepatitis, splenomegaly, periostitis and glomerulonephritis.

Investigation

All serological tests for syphilis are expected to be positive in secondary syphilis

RPR/VDRL titres in untreated cases are often > 1:8

4.1.1.3 Early Latent Syphilis

Definition

Early latent syphilis is diagnosed by a positive serology without symptoms and signs in a person known to be seronegative in the previous 2 years.

Management

Pharmacological treatment of early syphilis (primary, secondary and early latent syphilis) in non-pregnant adults

Type of infection	Preferred	Alternative
Primary syphilis Secondary syphilis Early latent syphilis	Benzathine penicillin 2.4MU IM STAT OR Procaine penicillin 600,000units IM q24h for 10 days	*For penicillin allergy:* Doxycycline 100mg PO q12h for 14 days
Note: *Patient should be warned on possible reactions to treatment i.e. Jarisch-Herxheimer reaction (JHR)*		

Advice

Patients should be advised to abstain from sex until 1 week after they and their partner(s) have completed treatment.

Contact tracing and management of sex partners

All sexual partners should be examined, investigated and treated epidemiologically.

Trace back according to sexual history and clinical stage of infection:

- Primary syphilis: **3 months** plus duration of symptoms or last negative test
- Secondary syphilis: **6 months** plus duration of symptoms or last negative test
- Early latent: **12 months** or most recent negative test

Sexual contacts of less than 90 days before the diagnosis should be epidemiologically treated for early syphilis, even if serology test results are negative.

Sexual contacts of more than 90 days before the diagnosis should be epidemiologically treated for early syphilis if serology test results are not immediately available and the opportunity for follow-up is uncertain.

If serology tests are positive, treatment should be based on syphilis stage.

All patients should be offered patient referral and provider referral as a method of contacting any sexual partners. The method agreed upon with the patient should be clearly documented.

Epidemiological treatment for all asymptomatic contacts is recommended including for pregnant women*.

* Pregnant women should be counselled on treatment benefits and risks.

Epidemiological treatment

Type of infection	Preferred	Alternative
Incubating syphilis/epidemiological treatment	Benzathine penicillin 2.4MU IM STAT	*For penicillin allergy:* Doxycycline 100mg PO q12h for 14 days

4.1.2. Late Syphilis

Definition

Syphilis diagnosed 2 years after infection. This includes late latent syphilis, benign tertiary syphilis (Gumma), cardiovascular syphilis and neurosyphilis

4.1.2.1 Late Latent Syphilis

Definition

Syphilis of more than 2 years duration/unknown duration; diagnosed by positive serology without any symptoms.

All patients should have a thorough clinical examination to exclude cardiovascular and neurological involvement.

4.1.2.2 Gumma (Benign Tertiary Syphilis)

Incubation period

1 to 45 years with an average of 15 years

Clinical presentation

Gumma is a destructive granulomatous lesion and commonly presents with skin or bone lesions. Liver, heart, brain, stomach and the respiratory tract may be affected.

Investigation

1. Serological test for syphilis
2. Treponemes can be demonstrated in the tissues by PCR

4.1.2.3 Cardiovascular Syphilis

Incubation period
15–30 years

Clinical presentation

Although syphilis may affect any large vessel, it is characterised by an aortitis affecting the proximal aorta. The aortitis may cause aortic incompetence (which may be complicated by heart failure), coronary ostial stenosis (presenting as angina), and aortic medial necrosis causing aortic aneurysm.

Additional investigations

1.CXR
2.Echocardiogram

Pharmacological Treatment of Late Latent, Gumma or Cardiovascular Syphilis *in Non-Pregnant Adults*

Type of infection	Preferred	Alternative
Late latent syphilis Gumma (benign tertiary) syphilis Cardiovascular syphilis	Benzathine penicillin 2.4MU IM weekly for 3 weeks (3 doses) OR Procaine penicillin 600,000units IM q24h for 14 days	*For penicillin allergy:* Doxycycline 100mg PO q12h for 28 days
Note: *For cardiovascular syphilis: Consider prednisolone 40-60mg q24h for 3 days starting 24 hours before the antibiotics.* *If a patient defaults benzathine penicillin treatment ≥ 2 weeks in between the weekly doses, the whole regimen needs to be restarted.*		

Advice

Patients should be advised to abstain from sex until 1 week after they and their partner(s) have completed treatment.

Contact tracing

Test current partner(s). If any doubt as to whether the patient has early latent or late latent syphilis, contact trace as for early latent syphilis.

Treatment failure in syphilis

Treated patients should be considered for re-treatment if clinical symptoms or signs persist or recur, RPR titre fails to decrease fourfold by one year or there is a sustained fourfold rise or higher in RPR titre. In the absence of reinfection, CSF examination should be done. If neurosyphilis has been excluded, re-treatment is indicated.

Pharmacological treatment for those with treatment failure (neurosyphilis excluded)

Weekly doses of benzathine penicillin 2.4MU IM for 3 weeks.

4.1.2.4 Neurosyphilis

T. pallidum can infect the CNS at any stage of syphilis and result in neurosyphilis. Clinical evidence of neurological involvement warrants CSF examination.

Early neurological signs such as cranial nerve dysfunction, meningitis, meningovascular syphilis, stroke and acute altered mental status are usually present within the first few months or years of infection. Late neurosyphilis includes meningovascular and parenchymatous syphilis.

Infection of the visual system (ocular syphilis) or auditory system (otosyphilis) can occur at any stage of syphilis but is commonly identified during the early stages, with or without additional CNS involvement. Ocular syphilis often presents as panuveitis. Other ocular presentations are conjunctivitis, anterior uveitis, posterior interstitial keratitis, optic neuropathy, and retinal vasculitis. Ocular syphilis can result in permanent vision loss. All persons with ocular symptoms and reactive syphilis serology need a full ocular examination, including cranial nerve evaluation. If cranial nerve dysfunction is present, a CSF evaluation is needed.

Otosyphilis typically presents with cochleo-vestibular symptoms (tinnitus, vertigo, and sensorineural hearing loss). Hearing loss can be unilateral or bilateral, have a sudden onset, and progress rapidly. Otosyphilis can result in permanent hearing loss.

Additional investigations

- CSF for protein, cell count, CSF VDRL test
- A negative CSF VDRL makes a diagnosis of neurosyphilis unlikely but does not exclude the diagnosis

NEUROSYPHILIS: CSF CRITERIA

1. WBC:

a. HIV negative: > 5 µL
b. HIV positive: > 20 µL **OR** 6-20 µL (on ART, VL undetectable, CD4 > 200)

(Regardless of HIV status)

2. Protein: > 0.45 g/l

3. VDRL: positive

Meningovascular Neurosyphilis

Incubation period

5 to 10 years

Clinical presentation

Headache, vertigo and cranial nerve involvement.

Parenchymatous Neurosyphilis

Incubation period

10 to 20 years

Clinical presentation

Patients may present with general paresis of the insane (brain syndrome) characterised by gradual personality change, ataxia, stroke or ophthalmic symptoms or with tabes dorsalis (spinal cord syndrome) presenting with lightning pain, sensory impairment and mobility problems. Both syndromes are important differential diagnoses in dementia, psychiatric disorders and mobility problems.

Pharmacological treatment for neurosyphilis

Type of infection	Preferred	Alternative
Neurosyphilis	Benzylpenicillin 4MU IV q4h for 14 days **OR** Procaine Penicillin 2.4MU IM q24h for 14 days **PLUS** Probenecid 500mg PO q6h for 14 days	*For penicillin allergy without anaphylaxis:* Ceftriaxone 2g IM/ IV q24h for 14 days **OR** *If anaphylaxis to penicillin:* Doxycycline 200mg PO q12h for 28 days
Note: *Consider Prednisolone 40-60mg q24h for 3 days starting 24 hours before the antibiotics.*		

Follow-up schedule for all stages of syphilis

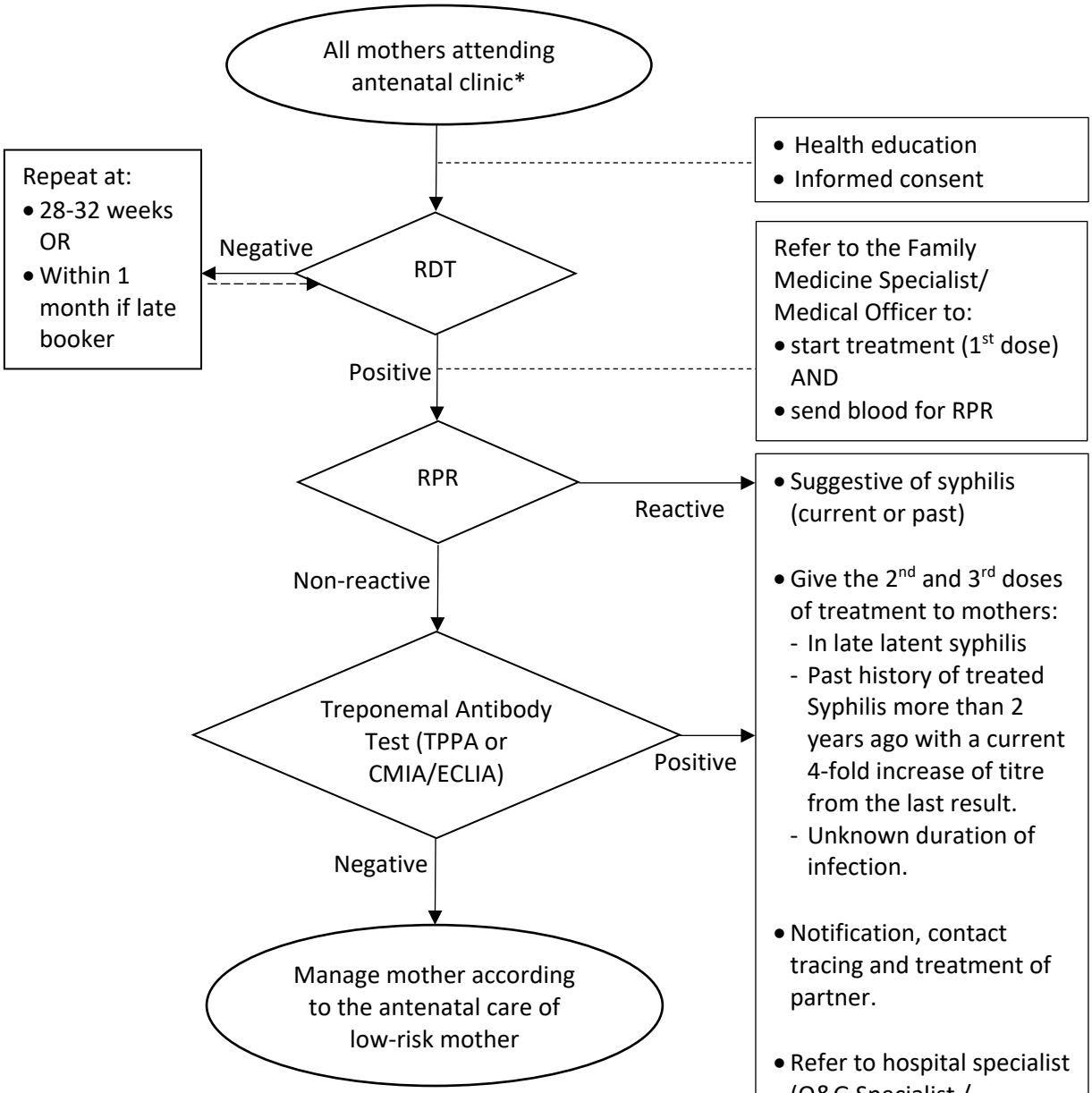
Review all patients clinically and with repeat RPR titre at **3 months**, **6 months** and **12 months** after completing treatment. A 4-fold drop (e.g., 1:8 to 1:2) indicates adequate response to treatment.

Patients should be re-examined with RPR titre every 6 monthly until RPR negative or at serofast state.

4.1.10 Syphilis in Pregnancy

Antenatal screening for syphilis with RPR/VDRL or RDT should be routinely performed on first visit and repeated at 28-32 weeks of gestation (in high-risk cases). Any woman who has a foetal death after 20 weeks gestation should be tested for syphilis. Serological confirmation of syphilis is similar to non-pregnant adults.

Flow chart for syphilis screening test for antenatal mother using Rapid Diagnostic Test (RDT) at Primary Care Clinics



*All mothers attending antenatal clinics:

i) 1st antenatal visit/booking
ii) Late bookers (presented at the third trimester ≥ 28 weeks)
iii) Unbooked/unscreened

References:

- WHO Guideline on Syphilis screening and treatment for pregnant women (2017): Strategy C: On-site rapid syphilis test followed (if positive) by first dose and RPR test (pg. 24).
- Director General of Health, Malaysia No 15/2023: Flow chart for screening and confirmatory tests of Syphilis (Algorithm 3: Syphilis testing using RDT).

Pharmacological treatment of syphilis in pregnant adults

Type of infection	Preferred	Alternative
Primary syphilis Secondary syphilis Early latent syphilis	Benzathine penicillin 2.4MU IM STAT OR Procaine penicillin 600,000units IM q24h for 10 days	*For penicillin allergy:* **Desensitise and treat with penicillin as there are no proven alternatives.* *If failed desensitisation:* Ceftriaxone 500mg IM q24h for 10 days OR Azithromycin 2g PO STAT
Late latent syphilis Gumma (benign tertiary) syphilis Cardiovascular syphilis	Benzathine penicillin 2.4MU IM weekly for 3 weeks (3 doses) OR Procaine Penicillin 600,000units IM q24h for 14 days	*For penicillin allergy:* Erythromycin Ethylsuccinate 800mg PO q6h for 28 days
Neurosyphilis	Benzylpenicillin 4MU IV q4h for 14 days OR Procaine Penicillin 2.4MU IM q24h for 14 days **PLUS** Probenecid 500mg PO q6h for 14 days	*For penicillin allergy without anaphylaxis:* Ceftriaxone 2g IM/IV q24h for 14 days
Note: *Doxycycline/Tetracycline is contraindicated in pregnancy.* *For cardiovascular and neurosyphilis: Consider Prednisolone 40-60mg q24h for 3 days starting 24 hours before the antibiotics.* *If macrolide is used, for neonate assessment and treatment at birth.* **The benefit of treatment outweighs the risk of allergic reaction in skin test and desensitisation. Refer appendix for the penicillin desensitisation protocol*		

Follow-up during pregnancy

Mothers should be advised to seek medical attention if they notice any change in foetal movements or have any contractions following treatment.
Monthly clinical and serological examination till delivery and thereafter follow-up is as in non-pregnant patients. In positive cases, RPR/VDRL should be repeated at delivery.

4.1.11 Congenital Syphilis

Definition

A condition caused by infection in utero with *Treponema pallidum*. There is a wide spectrum of severity, from infection which is not apparent to severe cases that are clinically apparent at birth.

Clinical presentation

An infant or child (aged less than 2 years) may have signs such as rash, snuffles, hepatosplenomegaly, condyloma lata, jaundice (non-viral hepatitis), pseudoparalysis, anaemia, or oedema (nephrotic syndrome and/or malnutrition).

An older child may have stigmata (e.g., interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinson teeth, saddle nose, rhagades, or Clutton joints).

Investigation

All neonates born to women who have reactive nontreponemal serologic tests (RPR/ VDRL) for syphilis at delivery should be examined thoroughly for evidence of congenital syphilis (e.g., nonimmune hydrops, conjugated or direct hyperbilirubinemia or cholestatic jaundice or cholestasis, hepatosplenomegaly, rhinitis, skin rash, or pseudo paralysis of an extremity).

Case classification of congenital syphilis:

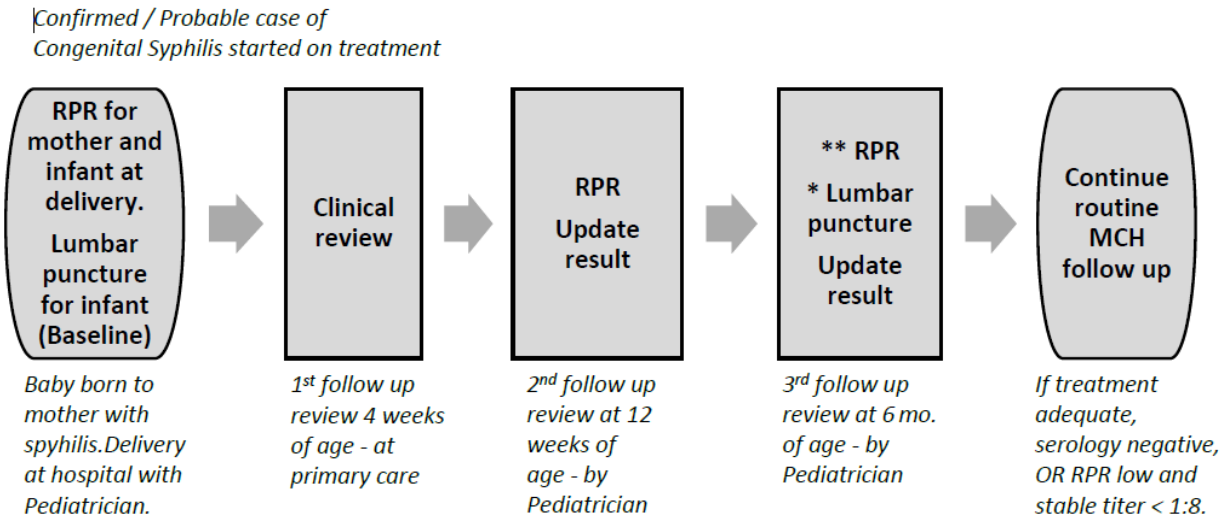
Congenital syphilis can be classified as confirmed, highly probable, possible or less likely and unlikely.

Confirmed syphilis	A case that is confirmed with serology tests
Highly probable syphilis	Neonate with • Abnormal physical examination that is consistent with congenital syphilis; • Serum quantitative nontreponemal serologic titre that is fourfold (or greater) higher than the mother's titre at delivery (e.g., maternal titre = 1:2, neonatal titre ≥1:8 or maternal titre = 1:8, neonatal titre ≥1:32); OR • An infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant; OR • An infant or child who has a reactive non-treponemal test for syphilis, **AND** any **one** of the following: – Any evidence of congenital syphilis on radiographs of long bones (e.g. osteochondritis, diaphyseal osteomyelitis, periostitis). – A reactive CSF-VDRL test. – In a non-traumatic lumbar puncture, an elevated CSF leukocyte (white blood cell, WBC) count or protein (without other cause): ○ Suggested parameters for abnormal CSF WBC and protein values: ○ *During the first 30 days of life, a CSF WBC count of >15 WBC/mm3 or a CSF protein >120 mg/dl is abnormal.* ○ *After the first 30 days of life, a CSF WBC count of >5 WBC/ mm3 or a CSF protein >40 mg/dl, regardless of CSF serology.* *(The treating clinician should be consulted to interpret the CSF values for the specific patient).*
Possible congenital syphilis	Any neonate who has a normal physical examination and a serum quantitative nontreponemal serology titre equal to or less than fourfold of the maternal titre at delivery (e.g., maternal titre = 1:8, neonatal titre ≤1:16) and **one** of the following: • The mother was not treated, was inadequately treated, or has no documentation of having received treatment. • The mother was treated with erythromycin or a regimen other than those recommended in these guidelines (i.e., a non-penicillin G regimen) • The mother received the recommended regimen but treatment was initiated < 30 days before delivery.

Congenital syphilis less likely	Any neonate who has a normal physical examination and a serum quantitative nontreponemal serology titre equal or less than fourfold of the maternal titre at delivery (e.g., maternal titre = 1:8, neonatal titre ≤ 1:16) and **both** of the following are true: • The mother was treated during pregnancy, treatment was appropriate for the infection stage and the treatment regimen was initiated ≥30 days before delivery. • The mother has no evidence of reinfection or relapse. **No evaluation is recommended.** Treatment: Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose
Congenital syphilis unlikely	Any neonate who has a normal physical examination and a serum quantitative nontreponemal serology titre equal to or less than fourfold of the maternal titre at delivery and both of the following are true: • The mother's treatment was adequate before pregnancy. • The mother's nontreponemal serology titre remained low and stable (i.e., serofast) before and during pregnancy and at delivery (e.g., VDRL ≤1:2 or RPR ≤1:4). No evaluation is recommended. *No treatment is required. However, any neonate with reactive nontreponemal tests should be followed serologically to ensure the nontreponemal test returns to negative (see Follow-Up). Benzathine penicillin G 50,000 units/kg body weight as a single IM injection might be considered, particularly if follow-up is uncertain and the neonate has a reactive nontreponemal test.*
Syphilitic stillbirth	A foetal death that occurs after a 20-week gestation or in which the foetus weighs greater than 500g and the mother had untreated or inadequately treated* syphilis at delivery.

Monitoring of serology tests for confirmed case/probable case congenital syphilis

(Source: *Garispanduan Pengukuhan Program Pencegahan Jangkitan HIV dan Sifilis Dari ibu-Ke-Anak, Edisi Kedua, 2021*)



Note:

At 6 months, continue ROUTINE MCH FOLLOW UP if treatment is adequate, serology negative, or RPR low and stable titre < 1:8. Monitoring should be continued every 3 months up to 24 months whenever indicated.

Lumbar puncture should be repeated at 6 months old if RPR static or increasing trend upon monitoring.

Consider retreatment if:

- *Signs and symptoms suggestive of congenital syphilis persist or recur at any time upon review OR*
- *RPR titre fails to decrease to 4-fold by 6 months after treatment OR Sustained 4-fold rise in RPR by 6 months after treatment*

Evaluation of infants born to sero-positive women

Infants should be evaluated if they were born to sero-positive women who:

- have untreated syphilis
- were treated for syphilis less than 1 month before delivery
- were treated for syphilis during pregnancy with a non-penicillin regimen
- did not have the expected decrease in RPR titre after treatment
- were treated but had insufficient serologic follow-up during pregnancy

Evaluation of Infant

- Thorough physical examination
- RPR (compare with mother's titre - repeated at delivery
- CSF analysis for cells, protein and CSF-VDRL test
- Long bones X-ray
- Chest X-ray

Pharmacological treatment decisions

Infants should be treated if they have any evidence of active disease:

1. An abnormal CSF finding (WBC >5/mm3 or protein >50 mg/dl) regardless of CSF serology
2. Serum RPR titre that are at least 4-fold higher than their mother's.
3. Positive treponemal antibody by CMIA/ECLIA

Type of infection	Preferred	Alternative
Congenital syphilis	Benzylpenicillin (Penicillin G) 50,000units/kg/dose IV q12h for the first 7 days of life, then q8h for the following 3-7 days OR Procaine Penicillin 50,000units/kg/dose IM q24h for 10-14 days	*<30 days old:* Ceftriaxone 75mg/kg/dose IM q24h for 10-14 days (Max: 2000mg/dose) *≥30 days old:* Ceftriaxone 100mg/kg/dose IM q24h for 10-14 days (Max: 2000mg/dose)
Note: *If drug administration is interrupted ≥ 1 day at any point during the treatment course, it is recommended that the entire course is restarted.* *Infants who should be evaluated but follow-up cannot be assured should be treated with Benzathine Penicillin 50,000 units/kg/dose IM STAT.*		

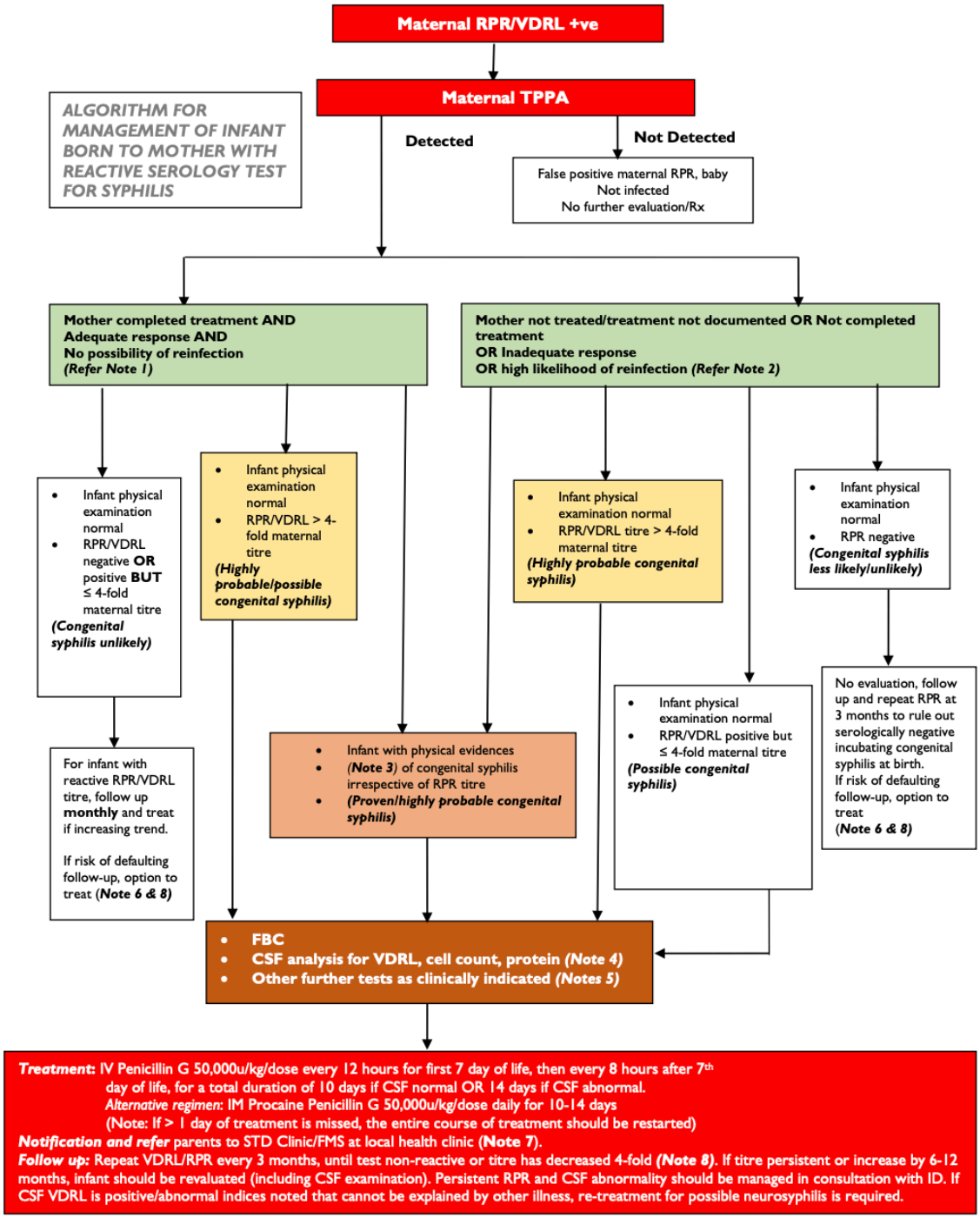
Follow-up schedules for untreated infants

Sero-positive untreated infants must be closely monitored at 1, 2, 3, 6, and 12 months of age. RPR should decrease by 3-months of age and usually disappear by 6 months of age.
Pharmacological treatment should be given if:

- Symptoms and signs persist or recur
- RPR titre increase fourfold or more by 3-months of age
- RPR still positive by 6 months of age
- TPHA still positive by 1 year of age

Treated infants must be monitored clinically and serologically at 1, 3, 6, 12, 18, and 24 months. Lumbar puncture should be repeated 6 monthly till normal.

Excerpt from draft of Paediatric Protocols for Malaysian Hospitals, 5th Edition, Ministry of Health. Chapter 30: Congenital Syphilis.



Footnotes to algorithm on previous page:

1. **Mother completed treatment is defined as**

• Had received adequate penicillin regime as per national/local treatment guideline. (Mother with late latent syphilis/unknown stage of disease requires 3 dose of IM benzathine Penicillin given *1 week apart)* **AND**

• Treatment completed more than 30 days prior to delivery with ***NO possibility*** or reinfection (i.e., single sexual partner/husband who are fully treated/not infected/***NOT*** recently diagnosed with syphilis/NO Risk of reinfection) **AND**

• Documented 4-fold decrease in RPR/VDRL titre **OR** remained low and stable (i.e., serofast) before and during pregnancy and at delivery (e.g., VDRL< 1:2/RPR< 1:4).

**If mother status unsure for any reasons, cases may be discussed with attending FMS/dermatologist to ascertain their treatment status

2. **Mother is considered as "not completed treatment"** if any of the criteria in ***note 1*** above is ***NOT met***
3. **Clinical features of congenital syphilis:** non-immune hydrops, IUGR, jaundice (direct/conjugated hyperbilirubinemia), hepatosplenomegaly, rhinitis, skin rash, pseudoparalysis of extremity.
4. **CSF analysis** (nontraumatic tap): Normal value differed by gestational age and higher in preterm infants. *Newborn* ≤16-19 WBCs/mm3 or protein level of ≤115-118 mg/dL. *2nd month of life* ≤9-11 WBCs/mm3 or protein level ≤89-91 mg/dL. *Older infant* 5 WBCs/mm3 and protein level of 40 mg/dL considered as upper limit of normal. For infant with abnormal initial CSF at birth, LP should be repeated if RPR remained positive after 6-12 months.
5. **Other tests, as clinically indicated**: long-bone x-ray, CXR, LFT, cranial ultra-sound, ophthalmologic examination and auditory brainstem response.
6. **For infant with a reactive RPR but not treated AND follow up cannot be ensured,** option to give single dose of IM Benzathine Penicillin G 50,000 units/kg. ***However, infants born to mother with untreated early syphilis at time of delivery are at increased risk of congenital syphilis, full course of treatment should be considered even if the infant RPR is nonreactive.***
7. **Notification:** ALL cases of suspected/probable/proven congenital syphilis **MUST** be notified to local health department irrespective of treatment was given or not.
8. **Follow up:** All sero-reactive infants/infant born to sero-reactive mother should receive careful follow up examination and serologic testing as mentioned above. VDRL/RPR titre ***should decline by age of 3 month*** and ***should be non-reactive by age of 6 month*** if the infants were not infected or were infected but adequately treated.

Additional Notes:

***** RPR indicates *rapid plasma reagin* test; and VDRL, *Veneral Disease Research Laboratory* slide test. RPR is currently the preferred ***nontreponemal test*** for syphilis in all MOH facilities. Nontreponemal test may be falsely negative/nonreactive in ***early primary syphilis***, ***latent acquired syphilis of long duration***, and ***late congenital syphilis***. Occasionally, RPR/VDRL test performed on serum sample containing high concentration of *T pallidum* antibody will be weakly reactive or falsely negative (known as *prozone phenomenon*); diluting the serum will result in a positive test.

* RPR titre are generally higher than VDRL, therefore when RPR/VDRL are used to monitor treatment response, same test must be used throughout the follow up period, preferably performed in the same laboratory, to ensure comparability of result.

* In order to compare infant RPR titre with maternal titre at birth, ensure mother blood taken at or immediately after delivery, and test performed in the same laboratory. Infant RPR test on umbilical cord sampling is not recommended as umbilical cord may be contaminated with maternal blood and could yield a false-positive result. Wharton's jelly within the umbilical cord also can yield a false negative result.

4.1.12 Syphilis in Older Infants and Children

After the newborn period, infants and children more than 1 month old, discovered to have syphilis with reactive serology tests, should be examined thoroughly and have maternal serology and records reviewed.
Any infant or child at risk for congenital or acquired syphilis should receive a full evaluation and should be screened for HIV infection.
Recommended evaluation:

- CSF analysis for VDRL, cell count and protein
- FBC including differential and platelet count
- Other test as indicated - long bone, chest, liver function tests, abdominal ultrasound, ophthalmologic examination, neuroimaging and hearing assessment

Pharmacological treatment for older infants and children

Type of infection	Preferred	Alternative
Congenital syphilis with or without neurologic involvement, in older infants and children	Benzylpenicillin (Penicillin G) 50,000units/kg/dose IV q4h-q6h (200,000 - 300,000units/kg/day) for 10 days **May consider Benzathine Penicillin 50,000units/kg (max: 2.4MU) IM STAT after the 10-day course of Benzylpenicillin to provide more comparable duration for treatment in those who have no clinical manifestation and normal CSF*	-
Congenital syphilis in older infants and children (no clinical manifestation and normal CSF)	Benzathine Penicillin 50,000units/kg (max: 2.4MU) IM weekly for 3 weeks (3 doses)	-
Note: *If drug administration is interrupted ≥ 1 day at any point during the treatment course, it is recommended that the entire course is restarted.*		

Follow-up schedule

Through follow up examinations and serology testing should be performed every 3 months until serology test becomes non-reactive or the titre has decreased fourfold. The serologic response after therapy might be slower for infants and children than neonates. If these titres increase at any point >2 weeks or do not decrease fourfold after 12–18 months, the infant or child should be evaluated (e.g., CSF examination), treated with a 10-day course of parenteral penicillin G, and managed in consultation with an expert.

Treponemal tests (e.g., CMIA, ECLIA, TPPA) should not be used to evaluate treatment response because the results are qualitative and persist after treatment. Passive transfer of maternal IgG treponemal antibodies might persist for > 15 months after delivery.

Infants or children whose initial CSF evaluations are abnormal do not need repeat lumbar puncture unless their serologic titres do not decrease fourfold after 12–18 months.

After 18 months of follow-up, abnormal CSF indices that persist and cannot be attributed to other ongoing illness indicate that retreatment is needed for possible neurosyphilis and should be managed in consultation with an expert.

Jarisch-Herxheimer Reaction (JHR)

A common acute febrile illness which presents as fever, headache, malaise, rigors and joint pains. It presents 6 to 12 hours after treatment and resolves within 24 hours. This is common in early syphilis but is usually not important unless there is neurological or ophthalmic involvement or in pregnancy when it may cause foetal distress and premature labour. It is uncommon in late syphilis but can potentially be life threatening if there is involvement of strategic sites (coronary ostia, larynx, nervous system). Antipyretics can reduce the reaction.

Anaphylaxis

Facilities for treatment of anaphylaxis should be available as penicillin is a common cause for anaphylaxis.
Treatment: Adrenaline 0.5mg IM STAT plus/minus hydrocortisone 100mg IV/IM STAT and chlorpheniramine 10mg IM STAT

References

1. 2021 STI Treatment Guidelines. Centre for Disease Control and Prevention (CDC). https://www.cdc.gov/std/treatment-guidelines/syphilis.htm
2. Australian STI Management Guidelines For Use In Primary Care. Updated Dec 2021. https://sti.guidelines.org.au/
3. Garis Panduan Pengukuhan Program Pencegahan Jangkitan HIV dan Sifilis Dari Ibu-Ke-Anak. Edisi Kedua, Jun 2021. Bahagian Kawalan Penyakit KKM
4. Guidelines on the management of Syphilis. British Association for Sexual Health and HIV. Updated June 2019. https://www.bashh.org/guidelines
5. Congenital Syphilis. Paediatric Protocols For Malaysian Hospitals. 4th Edition, 2018: 169-170.

4.1.13 Oral Penicillin Desensitisation Protocol

Drug desensitisation is a procedure to induce a state of temporary tolerance in a patient with confirmed drug hypersensitivity, be it type I allergic reactions (e.g., IgE-mediated penicillin/β-lactam antibiotics reactions) or non-allergic hypersensitivity reactions (e.g., cross intolerant non-steroidal anti-inflammatory drugs (NSAIDs) hypersensitivity reactions). Therefore, after a period of culprit drug discontinuation (about 2 - 5 half-lives), the procedure must be repeated if the medication needs to be taken again.

Desensitisation is required for persons who have a documented penicillin allergy and for whom no therapeutic alternatives exist such as syphilis in pregnancy and persons with neurosyphilis.

Penicillin G is the only known effective antimicrobial for preventing maternal transmission to the foetus and treating foetal infection. Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection. No proven alternatives to penicillin are available for treatment of syphilis during pregnancy. Pregnant women who have a history of penicillin allergy should be desensitised and treated with penicillin G. Although desensitisation exposes both mother and foetus to heightened risk of anaphylaxis and its consequences, it is indicated when there is a life- or pregnancy-threatening complication with no alternative medications available.

The group of patients whom oral penicillin desensitisation is absolutely contraindicated:

In these groups of patients whom oral penicillin desensitisation is ABSOLUTELY contraindicated, they may be treated with alternatives (appropriate to the scenario and stage of disease). It is imperative that the new-borns of mother (with syphilis) in this group to be treated with intravenous penicillin immediately post-delivery. Please discuss further with ID physician, obstetrician and/ or paediatrician.

1. Patients with poorly controlled asthma (FEV1 < 70% of their predicted value)
2. Unstable vital signs
3. Uncontrolled active cardiac disease
4. Patients who have had confirmed history of penicillin induced life-threatening non-immediate reactions, such as Stevens-Johnsons syndrome, toxic epidermal necrolysis syndrome, drug reaction with eosinophilia and systemic symptoms, or immuno-cytotoxic reactions.
5. Non-IgE mediated reactions to penicillin e.g., fixed drug eruption, maculopapular eruption, erythema multiforme and/or vasculitis.

Before the oral penicillin desensitisation

1. High risk categorisation of a true penicillin allergic patient should be sought. High risk categorisation includes at least one of:

    a) At least two (2) of the high-risk clinical history criteria: -

        i. Penicillin-induced immediate hypersensitivity reaction within the last 10 years.
        ii. Initial reaction compatible with immediate hypersensitivity reaction – pruritus with urticaria and/or angioedema, acute hoarseness of voice, acute rash/flushing, bronchospasm, hypotension, feeling faint, blurred vision, anaphylaxis.
        iii. No history of tolerating re-exposure to penicillin after the initial reaction
        iv. Documented elevated acute serum tryptase (>1.2 x baseline tryptase +2) during the index reaction and/or belonging to the high-risk clinical history group regardless of the in vitro or in vivo test.

    b) Elevated acute serum tryptase level during the index reaction (>1.2 x baseline tryptase +2).

    c) Positive skin testing

    d) Positive serum specific IgE to penicillin or penicillin specific IgE/total IgE ratio of $\geq$0.002.

2. An individualised risk-benefit evaluation should be performed, and the benefits must outweigh the risks involved.

3. If possible, non-selective β-blocker should be withheld 24 hours before and after starting the procedure and finishing the procedure, respectively. With more selective β-blocker, patients may be asked to skip the morning dose before starting the procedure, if possible. If it is not possible, patients must be counselled of the risks involved for desensitisation with concomitant use of β-blocker and, glucagon must be available onsite where the procedure is to be performed.

4. The morning dose of angiotensin converting enzyme (ACE) inhibitor should be skipped or converted to angiotensin receptor blocker. (*Special note: During pregnancy, ACE-inhibitor is contraindicated from 6 weeks of gestation onwards until delivery, while angiotensin receptor blocker is contraindicated throughout pregnancy*)

5. Informed consent must be taken from the patient.

6. Access to the intravenous line is obligatory before starting the procedure and vital signs monitoring at regular intervals is mandatory.

7. Emergency medications to treat anaphylaxis at the bedside.

8. For pregnant woman:
    a) Procedure to be carried out by the clinician in-charge in the high dependency unit/intensive care unit. The clinician in-charge must be well-versed in the desensitisation procedure and familiar with the management of anaphylaxis.
    b) Obstetric team on standby.
    c) Foetal monitoring.

Oral Penicillin Desensitisation Protocol
by using Syrup Penicillin V 125mg/5ml (200, 000 unit/5ml)
[1mL = 40, 000 units penicillin]

1. **Patient's Information:**

Name of patient:		IC Number/RN:		Ward:	
Date:		Time start:		Time end:	

2. **Preparation and Administration Guide:**

Dose no	Time (mins)	Time given	Penicillin concentration (units/mL)	Amount to give patient (mL)	Dose (units)	Cumulative dose given (units)	SN Sign	Any reaction	
1	0		1000	0.1	100	100			Dose no 1-7: Take **1mL of syrup penicillin V 125mg/5mL** and dilute with **39mL water**.
2	15		1000	0.2	200	300			
3	30		1000	0.4	400	700			
4	45		1000	0.8	800	1500			
5	60		1000	1.6	1600	3100			
6	75		1000	3.2	3200	6300			
7	90		1000	6.4	6400	12,700			
8	105		10,000	1.2	12,000	24,700			Dose no 8-10: Take **1mL of syrup penicillin V 125mg/5mL** and dilute with **3mL water**.
9	120		10,000	2.4	24,000	48,700			
10	135		10,000	4.8	48,000	96,700			
11	150		40,000	2.0	80,000	176,700			Dose no 11-14: Use **Undiluted**
12	165		40,000	4.0	160,000	336,700			
13	180		40,000	8.0	320,000	656,700			
14	195		40,000	16.0	640,000	1,296,700			

Notes: 1. Each dose is to be further diluted in 15-30mL water before administering it to the patient.
2. To monitor/observe for any allergic reactions (rash, itchiness, shortness of breath, hypotension, angioedema – facial, lip, periorbital swelling). If any allergic reactions occur, stop the desensitisation & inform the doctor immediately.
3. To observe 30 minutes prior to a full parenteral therapeutic dose

Prepared by: Department of Pharmacy Hospital Kuala Lumpur (September 2022)
Reference: Chastain DB, Hutzley VJ, Parekh J, Alegro JVG. Antimicrobial Desensitization: A Review of Published Protocols. *Pharmacy (Basel)* 2019 Aug 9;7(3):112.

During procedure

1. Breakthrough reactions (objective symptoms of drug hypersensitivity) may occur at any step of the desensitization, most commonly towards the end of the procedure.
2. These breakthrough reactions must be treated immediately and mandatory to stop the next step of the procedure.
3. Management of hypersensitivity reactions during desensitisation

Severity	Management
Mild: Nausea, vomiting, altered taste sensation, sweats, cough, itching, rash, or wheals, shaking, periorbital swelling, chills, local skin rash, headache, abdominal pain	• Perform physical examination to look for objective symptoms • For symptoms such as wheals, periorbital swelling, skin itchiness, administer nonsedating oral antihistamines like cetirizine or loratadine • If no objective symptoms, observe closely
Moderate: Tachycardia, bradycardia, bronchospasm, wheezing, dyspnoea, generalised cutaneous reaction, throat tightness, lip/tongue swelling hoarseness of voice and trouble speaking	• Ask about symptoms to look for possibility of anaphylaxis • Perform physical examination to look for evidence of anaphylaxis • Administer oxygen, nebulised salbutamol if bronchospasm • Hydrocortisone 200mg IM STAT if indicated • If not improving or has potential of developing laryngeal oedema (swollen lips/tongue/throat tightness/hoarseness of voice/trouble speaking) or has generalised urticaria, to give adrenaline 0.5mg SC STAT. May repeat as needed.
Severe: Laryngeal oedema, anaphylaxis (involvement of ≥2 organ systems), hypotension, unresponsive, convulsions, arrhythmias, cardiopulmonary arrest	• Assess airway, breathing and circulation and call for assistance • Lie patient flat with legs elevated • Adrenaline 0.5mg IM STAT, repeat dose every 3-5 minutes as needed or start adrenaline IV infusion as per hospital guideline • Administer hydrocortisone 200mg IV /antihistamines/bronchodilators • Cardiac monitoring • Administer oxygen as needed • If hypotensive – insert 2 large bore IV cannula, IV normal saline bolus 20mls/kg. if still hypotensive, to give up to 50mls/kg in the first 20 minutes, add on a selective vasoconstrictor • For upper airway obstruction/stridor, also administer continuous nebulisation of adrenaline. • Patient is to be admitted for close observation.

4. The clinician in-charge of the procedure should assess if the patient is suitable to continue and finish the rest of the procedure.
5. If it is deemed suitable to continue the procedure, the clinician in-charge should consider re-starting at the last step that does not cause a breakthrough reaction.

6. Desensitisation should definitely be abandoned in patients with near fatal reactions or clinical syndromes such as serum sickness-like and/or blood cell dyscrasias reactions.

Post-procedure

1. After successful desensitisation, penicillin therapy should be given without interruption until completion.
2. Patients requiring 3 doses of benzathine penicillin IM (7.2 million units total, administered as 3 doses of 2.4MU IM each at 1-week intervals) may be given the two subsequent doses as regular injections after being successfully desensitised during the first dose administration. This is because benzathine penicillin has a long half-life, maintaining high plasma levels up to three weeks. Nevertheless, as a safety precaution, these patients should be admitted to the hospital, given a single test dose of penicillin V 400,000u PO and observed for one hour.
3. If there is no reaction, proceed with benzathine penicillin 2.4MU IM and patients should be monitored overnight.
4. If for any reason penicillin is required to be separated in time that exceeds 2-5 half-lives of the penicillin drug to be used, the whole desensitisation procedure must be repeated.

Potential adverse events:

1. Urticaria
2. Pruritus
3. Anaphylaxis
4. Uterine contraction (with subsequent risk of spontaneous abortion)
5. Jarisch-Herxheimer reaction
6. Serum sickness-like reactions (SSLRs) which occur several days to several weeks after antibiotic administration and present with rash (primarily urticaria) and joint complaints (arthralgia/arthritis), with or without fever.

References

1. Alvarez-Cuesta E, Madrigal-Burgaleta R, Broyles AD, Cuesta-Herranz J, Guzman-Melendez MA, Maciag MC, Phillips EJ, Trubiano JA, Wong JT, Ansotegui I; Steering Committee Authors; Review Panel Members. Standards for practical intravenous rapid drug desensitization & delabeling: A WAO committee statement. World Allergy Organ J. 2022 May 31;15(6):100640.
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4.2 GONORRHOEA

Aetiology

Neisseria gonorrhoeae

Incubation period

1-14 days (Men become symptomatic 2-5 days and women become symptomatic within 10 days)

Clinical presentation

In males:

- Asymptomatic
- Purulent or mucopurulent urethral discharge
- Dysuria
- Symptoms of proctitis (in receptive anal intercourse)anal irritation, painful defecation, constipation, scant rectal bleeding, painless mucopurulent discharge, anal pruritus, and tenesmus
- Signs of epididymo-orchitis
- Signs of prostatitis
- Inguinal lymphadenitis, penile oedema, and balanitis

In females:

- Asymptomatic
- Nonspecific vaginal discharge (purulent or mucopurulent cervical discharge on cervical examination)
- Dysuria
- Intermenstrual or post-coital bleeding
- Dyspareunia
- Lower abdominal pain
- Acute and chronic symptoms and signs of pelvic inflammatory disease
- Symptoms of proctitis (in receptive anal intercourse)- anal irritation, painful defecation, constipation, scant rectal bleeding, painless mucopurulent discharge, anal pruritus, and tenesmus

Complications:

- Pelvic inflammatory disease (PID)
- Ectopic pregnancy
- Infertility
- Accessory gland infection (Bartholin in women and other accessory glands in men)
- Gonococcal conjunctivitis
- Disseminated gonococcal infection: skin lesions, arthralgia, arthritis, tenosynovitis, hepatitis, myocarditis, endocarditis, and meningitis
- Ophthalmia neonatorum
- Periurethral abscess or fistula

- Urethral stricture
- Perianal abscess
- Perihepatitis (Fitz-Hugh-Curtis Syndrome)

Investigations

1. Gram stain of urethral, cervical or rectal discharge
   - Presence of intracellular gram-negative diplococci (within polymorphonuclear leucocytes)
   - Male: Sensitivity 95% (symptomatic), 50-75% (asymptomatic), Specificity 99%
   - Female: Sensitivity 45 - 65%, Specificity 90%

2. Nucleic acid amplification tests (NAAT)
   - NAATs have high sensitivity (>95%) in both symptomatic and asymptomatic infection, and it is more sensitive than culture
   - Vulvovaginal, anorectal and pharyngeal swabs may either be self-collected or clinician-collected
   - Extra-genital specimens from rectal and pharyngeal sampling should be routine in all MSM and be guided by an assessment of risk and symptoms in everyone else

3. Culture and sensitivity (C&S)
   - Culture is still the gold standard for gonorrhoea identification
   - C&S provides antimicrobial susceptibility testing and monitors emerging resistance
   - Types of specimens: urethral, endocervical, neovaginal, anorectal and pharyngeal swabs
   - Culture accuracy depends on stringent incubation and transport conditions and should reach the laboratory within 24 hours e.g. incubating on selective agar such as Modified Thayer Martin or GC agar and incubated in an increased carbon dioxide (CO_2) environment
   - Clinicians must specifically request 'gonococcal culture', as gonococci require specific culture conditions
   - All individuals with gonorrhoea diagnosed by NAAT should have cultures taken from infected sites for susceptibility testing prior to treatment but treatment should be administered without waiting for culture results

Site	Preferred Specimen	Alternative specimen
Penile urethra	First pass urine (FPU)	Urethral swab specimen
Female urethra and endocervix	Self-collected vulvovaginal swab	Endocervical swab
Rectum	Anorectal swab	-
Pharynx	Pharyngeal swab	-

Management

i. Pharmacological treatment

Type of infection	Preferred	Alternative
Uncomplicated (urogenital and anorectal)	Ceftriaxone 500mg IM STAT (Use 1g if weight more than 150kg)	Gentamicin 240mg IM STAT AND Azithromycin 2g PO STAT
Uncomplicated (pharynx)		Discuss with expert
Gonococcal conjunctivitis	Ceftriaxone 1g IM STAT *one-time lavage of the infected eye with saline should be considered	Refer Ophthalmologist
Disseminated Gonococcal Infection (DGI) (Hospitalisation and physician consultation are recommended)	Ceftriaxone 1g IM/IV daily Duration of parenteral treatment: At least 7 days for DGI with arthritis-dermatitis syndrome 10-14 days for DGI with meningitis 4 weeks for DGI with endocarditis	Refer relevant subspecialities

Note: If chlamydia infection has not been ruled out, all non-pregnant patients should receive oral doxycycline 100mg BD for 7 days. During pregnancy, oral azithromycin 1 gram as a single dose is recommended.

ii. Contact tracing/advice/epidemiological treatment

- Sexual partners within the last 60 days must be epidemiologically treated irrespective of the test results
- Sexual partners prior to 60 days should be evaluated and treated if necessary
- Newborns of mothers with gonorrhoea infections must be screened for gonorrhoea
- Sex partners should be instructed to abstain from condomless sexual intercourse for 7 days after they and their sex partners have been treated, and after resolution of symptoms.

iii. Follow-up

- For persons with pharyngeal gonorrhoea or treated with anything other than the first line recommended regimen when antimicrobial susceptibility is unknown, a routine test-of-cure (using either culture or NAAT) is recommended 7 to 14 days after completing treatment.
- Routine test-of-cure for gonorrhoea of the cervix, urethra or rectum is not recommended
- Symptoms that persist after treatment should be evaluated by culture for *N. gonorrhoeae* (with or without simultaneous NAAT) and antimicrobial susceptibility testing

References

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4.3 CHLAMYDIA

Chlamydia infection in the ano-genital tract

Chlamydia trachomatis is the commonest bacterial STI and the prevalence is highest in persons aged < 25 years. The majority of infections in both men and women are asymptomatic.

Aetiology

Chlamydia trachomatis serovars D to K

Incubation period

7-21 days (usually shorter 5-15 days)

Clinical presentation

In males:

- Asymptomatic
- Mucopurulent urethral discharge
- Dysuria
- Signs of epididymo-orchitis
- Ano-rectal discomfort + discharge (in receptive anal intercourse)

In females:

- Majority asymptomatic
- Mucopurulent vaginal discharge
- Dysuria
- Intermenstrual or post-coital bleeding
- Lower abdominal pain
- Acute and chronic symptoms and signs of pelvic inflammatory disease
- Cervicitis
- Ano-rectal discomfort + discharge (in receptive anal intercourse)

Complications

- Pelvic inflammatory disease (PID)
- Ectopic pregnancy
- Infertility
- Sexually acquired reactive arthritis (SARA)
- Periurethral and perianal abscess
- Pregnancy related complications (premature rupture of membranes, pre-term delivery, low birth weight infants)
- Peri-hepatitis
- Prostatitis

Investigations

1. Gram stain of urethral, cervical or rectal discharge (not diagnostic)
    - Increased polymorphonuclear neutrophils (PMNs) (average of >5 per high power field in a urethral smear and >20 per high power field in an endocervical smear)
    - To exclude Gram-negative intracellular diplococci

2. Nucleic acid amplification tests (NAAT)

Site/Specimen	**Consideration**
Urethra - first pass urine (FPU)	In men, FPU is as sensitive or more sensitive than urethral sampling. Urethral swabs are less acceptable than urine samples for patients. In women, FPU can be considered if endocervical swabs/ self-collected vaginal swabs cannot be taken.
Self-collected vaginal swab	Self-collected vulvo-vaginal swabs are the specimen of choice
Clinician-collected endocervical swab	Best test if a speculum examination is done
Anorectal swab	Any patient with ano-rectal symptoms All men who have sex with men (MSM) Self-collection or during a clinical examination
Pharyngeal swab	All men who have sex with men (MSM)

Note:
Chlamydia serology is not recommended for diagnosis of Chlamydia infection.

Management

Pharmacological treatment

Type of infection	**Preferred**	**Alternative**
Uncomplicated (urogenital, anorectal, pharyngeal)	Doxycycline 100mg PO q12h for 7 days	Azithromycin 1g PO STAT
In pregnancy	Azithromycin 1g PO STAT	Amoxicillin 500mg PO q8h for 7 days

Test of cure (TOC)

TOC is not routinely recommended for uncomplicated genital chlamydia infection, because residual, non-viable chlamydial DNA may be detected by NAAT for up to 4 weeks following treatment.

TOC is recommended in pregnancy, where poor compliance is suspected and where symptoms persist and should be performed no earlier than 4 weeks after treatment to prevent false positive results

Advice

Patients should be instructed to abstain from condomless sexual intercourse until they and their sex partner(s) have been treated (after completion of a seven-day regimen) and any symptoms have resolved

Contact tracing

- Sexual partners within the last 60 days must be epidemiologically treated irrespective of the test results
- Newborns of mothers with chlamydial infections must be screened

References

1. 2021 STI Treatment Guidelines. Centre for Disease Control and Prevention (CDC). Last Reviewed: April 11, 2023. https://www.cdc.gov/std/chlamydia/default.htm
2. Australia STI Management Guidelines for Use in Primary Care. Last updated: December, 2021. https://sti.guidelines.org.au/

4.4 EPIDIDYMO-ORCHITIS

Definition

- A syndrome consisting of pain, swelling and inflammation of the epididymis and/or the testes.
- Route of infection: local extension and due mainly to infections from the urethra.

Aetiology

- Usually under 35 years of age; most often caused by a sexually transmitted pathogen e.g., *C. trachomatis* and *N. gonorrhoeae*.
- Over 35 years of age; usually due to non-sexually transmitted gram negative enteric/urinary organisms e.g. *E.coli.*
- Anatomical and functional abnormalities are often present in this group and should be further investigated.

Important differential diagnoses

- Testicular torsion (surgical emergency, should be considered in all patients and be excluded first)
- Appendix testis torsion
- Testicular mass
- Hydrocoele
- Spermatocoele
- Varicocoele
- Testicular rupture/trauma
- Other infections like TB or mumps

Clinical presentation

- Asymptomatic
- Unilateral pain and swelling of the testes
- Dysuria
- Symptoms of urethritis or a urethral discharge
- Pyrexia
- Palpable swelling of the epididymis
- Tenderness on palpation
- Erythema/oedema of the scrotum

Investigations

- Gram-stain of urethral smear to look for polymorphs and intracellular gram-negative diplococci
- Urethral swab for *N. gonorrhoeae* culture
- Urine NAAT for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*
- Urine FEME and MSU culture to exclude urinary tract infection
- Surgical review/USG testes if concerned

Management

i. General

- Scrotal support
- Analgesia – NSAIDs

ii. Pharmacological treatment

Type of infection	Preferred	Alternative
STI related	Ceftriaxone 500mg IM STAT **PLUS** Doxycycline 100mg PO q12h for 10 days	-
STI related but unlikely gonorrhoea	Doxycycline 100mg PO q12h for 10-14 days	-
Non STI related (enteric /urinary organisms)	Levofloxacin 500mg PO q24h for 10 days	Ofloxacin 200mg PO q12h for 14 days

iii. Contact tracing and advice

- Abstain from sexual intercourse until patient and partner have completed treatment.
- Trace partner/s for screening and treatment.
- Partner notification: Appropriate to infections isolated.

iv. iv. Follow up

- If no clinical improvement after 3 days: Review diagnosis.
- Review at 2 weeks to assess treatment compliance, partner notification and resolution of symptoms.
- Look out for complications i.e., hydrocoele, abscess, infarction, infertility.

References

1. CDC Sexually Transmitted Infections Treatment Guidelines 2021
2. United Kingdom British association for sexual health and HIV national guideline for the management of epididymo-orchitis, 2020

4.5 NON-GONOCOCCAL URETHRITIS

Aetiology

- *Chlamydia trachomatis* (11% - 50%)
- *Mycoplasma genitalium* (6% - 50%)
- *Ureaplasma spp.* (11% - 26%)
- *Trichomonas vaginalis* (1% - 20%)
- Adenoviruses (2% - 4%)
- Herpes simplex virus (HSV) (2% - 3%)

Incubation period

- Variable, often longer
- 1 week to 3 weeks (up to 6 weeks)

Clinical presentation

- Urethritis is characterised by urethral inflammation, which results from infectious and non-infectious causes
- It may be symptomatic or asymptomatic
- Urethral discharge, may be muco-purulent or mucoid and may only be present on urethral milking
- Dysuria
- Urethral itching
- Penile irritation
- Urinary frequency
- Other clinical signs include balanoposthitis, epididymo-orchitis and SARA (Sexually acquired reactive arthritis)

Investigations

- Urethral swab for gram stain
    - Gram-stained urethral smear containing 5 or more PMNL per high power field
    - To exclude gram-negative intracellular diplococci
    - There is little justification for performing urethral microscopy in asymptomatic men
- Urine FEME to look for leukocytes
- Urine C&S to exclude UTI
- Urine for Chlamydia/Gonorrhoea (CT/GC) NAAT
- Urethral swab wet mount microscopy for *Trichomonas vaginalis*
- Multiplex PCR (for recurrent/persistent NGU)

Management

i. Pharmacological treatment

Type of infection	Preferred	Alternative
1st episode of NGU	Doxycycline 100mg PO q12h for 7 days	Azithromycin 500mg PO STAT, then 250mg q24h for 4 days
Recurrent and persistent NGU	***If treated with Doxycycline first line:*** Azithromycin 500mg PO STAT, then 250mg q24h for 4 days **PLUS** Metronidazole 400mg PO q12h for 5 days ***If treated with Azithromycin first line:*** Moxifloxacin 400mg PO q24h for 10-14 days **PLUS** Metronidazole 400mg PO q12h for 5 days	

ii. Contact tracing and advice

Sexual partner(s) should be evaluated and treated (look back period: preceding 60 days)

- Empiric treatment with a drug regimen effective against Chlamydia should be considered for sexual partner(s)
- Abstain from sexual intercourse until the patient has completed treatment, their partner(s) have been treated and symptoms resolved at least for 1 week
- Offer HIV and syphilis test
- Advice on safer sex and consistent condom use

iii. Follow-up

Test of cure (TOC) in asymptomatic patients is not recommended

References

1. 2015 UK National Guideline on the management of non-gonococcal urethritis. Updated November 2018
2. CDC Sexually Transmitted Infections Treatment Guidelines 2021
3. National Antimicrobial Guideline 2019 (STI Chapter). MOH

4.6 OPHTHALMIA NEONATORUM

Definition

Conjunctivitis which occurs in the first 4 weeks of life in a neonate with clinical signs of erythema and oedema of the eyelids and palpebral conjunctivae, purulent eye discharge with one or more polymorph nuclear per oil immersion field on a Gram-stained conjunctival smear.

Aetiology

- *Chlamydia trachomatis* (the commonest causative organism)
- *Neisseria gonorrhoeae*
- Herpes simplex virus (HSV 1 & 2)
- Other bacterial agents: *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Pseudomonas* and Enteric gram-negative organism

Incubation Period

C trachomatis conjunctivitis: 5-14 days
Gonococcal conjunctivitis: 2-5 days
Herpes simplex conjunctivitis: 6-14 days.

Clinical presentation

An initial watery conjunctival exudate may rapidly become purulent, thick and blood stained.

The conjunctiva and eyelid are oedematous. These may lead to development of keratitis, iridocyclitis, corneal ulceration, perforation, pannus formation, scarring, and eventually blindness if left untreated.

In some infants with Chlamydia-associated conjunctivitis, the infection persists for a longer period and the babies may develop pharyngitis and pneumonia if left untreated.

Neonatal herpes simplex infection can be generalized, with involvement of the skin, eye and mucosa. Neonates may present with vesicles around the eye with corneal involvement. These infants need a lumbar puncture and assessment by an ophthalmologist.

Diagnosis:

- Essentially a clinical diagnosis
- Laboratory investigations to determine aetiology

Investigations

- Eye swab for Gram stain (fresh specimen to reach laboratory in 30 mins)
- Gram stain of intracellular gram-negative diplococci - high sensitivity and

specificity for Neisseria gonorrhoeae.
- Eye swab for culture and sensitivity
- NAAT for *N. gonorrhoeae & C. trachomatis*
- Swab for HSV NAAT

Management

- Refer patients to an ophthalmologist for assessment.
- Careful handling of neonate to prevent direct spread to others
- Ophthalmia neonatorum due to gonococcal or chlamydia trachomatis infection is a notifiable disease
- Check RPR of the infant and mother to exclude associated congenital syphilis and screen for C. trachomatis, HSV and HIV.

Treatment for ophthalmia neonatorum

Type of infection	**Preferred**	**Alternative**
Gonococcal ophthalmia (systemic)	Ceftriaxone 25-50mg/kg (max 250mg) IV/IM STAT	Cefotaxime 100mg/kg IV/IM STAT
Gonococcal ophthalmia (disseminated)	Ceftriaxone 25-50mg/kg/dose IV/IM q24h Duration of treatment: Disseminated infection: 7 days Meningitis: 10-14 days	Cefotaxime 25mg/ kg/ dose IV/IM q12h Duration of treatment: Disseminated infection: 7 days Meningitis: 10-14 days
Gonococcal ophthalmia (local)	Irrigate eyes with sterile normal saline at least hourly to eliminate discharge Topical antibiotics are optional	
Chlamydial ophthalmia (systemic)	Erythromycin base or ethyl succinate 50mg/kg/day PO in 4 divided doses for 14 days *- May need repeat course of erythromycin for further 2 weeks if poor response as elimination after first course ranges from 80-100%*	Azithromycin 20mg/kg PO q24h for 3 days

	If subsequent treatment failure: Trimethoprim/sulfamethoxazole 0.5mL/kg/day PO in 2 divided doses *(Formulation: trimethoprim 40mg/sulfamethoxazole 200mg per 5mL suspension)*	
Herpes simplex conjunctivitis	Acyclovir 10mg/kg/dose IV q8h for 2 weeks	
Note: *Chlamydial ophthalmia: Systemic treatment is essential. Local treatment may be unnecessary if systemic treatment is given.* *Both erythromycin and azithromycin are associated with increased risk of infantile hypertrophic pyloric stenosis (IHPS).*		

Contact tracing

- Parents should be referred to an STI clinic for STI screening, in particular C trachomatis, HSV and HIV
- The mother should be treated on epidemiological grounds.

Follow-up

On discharge, infants should be seen at 2 weeks to have a repeat eye swab gram stain and culture. If clinical symptoms and signs persist, consider a second course of treatment.

References

1. 2021 STI Treatment Guidelines. Centre for Disease Control and Prevention (CDC). https://www.cdc.gov/std/treatment-guidelines/syphilis.htm
2. Ophthalmia Neonatorum. Paediatric Protocols For Malaysian Hospitals. 4th Edition 2018.167-168.
3. Zikic A, Schünemann H, Wi T, Lincetto O, Broutet N, Santesso N. Treatment of neonatal chlamydial conjunctivitis: a systematic review and meta-analysis. J Pediatric Infect Dis Soc 2018;7:e107–15.
4. Zloto O, Gharaibeh A, Mezer E, Stankovic B, Isenberg S, Wygnanski-Jaffe T. Ophthalmia neonatorum treatment and prophylaxis: IPOSC global study. Graefes Arch Clin Exp Ophthalmol. 2016 Mar;254(3):577-82.

4.7 PELVIC INFLAMMATORY DISEASE

Definition

PID comprises a spectrum of inflammatory disorders of the upper female genital tract, usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophoritis, tuboovarian abcess and/or pelvic peritonitis.

Aetiology

The aetiology of PID is often polymicrobial. Common organisms include:

Sexually transmitted organisms	**Non sexually transmitted pathogen**
Neisseria gonorrhoea and *Chlamydia Trachomatis* **Affecting younger age group* *Mycoplasma genitalium* has also been associated with upper genital tract infection in women	Anaerobes, *Gardnerella vaginalis, Haemophilus influenzae*, enteric Gram-negative rods, *Streptococcus agalactiae, Cytomegalovirus* (CMV), *Mycoplasma hominis* and *Ureaplasma urealyticum*

Pathogen negative PID is also commonly encountered. It may be due to:

- A false positive diagnosis where the woman does not have a STI or PID
- PID of another microbiological aetiology or associated with a past STI
- PID where the cervical infection has cleared

The risk of pelvic infection appears to increase within the 3 weeks of IUCD insertion, however the risk is very low at less than 1%.

Clinical presentation:

PID is usually symptomatic, but may be asymptomatic.

- Lower abdominal pain which is typically bilateral
- Deep dyspareunia
- Abnormal vaginal bleeding, including post coital, intermenstrual and menorrhagia
- Abnormal vaginal or cervical discharge which is often purulent
- Fever (> 38°C)
- Adnexal tenderness on bimanual vaginal examination
- Cervical motion tenderness on bimanual vaginal examination

These clinical symptoms and signs have low sensitivity and specificity, therefore a diagnosis of PID based solely on positive examination findings without lower abdominal pain, should be made with caution.

Other causes of abdominal/pelvic pain such as endometriosis, complication of ovarian cyst, acute appendicitis and urinary tract infection have to be excluded.

Investigations

Endocervical swabs for microscopy, culture and sensitivity for gonorrhoea and NAAT for Chlamydia are highly recommended.

The absence of endocervical or vaginal pus cells on Gram-stain examination of a vaginal smear has a good negative predictive value (95%) for a diagnosis of PID but their presence is non-specific. (poor positive predictive value of 17%)

All females in the reproductive age group should be offered pregnancy test to rule out ectopic pregnancy and screened for sexually transmitted infections including HIV.

Ultrasound scanning is of limited value for uncomplicated PID but is helpful if an abscess or hydrosalpinx is suspected.
MRI or CT scanning of the pelvis may be helpful in differentiating PID from alternative diagnoses but are not routinely indicated.

Management

Empirical treatment should be started immediately if there are any suspicions of PID because of the lack of definitive clinical diagnostic criteria and potential consequences of untreated PID. Delaying treatment increases the risk of long-term sequelae such as ectopic pregnancy, infertility and chronic pelvic pain.

Outpatient treatment is appropriate for patients with mild to moderate PID. Hospital admission (preferably under gynaecological care) is indicated in these situations:

- A surgical emergency cannot be excluded
- Lack of response or intolerance to oral therapy
- Clinically severe disease (pyrexia>38 C, signs of peritonitis)
- Presence of a tubo-ovarian abscess
- PID in pregnancy

Appropriate analgesia should be provided.

Pharmacological treatment

Type of regimens	Preferred	Alternative
Outpatient	Ceftriaxone 500mg IM STAT **PLUS** Doxycycline 100mg PO q12h for 14 days **PLUS** Metronidazole 400mg PO q12h for 14 days	If cephalosporin allergy and low risk for gonorrhoea: Levofloxacin 500mg PO q24h for 14 days **PLUS** Metronidazole 400mg PO q12h for 14 days OR Moxifloxacin 400mg PO q24h for 14 days
	Note: Do not replace intramuscular Ceftriaxone with an oral Cephalosporin (e.g.cefixime) because there is no clinical trial evidence to support its use, and tissue levels are likely to be lower which might impact on efficacy	
Type of regimens	**Preferred**	**Alternative**
Inpatient	Ceftriaxone 2g IV q24h* **PLUS** Doxycycline 100mg PO q12h **PLUS** Metronidazole 400mg PO or 500mg IV q12h Duration of treatment: 14 days	Ampicillin/sulbactam 3g IV q6h **PLUS** Doxycycline 100mg PO q12h OR Clindamycin 900mg IV q8h* **PLUS** Gentamicin loading dose 2mg/kg IV, followed by maintenance dose 1.5mg/kg IV q8h OR 3-5mg/kg IV q24h* *followed by,* Clindamycin 450mg PO q6h or 600mg PO q8h OR Doxycycline 100mg PO q12h **PLUS** Metronidazole 400mg PO q12h Duration of treatment: 14 days
	*Note: *Patients with clinical improvement after 24-48 hours can be transitioned to oral therapy to complete the 14 days of treatment.*	

Pregnancy and Breastfeeding

PID in pregnancy is uncommon but associated with an increase in both maternal and foetal morbidity, therefore parenteral therapy is advised although none of the suggested evidence-based regimens are of proven safety in this situation.

There is insufficient data from clinical trials to recommend a specific regimen and empirical therapy with agents effective against gonorrhoea, *C. trachomatis* and anaerobic infections should be considered taking into account local antibiotic sensitivity patterns (e.g., parenteral ceftriaxone, erythromycin and metronidazole switching to oral therapy following clinical response and completing 2 weeks of treatment).

Surgical treatment

Laparoscopy may help early resolution of the disease by dividing adhesions and draining pelvic abscesses but ultrasound guided aspiration of pelvic fluid collections is less invasive and may be equally effective. Laparotomy may be required to assess and treat clinically severe pelvic infection

General advice

- The risk of PID is highest in women aged under 25 not using barrier contraception and with a history of a new sexual partner.
- Patients should be advised to avoid unprotected intercourse until they, and their partner(s), have completed treatment and follow-up.
- A detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s) should be provided and reinforced with clear and accurate written information.
- The decision to remove an intrauterine device (IUD) in a woman with suspected PID needs to be balanced against the risk of pregnancy in those who have had otherwise unprotected intercourse in the preceding 7 days. Consider removal of IUD if no response to treatment within 48-72 hours. Hormonal emergency contraception may be appropriate for some women in this situation.

Contact tracing

- Sexual partners within the last 60 days must be epidemiologically treated for Chlamydia and Gonorrhoea irrespective of the test results.
- Partners should be advised to avoid intercourse until they and the index patient have completed the treatment course.

Follow Up

Review at 72 hours is recommended to assess adherence and response to treatment. Lack of clinical improvement suggests the need for further investigation, parenteral therapy and/or surgical intervention.

Further review in 2 – 4 weeks after therapy to ensure:

- Adequate clinical response to treatment
- Compliance with oral antibiotics
- Screening and treatment of sexual contacts
- Awareness of the significance of PID and its sequelae
- Repeat pregnancy test, if clinically indicated

References:

1. Malaysian Guidelines in the Treatment of Sexually Transmitted Infections. Fourth Edition 2015.
2. Sexually Transmitted Disease Treatment Guideline 2020: Centre for disease Control And Prevention (CDC)
3. United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease (BASHH) 2018
4. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: World Health Organization; 2021.
5. Ministry of Health Malaysia National Antimicrobial Guideline 2019.

4.8 TRICHOMONIASIS

Aetiology

Trichomonas vaginalis is a flagellated protozoan which is a parasite of the genital tract. The growth and multiplication of *T. vaginalis* is greatest in moist environments at normal body temperature, with a pH of 4.9 to 7.5.

TV is almost exclusively sexually transmitted. Due to site specificity, an infection can only follow intravaginal or intraurethral inoculation of the organism. It has been isolated in 14–60% of male partners of infected females and in 67–100% of female partners of infected men.

Incubation period

4 days to 4 weeks

Clinical presentation

In male:

15-50% of infections are asymptomatic. Infected men usually present as sexual partners of infected women.

Common symptoms:

- Urethral discharge and/or dysuria
- Urethral irritation
- Urinary frequency

Rare symptoms:

- Copious purulent urethral discharge
- Superficial penile ulceration

Examination findings:

- No abnormalities, even in the presence of symptoms, suggesting urethritis
- Urethral discharge in 20-60% of cases
- Rarely balanoposthitis

In female:

10-50% of infections are asymptomatic.

The organism is most often found in the:

- Vagina
- Urethra
- Paraurethral glands

Common symptoms:

- Vaginal discharge
- Vulval itching

- Dysuria
- Offensive odour

Occasionally, patient may complaint of lower abdominal discomfort, vaginitis and abnormal vaginal bleeding (post coital bleeding).

Examination findings:

- No abnormalities in 5-15% of women
- Vaginal discharge in up to 70% (classical frothy yellow discharge)
- Varying in consistency from thin and scanty to profuse and thick
- Strawberry cervix

Only 2% are visible to the naked eye, higher rates are seen on colposcopic examination.

Investigations

1. Microscopy examination
    - Saline wet smear sensitivity of 40-60%
    - In female, smear is taken from posterior fornix of the cervix
    - Detection of motile trichomonads by light-field microscopy
    - Microscopy should be performed as soon as possible after specimens collection as motility diminishes with time

2. NAAT
    - if available
    - Sensitivity of 88-100% and specificity of 92-100%

Management

There is a spontaneous cure rate in the order of 20-25%.

To effect a permanent cure, treatment is required due to the frequency of infection of the urethra and paraurethral glands in females.

Recommended regime

Preferred	**Alternative**
Metronidazole 400mg PO q12h for 7 days OR Metronidazole 2g PO STAT*	-
Note: **Single high dose of metronidazole is associated with gastrointestinal side effects and higher failure rate, especially if partners are not treated concurrently.*	

Pregnancy and breastfeeding

There is evidence that suggests *T. vaginalis* infection can have a detrimental outcome on pregnancy and is associated with pre-term delivery and low birth weight. However, further research is needed to confirm this association. Screening of asymptomatic individuals for TV infection in pregnancy is not currently recommended.

Meta-analyses have concluded that there is no evidence of teratogenicity from the use of metronidazole in women during the first trimester of pregnancy. Metronidazole can be used in all stages of pregnancy and during breastfeeding. In the absence of data on the use of single high stat doses in pregnancy and the theoretical risk of a threshold dose above which teratogenicity may occur in humans, single dose regimens are not recommended.

Contact tracing

Sexual partners should be treated simultaneously. Patients should be advised to avoid sexual intercourse (including oral sex) for at least 1 week, and until they and their partner have completed treatment.

Follow-up

Test of cure with NAAT is only recommended if the patient remains symptomatic following treatment, or if symptoms recur. This includes pregnant women treated for TV.

References

1. Malaysian Guidelines in the Treatment of Sexually Transmitted Infections, Fourth Edition. Putrajaya: Ministry of Health, Malaysia; 2015
2. Guidelines | British Association for Sexual Health and HIV. (2021). https://www.bashhguidelines.org/media/1310/tv-2021.pdf
3. Centers for Disease Control and Prevention. (2021). https://www.cdc.gov/std/treatment-guidelines/trichomoniasis.htm
4. Guidelines for the Management of Symptomatic STI, WHO 2021

4.9 VULVOVAGINAL CANDIDIASIS

Aetiology

- *Candida albicans* in 90% of cases
- *C. glabrata* in 8% of cases
- Other non-albicans species, such as *C. tropicalis*, *C. krusei* and *C. parapsilosis* in the remainder of cases

Clinical presentation

Symptoms

- Vulvar itchiness or burning sensation
- Vaginal soreness or irritation
- Dyspareunia (pain during sexual intercourse)
- Dysuria
- Vaginal discharge – thick, curdy, white, although discharge can appear normal or absent

Signs

- Vulva may be erythematous and excoriated
- Vulva and labia may be swollen
- Pustulopapular lesions peripheral to the erythematous area of the vulva may be present
- Speculum examination shows erythematous vaginal wall, and an adherent discharge may be seen, either curd-like or white. The cervix often appears normal.

Recurrent vaginal candidiasis

- 4 or more episodes in a 12-month period (may occur in nearly 10% of women).
- Infection should be confirmed by culture on at least one occasion.
- Predisposing factors: diabetes mellitus, human immunodeficiency virus (HIV) infection or other causes of immunosuppression, corticosteroid use, frequent broad spectrum antibiotic use and non-compliance to antifungal therapy.

Investigations

1. Microscopy

    - Gram stain of vaginal discharge demonstrating presence of blastopores and pseudohyphae.
    - 10% potassium hydroxide preparation is also useful in identifying yeast or hyphae

2. Culture

    - Should be done for symptomatic women with negative microscopic examination

Management

Pharmacological treatment

Type of infection	Preferred	Alternative
Uncomplicated infection	Clotrimazole 500mg as a single vaginal pessary STAT	Fluconazole 150-200mg PO STAT
Complicated infection (severe vaginitis symptoms)	Fluconazole 150-200mg PO q72h for 2 or 3 doses	
Recurrent infection	Fluconazole 150-200mg PO q72h for 3 doses, then weekly for 6 months *Treat each episode with longer course of azole cream	Clotrimazole 500mg vaginal pessary weekly for 6 months
Infection in pregnancy	Clotrimazole 500mg as a single vaginal pessary STAT If indicated, treat with topical therapy as oral azole is contraindicated	

General treatment advice

- Intravaginal and oral azoles have similar efficacy
- Both vulvar and vaginal sites should be treated
- Addition of 1% hydrocortisone cream may provide symptomatic relief
- No evidence that specific diet or use of probiotic influence recurrence
- Reconsider diagnosis if no response to therapy
- No hepatic monitoring is required for fluconazole use at the above doses
- Avoid local irritants e.g., soap, spermicide, vaginal lubricant and vaginal hygiene products
- Latex barrier contraception e.g., condoms can be damaged by antifungal creams
- Pregnant women may need longer course of topical treatment (7 days minimum)

Pregnancy and breastfeeding

Symptomatic candidiasis is common in pregnancy. Evidence is incomplete to suggest increased risk for preterm birth or other adverse perinatal outcomes, in pregnant women with either symptomatic or asymptomatic vulvovaginal candidiasis. There is conflicting evidence over the safety of fluconazole and other oral azoles in pregnancy thus best avoided. Vaginal clotrimazole and topical azoles are choice of treatment in pregnancy and breastfeeding.

Contact tracing

- Contact tracing is not required
- No evidence to support treatment of asymptomatic male sexual partners

Follow-up

- Not indicated for uncomplicated infection.
- 7-14 days after completion of therapy for recurrent candida infections

References:

1. Malaysian Guidelines in the Treatment of Sexually Transmitted Infections. Fourth Edition 2015.
2. Australian STI Management Guidelines for Use In Primary Care. Updated Dec 2021. https://sti.guidelines.org.au/
3. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
4. Workowski K.A et.al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep 2021;70 (4), 82-3.
5. Ministry of Health Malaysia National Antimicrobial Guideline 2019.

4.10 BACTERIAL VAGINOSIS

Aetiology

BV is the most common cause of vaginal discharge in women of reproductive years. The normal *Lactobacillus*-dominated flora is overwhelmed by an overgrowth of anaerobic organisms known as BV-associated bacteria (BVAB) e.g., *Gardenella vaginalis, Mobiluncus spp and Bacteroides spp*.

Lactobacilli metabolises glycogen to produce lactic acid which maintains an acidic pH between 3.5 and 4.5. They produce additional factors which inhibit the growth of other organisms such as hydrogen peroxide and bacteriocins. By binding to epithelial cells, they block attachment sites for other bacteria.

In vitro, the BVAB growth is superior to that of lactobacilli at pH levels above 5.0. Many species grow together symbiotically with metabolites of one being substrates for another.

The vaginal flora is in a dynamic state throughout the menstrual cycle. pH is lowest and glycogen levels highest mid-cycle, and even in women who do not get BV there may be lower levels of lactobacilli and higher levels of BV-associated organisms around the time of menstruation.

BV is associated with:

- Change of sex partner
- Increasing lifetime partners
- Smoking
- Intrauterine device (IUD) use
- Presence of an STI, e.g., chlamydia, gonorrhoea, pelvic inflammatory disease

BV is less common in women using hormonal contraception and/or condoms than in those using no contraception.

Trigger factors for BV are:

- Unprotected sexual intercourse
- Menstruation
- Vaginal douching

Prevalence

Prepubertal girls

Prepubertal girls do not get BV, probably because there is insufficient glycogen to support a high concentration of bacteria.

Post-menopausal women

Post-menopausal women can be expected to have a different vaginal microbiome. It is not common for post-menopausal women to present with symptoms of BV.

Men
Men do not get BV, although sometimes they present with an offensive smell from the sub preputial space and the Gram stain looks very similar to BV. This is usually associated with poor hygiene and antibiotic treatment is not usually required.

Clinical presentation

The principal symptoms and signs of BV are, an offensive fishy smell detectable in approximately 50% of cases and a watery homogeneous vaginal discharge, which can be white or yellow. Approximately 50% are asymptomatic.

Usually, there is no redness or inflammation unless due to another co-existing condition. Occasionally (in less than 10% of cases) there is vulval irritation or soreness.

The main differential diagnoses are:
- Trichomoniasis
- Candidiasis
- Cervicitis due to chlamydia or gonorrhoea

Diagnosis

1. Amsel's criteria
2. Hay/Ison criteria

Amsel's criteria
At least 3 out of 4 criteria are present for diagnosis of BV:
1. Thin, white, homogeneous discharge
2. Clue cells on microscopy of wet mount
3. pH of vaginal fluid >4.5
4. Release of a fishy odour on adding 10% KOH

Investigations

1. Sample: Vulvovaginal swab for Gram stain with Hay/Ison criteria.

The Hay/Ison criteria are defined as follows:

Grade 1 (Normal):	Lactobacillus morphotypes predominate
Grade 2 (Intermediate):	Mixed flora with some lactobacilli present, but Gardnerella or Mobiluncus morphotypes also present
Grade 3 (Bacterial Vaginosis):	Predominantly Gardnerella and/or Mobiluncus morphotypes. Few or absent Lactobacilli.
Grade 4	Gram-positive predominate

2. NAATs
    - Should be used among symptomatic women only

Management

Antibiotics with good anti-anaerobic activity are the most effective for treating BV. The most established treatment is a course of oral metronidazole, which in a systematic review was shown to have the best cure rates after 30 days.

Treatment is indicated for women with BV who have symptoms. Relapse is common with recurrence rates of 30% after one month and up to 60% after six months, but spontaneous resolution can also occur.

Recommended regimes:

Preferred	**Alternative**
Metronidazole 400mg PO q12h for 5-7 days OR Metronidazole 2g PO STAT*	Clindamycin 300mg PO q12h for 7 days
Note: **Single high dose of metronidazole is associated with gastrointestinal side effects.*	

Pregnancy and breast feeding

In pregnancy, BV is associated with an increased risk of second-trimester miscarriage (about 3-5-fold) and preterm birth (1.5-7-fold).

There is currently no consensus as to screen for or treat bacterial vaginosis in the general pregnant population in order to prevent adverse outcomes, such as preterm birth. Treatment with either oral or vaginal antibiotics is acceptable for achieving a cure in pregnant women with symptomatic bacterial vaginosis who are at low risk of adverse obstetric outcomes. Women at increased risk for preterm birth may benefit from routine screening and treatment of bacterial vaginosis.

Even though metronidazole crosses the placenta, meta-analyses have concluded that there is no evidence of teratogenicity from its use in women during the first trimester of pregnancy.

Metronidazole is secreted in breast milk; however, several studies identified no evidence of metronidazole-associated adverse effects in breastfed infants.

Additional advice

- Avoid douching
- Avoid the use of shower gel and antiseptic soap in a bath

Contact tracing

Routine screening and treatment of male partners are not indicated.

Follow up

Tests of cure are not indicated.

References

1. Malaysian Guidelines in the Treatment of Sexually Transmitted Infections, Fourth Edition. Putrajaya: Ministry of Health, Malaysia; 2015

2. British Association for Sexual Health And HIV. (2023). https://www.bashhguidelines.org/media/1041/bv-2012.pdf

4.11 GENITAL HERPES

Aetiology

1. HSV-1 (the usual cause of oro-labial herpes and now the most common cause of genital herpes) **OR**
2. HSV-2 (historically the most common cause of genital herpes, and more likely to cause recurrent anogenital symptoms).

Incubation Period

2 - 14 days

Terminology

1. Initial episode

The first episode with either herpes simplex virus type 1 (HSV-1) or type 2 (HSV-2). Depending on whether the individual has had prior exposure to the other type, this is further subdivided into:

i. **Primary infection**:

- First infection with either HSV-1 or HSV-2 in an individual with no pre-existing antibodies to either type. More than 50% of primary genital infections in young people are caused by HSV-1.
- Lesions usually heal within a month.
- Following primary infection, the virus becomes latent in local sensory ganglia, periodically reactivating to cause symptomatic lesions or asymptomatic, but infectious, viral shedding.
- Median recurrence rate after a symptomatic first episode is 0.34 recurrences per month for HSV-2 and 0.08 recurrences per month for HSV-1.
- Recurrence rates decline over time in most individuals, although this pattern is variable

ii. **Non-primary infection:**

- First noted symptoms with either HSV-1 or HSV-2 in an individual with pre-existing antibodies to the other type.
- Symptoms and signs are less severe as compared to the primary infection.
- Lesions usually heal within 1-2 weeks.

2. Recurrent episode

- Recurrence of clinical symptoms due to reactivation of pre-existent HSV-1 or HSV-2 infection after a period of latency. Recurrences are more common in the first year with HSV-2.
- Symptoms are milder than primary infection

- Certain factors may precipitate an attack such as trauma, menstruation, concurrent infection or fever, immune suppression, stress and UV light.
- Lesions usually heal within 1-2 weeks.

3. Asymptomatic herpes/viral shedding

- 80% of patients have no symptoms following infection.
- Shedding of the virus may occur from intact epithelial surfaces in the absence of symptoms.
- Responsible for transmission of HSV in a majority of cases (70%).
- Occurs most commonly in
  - Patients with genital HSV-2 infection
  - In the first year after the first episode of genital infection
  - In individuals with frequent symptomatic recurrences

Transmission risk

- Risk is greatest during lesional recurrences or prodrome, and patients should be advised to abstain from sexual contact during this time.
- However, subclinical viral shedding can occur in the absence of lesions.
- Thus, consistent condom is important to prevent transmission to both males and females.

Clinical presentation

Symptoms

- The patient may be asymptomatic and the disease unrecognised.
- Local symptoms consist of painful ulceration, dysuria, and vaginal or urethral discharge.
- Systemic symptoms consist of fever and myalgia. They are much more common in primary than in non-primary or recurrent disease. Rarely, these may be the only evidence of infection.

Signs

- Blistering and ulceration of the external genitalia or perianal region (+/-cervix/ rectum).
- Tender inguinal lymphadenitis.
- In first episodes, lesions and lymphadenitis are usually bilateral.
- In recurrent disease, lesions are usually unilateral for each episode and limited to the infected dermatome.
- Excoriation marks, folliculitis, fissure or erythema over the genital region in atypical herpes genitalis

Complications

- Superinfection of lesions with candida and streptococcal species (typically occurs in the second week of lesion progression).
- Autonomic neuropathy, resulting in urinary retention.
- Aseptic meningitis.

Diagnosis

Diagnosis is mainly based on clinical presentation. However, laboratory investigations may be needed to confirm atypical presentation or to rule out other differential diagnosis.

Investigations

1.HSV nucleic acid by NAAT

- Sample: vesicular fluid of exudate from vesicles or swab from mucocutaneous genital lesions
- Useful for all stages but not widely available
- Detects type specific DNA sequence within glycoprotein G gene
- Increases HSV detection rates in muco-cutaneous swabs by 11–71% compared to viral culture
- Sensitivity and specificity >90%

2. Viral culture

- Traditionally is the gold standard for diagnosing HSV infection (early & atypical)
- Low sensitivity
- Specificity is virtually 100% (if typing is performed)

3. Type specific serologic test

- A type-specific immune response can take 8-12 weeks to develop following primary infection
- Detects HSV-specific EIAs based on glycoprotein G
- Has a sensitivity of 80-98% and a specificity of 96% or more
- Caution is needed in interpreting results because even highly sensitive and specific assays have poor predictive values for low prevalence populations
- HSV type-specific serology test is not routinely recommended in asymptomatic patients.

4. Tzanck Smear

- Specimen obtained from base of ulcer, not vesicle fluid
- Look for multinucleated giant cells
- Insensitive, nonspecific and should not be relied on for diagnosis of HSV infection

Management

1. First-episode genital herpes

Indications for therapy

First episodes of genital herpes are frequently associated with a prolonged disease course. Untreated, many patients suffer general and local complications. Therapy should be instigated at the earliest opportunity and on clinical suspicion alone.

Antivirals

- Patients presenting within five days of the start of the episode, or while new lesions are still forming, should be given oral antiviral drugs.
- Acyclovir and valacyclovir are all effective in reducing the severity and duration of the episode.
- No therapy alters the natural course of genital herpes infection.
- Topical agents are not recommended as they are less effective than oral agents and easily generate resistance.
- Recommended regimens (refer table below)

Supportive measures

- Saline/diluted potassium permanganate Sitz bath/dabs
- Appropriate analgesia
- Topical Lignocaine/lidocaine (gel or ointment)
- Treatment of secondary infection
- In women with severe dysuria, urination with the genitals submerged in water along with spreading the labia can alleviate symptoms

Management of complications

- Hospitalization may be required for urinary retention, meningism and severe constitutional symptoms
- If catheterization is required, the suprapubic route may be considered
  - To prevent the theoretical risk of ascending infection
  - To reduce the pain associated with the procedure
  - To allow normal micturition to be restored without multiple removals and re-catheterizations

2. Recurrent genital herpes

- Recurrences are self-limiting and generally cause minor symptoms
- Management decisions should be made in partnership with the patient according to the severity of symptoms and the frequency of recurrence
- Strategies include
  - Supportive therapy only (as mentioned above)
  - Episodic antiviral treatment
  - Suppressive antiviral therapy

Episodic antiviral treatment

- Indication: for patients with severe and/or prominent prodromal symptoms
- Patient-initiated treatment which is started within 24 hours of symptoms is most effective and has been shown to abort lesions in up to one-third of patients
- Oral acyclovir and valacyclovir are effective at reducing the duration and severity of recurrent attacks by a median of 1-2 days
- Regime for short course therapies and alternative longer five-day courses (refer table below)
- Head-to-head studies found no advantage of any particular antiviral or duration of treatment

Suppressive Antiviral Therapy

- Suppressive therapy is indicated in patients with recurrent episodes of ≥6 per year
- It reduces the number of recurrences by 70-80% with improvement in QoL but it does not eliminate subclinical viral shedding
- More recent studies in patients with milder disease indicate that they will still benefit from a reduced rate of recurrence with suppressive treatment.
- Experience with suppressive antiviral therapy is most extensive with acyclovir. Safety and resistance data on patients on long-term intermittent therapy with acyclovir now extend to over 20 years of continuous surveillance and 6 years for long term continuous therapy.
- Treatment regime: refer table below
- Full suppressive effect is usually achieved 5 days into treatment.

3. Severe disease/complication that needs hospitalization (disseminated infection, pneumonitis, hepatitis or CNS complication e.g., meningitis or encephalitis)

Refer table below for treatment.

Information for patients

The following information should be discussed when counselling patients with genital herpes:

- The course of infection, including subclinical shedding
- Treatment options
- The risk of transmission and interventions (consistent condom use)
- The risk of transmission to the infant at birth (for pregnant patients)
- Partner notification
- Transmissions can occur from an asymptomatic partner some years before the current relationship

Management of genital herpes in pregnancy

Foetal transmission risk

- Factors associated with transmission include type of maternal infection (primary or recurrent), presence of transplacental maternal neutralising antibodies, duration of rupture of membranes before delivery, use of foetal scalp electrodes and mode of delivery.
- The risks are greatest when a woman acquires a new infection (primary genital herpes) in the third trimester, particularly within 6 weeks of delivery, as viral shedding may persist and the baby is likely to be born before the development of protective maternal antibodies.
- Rarely, congenital herpes may occur as a result of transplacental intrauterine infection.

Management of pregnant women with first episode of genital herpes

1. First or second trimester acquisition (until 27^{+6} weeks of gestation)

- Management of the woman should be in line with her clinical condition and will usually involve the use of oral (or intravenous for disseminated HSV) Acyclovir in standard doses (400mg three times daily, for 7-10 days).
- Acyclovir use is associated with a reduction in the duration and severity of symptoms and a decrease in the duration of viral shedding.
- Acyclovir is not licensed for use in pregnancy but is considered safe and has not been associated with an increased incidence of birth defects.
- Paracetamol and topical lidocaine 2% gel can be offered as symptomatic relief.
- The obstetrician should be informed.
- Providing that delivery does not ensue within the next 6 weeks, the pregnancy should be managed expectantly and vaginal delivery anticipated.

2. Third trimester acquisition (from 28 weeks of gestation)

- Treatment should not be delayed.
- Management of the woman should be in line with her clinical condition and will usually involve the use of oral (or intravenous for disseminated HSV) Acyclovir in standard doses (400mg three times daily), until delivery.
- Caesarean section should be the recommended mode of delivery for all women developing first episode genital herpes in the third trimester, particularly those developing symptoms within 6 weeks of expected delivery, as the risk of neonatal transmission of HSV is very high at 41%.
- It can be difficult to distinguish clinically between primary and recurrent genital HSV infections, as in up to 15% of cases where a woman presents with a first episode of clinical HSV infection, will actually be a recurrent infection.
  Thus, the plan of delivery should be based on the assumption that all first episode lesions are primary genital herpes.

Management of pregnant women with recurrent genital herpes

- Women with recurrent genital herpes should be informed that the risk of neonatal herpes is low, even if lesions are present at the time of delivery (0-3% for vaginal delivery).
- The majority of recurrent episodes of genital herpes are short-lasting and resolve within 7-10 days without antiviral treatment. Supportive treatment measures using saline bathing and analgesia with standard doses of paracetamol alone will usually suffice.
- Vaginal delivery should be anticipated in the absence of other obstetric indications for caesarean section.
- Daily suppressive Acyclovir 400mg three times daily can be considered from 36 weeks of gestation as it reduces viral shedding and recurrences at delivery, thus reducing the need for caesarean section.

Management of women with primary or recurrent genital lesions at the onset of labour

- Management of a woman with genital herpes at the onset of labour will be based on clinical assessment as there will not be time for confirmatory laboratory testing.
- A viral swab from the lesion(s) should nonetheless be taken, since the result may influence the management of the neonate.
- The neonatologist should be informed.

i. Primary episode

- Caesarean section should be recommended to all women presenting with primary episode genital herpes lesions at the time of delivery, or within 6 weeks of the expected date of delivery, to reduce exposure of the foetus to HSV which may be present in maternal genital secretions.
- If the baby is delivered vaginally, the risk of neonatal herpes is estimated to be 41%.

ii. Recurrent genital herpes

- Women presenting with recurrent genital herpes lesions at the onset of labour should be advised that the risk to the baby of neonatal herpes is low (0–3% for vaginal delivery). Vaginal delivery should be offered.

Management of the neonate

i. Management of babies born by caesarean section in mothers with primary HSV infection in the third trimester

These babies are at low risk of vertically transmitted HSV infection so conservative management is recommended

- Liaise with the neonatal team
- Swabs from the neonate are not indicated

- No active treatment is required for the baby
- Normal postnatal care of the baby is advised with a neonatal examination at 24 hours of life, after which the baby can be discharged from the hospital if well and feeding is established.
- Parents should be educated regarding good hand hygiene and due care to reduce the risk of postnatal infection. They should be advised to look for: skin, eye and mucous membrane lesions, lethargy/irritability, and poor feeding.

ii. Management of babies born by vaginal delivery in mothers with a primary HSV infection within the previous 6 weeks

If the baby is well:

- Swabs of the skin, conjunctiva, oropharynx and rectum should be sent for herpes simplex PCR.
- A lumbar puncture is not necessary.
- Empirical treatment with intravenous Acyclovir (20mg/kg every 8 hours) should be initiated until evidence of active infection is ruled out.
- Strict infection control measures should be put in place for both mother and baby
- Breastfeeding is recommended unless the mother has herpetic lesions around the nipples. Parents should be warned to report any early signs of infection such as poor feeding, lethargy, fever or any suspicious lesions.

If the baby is unwell or presents with skin lesions:

- Swabs of the skin, lesions, conjunctiva, oropharynx and rectum should be sent for herpes simplex PCR.
- A lumbar puncture should be performed even if CNS features are not present.
- Intravenous Acyclovir (20mg/kg every 8 hours) should be initiated until evidence of active infection is ruled out.

iii. Management of babies born to mothers with recurrent HSV infection in pregnancy with or without active lesions at delivery

- In the case of recurrent genital herpes infections in the mother, maternal IgG will be protective in the baby and hence the infection risk is low
- Conservative management of the neonate is advised
- Surface swabs from the neonate are not indicated
- No active treatment is advised for the baby
- Parents should be educated regarding good hand hygiene to reduce the risk of postnatal infection.
- Parents should be advised to look for: skin, eye and mucous membrane lesions, lethargy/irritability and poor feeding.

Treatment

Type of infection	Preferred	Alternative
First episode	Acyclovir 400mg PO q8h for 7-10 days	Valacyclovir** 1g PO q12h for 7-10 days
Recurrent episode	*Short course:* Acyclovir 800mg PO q8h for 2 days *5-day course:* Acyclovir 800mg PO q12h for 5 days	*Short course:* Valacyclovir** 500mg PO q12h for 3 days *5-day course:* Valacyclovir** 1g PO q24h for 5 days
Suppressive therapy *(if ≥ 6 recurrences/year, severe, prolonged or with psychosocial problems)*	Acyclovir 400mg PO q12h for up to 1 year, then reassess *In break-through recurrences*: increase to Acyclovir 400mg PO q8h	Valacyclovir** 500mg PO q24h for up to 1 year, then reassess *If ≥ 10 recurrences/year:* Valacyclovir** 1g PO q24h for up to 1 year, then reassess
Severe disease (needing hospitalization)	Acyclovir 5-10mg/kg/dose IV q8h for 10-14 days	
First episode (in pregnancy)	Acyclovir 400mg PO q8h for 7-10 days For 3rd trimester acquisition: Continue treatment till delivery	Valacyclovir** 500mg PO q12h for 7-10 days
Recurrent episode (in pregnancy)	Acyclovir 400mg PO q8h Treatment recommended starting at 36 weeks gestation	Valacyclovir** 500mg PO q12h Treatment recommended starting at 36 weeks gestation
Neonatal herpes	Acyclovir 20mg/kg/dose IV q8h Duration of treatment:	

Type of infection	Preferred	Alternative
	Skin and mucous membranes: 14 days Disseminated/CNS: 21 days	
*Note: ** Not listed in MOH Drug formulary*		

References

1. Management of Genital Herpes in Pregnancy. RCOG/ BASH 2014
2. Suppression of Recurrent Genital Herpes Among Pregnant Women CDC 2021 STI Tx Quick Guide
3. CDC Sexually Transmitted Infections Treatment Guidelines, 2021
4. 2017 European guidelines for the management of genital herpes

4.12 GENITAL WARTS

Aetiology

Genital warts are caused by Human papilloma virus (HPV). HPV is a group of nonenveloped, dsDNA viruses belonging to the family *Papovaviridae.* Approximately 150 types of HPV have been identified and at least 40 of which infect the genital area.

- High risk (Oncogenic) HPV
  - e.g., HPV type 16, 18, 31, 33, 45, 52, 58
  - causes majority of cervical, penile, vulvar, vaginal and oropharyngeal cancer and precancer.
- Low risk HPV infection
  - e.g., HPV 6, 11
  - causes genital warts and recurrent respiratory papillomatosis.

Transmission Risk

- A highly contagious virus –more than 75% of sexual partners develop warts when exposed
- Sexually active persons are usually exposed to HPV during their lifetime
- Can persist undetected for the duration of an individual's lifetime
- The risk of acquiring HPV increases with the number of sexual partners.
- Transmission of genital HPV infection
  - penetrative and non-penetrative sexual activity (vaginal, anal, and oral; same and opposite sex)
  - Perinatal – rarely HPV type 6 & 11 can cause respiratory papillomatosis (route whether transplacental, perinatal or postnatal is not completely understood)
- Digital lesions - usually in children
- Fomites - no good evidence

Clinical presentation

- Mostly asymptomatic
- Lump/s
- Itching, burning, bleeding
- Disfigurement
- Psychological distress

Clinical types of genital HPV infection

i. Condylomata acuminata
ii. Flat topped papules/plaques
iii. Verruca vulgaris type or keratotic warts
iv. "Giant condyloma" (Buschke – Lowenstein)
v. Laryngeal papilloma

Common anatomic site

- Vaginal introitus, foreskin of the uncircumcised penis, shaft of the circumcised penis
- Multiple sites in the anogenital epithelium or within the anogenital tract (e.g., cervix, vagina, urethra, perineum, perianal skin, anus, or scrotum)
- Intraanal warts more common with receptive anal intercourse
- Extragenital lesions may be seen on oral cavity, larynx, conjunctivae, and nasal cavity

Investigations

- Usually made by visual inspection
- Cervical cytology
- Biopsy indicated for
  - atypical lesion
  - diagnostic uncertainties
  - lesions not responding to standard therapy
  - ruling out malignancy
  - all suspected cervical lesion

HPV testing is not recommended for anogenital warts because test results are not confirmatory and do not guide genital wart management

Management

- Treatment choice depends on the number, size, site, morphology, patient preference, cost, convenience, adverse effects, pregnancy, and provider experience
- Information on management of treatment and side effects is recommended
- Does not eradicate HPV infectivity or reduce the risk of genital cancer

Type of infection	Patient-applied	Provider-administered
External anogenital warts (i.e., penis, groin, scrotum, vulva, perineum, external anus or perianal)	Imiquimod 5% cream† 3 times/week at bed-time for <16 weeks *OR* Imiquimod 3.75% cream†** q24h at bedtime for <8 weeks *OR* Podofilox 0.5% solution or gel†** q12h for 3 days, followed by 4 days of no therapy. Cycle may be repeated as necessary, up to 4 cycles. *OR* Sinecatechins 15% ointment†**	Cryotherapy with liquid nitrogen or cryoprobe OR Surgical removal (Tangential scissor excision, tangential shave excision, curettage, laser, or electrosurgery) OR Trichloroacetic acid (TCA) 40-100%** weekly or bichloroacetic acid (BCA) 80%–90%** solution

Type of infection	Patient-applied	Provider-administered
Urethral Meatus Warts	-	Cryotherapy with liquid nitrogen OR Surgical removal
Vaginal warts Cervical warts Intra-anal warts	-	Cryotherapy with liquid nitrogen OR Surgical removal OR Trichloroacetic acid (TCA) 40-100%** weekly or bichloroacetic acid (BCA) 80%–90%** solution
Note: *†Might weaken condoms and vaginal diaphragms.* *** Not listed in MOH Drug formulary* *The use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation.* *Management of cervical warts should include consultation with a specialist. For women who have exophytic cervical warts, a biopsy evaluation to exclude HSIL should be performed before treatment is initiated.* *Management of intra-anal warts should include consultation with a colorectal specialist.*		

Follow-Up

- Anogenital warts typically respond within 3 months of therapy.
- Factors that might affect response to therapy include immunosuppression and treatment compliance.

Contact Tracing

- Current sexual partner may benefit from a physical examination to detect genital warts and tests for other STIs
- Persons should inform current partners about having genital warts because the types of HPV that cause warts can be passed on to partners.
- Tracing of previous sexual partner is not recommended

Pregnancy

- Podofilox, podophyllin, and sine catechins should not be used during pregnancy.
- Imiquimod should be avoided until more data are available.
- Anogenital warts can proliferate and become friable during pregnancy.

- Resolution of genital warts might be incomplete or poor until pregnancy is complete.
- Rarely, HPV types 6 and 11 can cause respiratory papillomatosis among infants and children, although the route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood.
- Whether caesarean delivery prevents respiratory papillomatosis among infants and children is unclear. Therefore, caesarean delivery should not be performed solely to prevent transmission of HPV infection to the newborn.
- Caesarean delivery is indicated for women with anogenital warts if the pelvic outlet is obstructed or if vaginal delivery would result in excessive bleeding.
- Pregnant women with anogenital warts should be counseled about the low risk for warts on the larynx of their infants or children (recurrent respiratory papillomatosis).

Prevention

- Condoms used consistently and correctly can lower the chances of acquiring and transmitting HPV and developing HPV-related diseases (e.g., genital warts or cervical cancer).
- Vaccine is available for males and females. It can be administered regardless of history anogenital warts, abnormal pap smear test or HPV test, or anogenital precancerous lesions.
- Routine (every 3 years) pap smear screening is recommended for women with anogenital warts and those who have received HPV vaccine
- Abstaining from sexual activity is the most reliable method

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1. Workowski KA, Bolan G.A Centers for Disease Control and Prevention. Sexually Transmitted Disease Treatment Guidelines MMWR /July 23,2021/vol 70/ No 4.
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4.13 CHANCROID

Aetiology

Haemophilus ducreyi

Incubation Period

3 to 10 days

Clinical Presentation

Divided into those at the site of primary inoculation and at the regional lymph nodes

1. At the site of primary inoculation

Initial lesions consist of erythematous papules which quickly progress into pustules that rupture after a few days and develop into superficial ulcers.

In males, ulcers are found on the prepuce near the frenulum or in the coronal sulcus. In females, ulcers are found at vulva, cervix, perianal areas and the entrance to the vagina, particularly the fourchette.

The ulcers are classically described as:

- Multiple, painful
- Not indurated ("soft sore")
- With a necrotic base and purulent exudate
- Bordered by ragged undermined edges
- Bleeds easily on contact
- Autoinoculation from primary lesions on opposing skin may result in so-called "kissing ulcers"

2. At the regional lymph nodes

Painful unilateral inguinal adenitis is a characteristic feature (50%), leading to the formation of buboes (purulent abscess of the inguinal lymph nodes). Buboes are fluctuant and may rupture, releasing thick pus, and may result in extensive ulceration. A probable diagnosis of chancroid can be made if all the following criteria are met:

- The patient has one or more painful genital ulcers
- The patient has no evidence of *T.pallidum* infection or by serologic testing for syphilis performed at least 7-14 days after the onset of ulcers
- The clinical presentation, the appearance of genital ulcers, and if present, the presence of regional lymphadenopathy is typical for chancroid
- Test results for herpes simplex virus (HSV-1 or HSV-2 PCR) performed on the ulcer exudate or fluid are negative

Investigations

1. Gram stain of scrapings from the ulcer base or pus aspirated from the bubo

Gram negative coccobacilli, with characteristic appearance ("school of fish").

2. Culture

- Genital specimens for *H.ducreyi* should be collected from the base and the (undermined margins of the chancroid lesion after cleansing the area by flushing with sterile physiological saline).
- Collect the material from the ulcer with calcium alginate, Dacron or sterile cotton swabs.
- *H. ducreyi* will only survive a few hours on the swab and direct plating on selective media is preferable as it results in the highest chance of positive culture.
- If bedside plating is not possible, the swab should be sent within 4 hours to the laboratory using Amies transport media**.**

3. PCR (>95% sensitivity)

Using multiplex PCR detecting *H. ducreyi, T. pallidum,* and *Herpes Simplex Virus* direct from genital ulcer specimen

4. Screening for other possible causes of genital ulcers:

Testing for syphilis and herpes simplex virus should always be done because the three diseases may be clinically difficult to distinguish from each other and because co-infections occur. Other causes of genital ulcers include:

- Treponema pallidum
- Genital herpes
- Lymphogranuloma venereum (LGV)
- Granuloma inguinale (Donovanosis)
- HIV
- Neoplasia

Management

i. Pharmacological treatment

Preferred	**Alternative**
Azithromycin 1g PO STAT	Ceftriaxone 250mg IM STAT OR Ciprofloxacin 500mg PO q12h for 3 days OR Erythromycin ethylsuccinate 800mg PO q8h for 7 days

Preferred	Alternative
Note: In pregnancy/breasfeeding, to use azithromycin, ceftriaxone or erythromycin.	

ii. Surgical treatment

Management of fluctuant buboes

- Needle-aspirate fluctuant buboes from adjacent healthy skin is simpler and safer than incision
- Incision and drainage might be preferred because of reduced need for subsequent drainage procedures, but is more prone to sinus formation
- Aspirate from top of bubo not from the base

iii. Epidemiological treatment

Sexual contacts within 10 days before onset of the patient's symptoms should be examined and treated even in the absence of symptoms

iv. Advice

- Patients should be advised to avoid unprotected sexual intercourse until they and their partner(s) have completed treatment and follow-up
- Symptoms should resolve within one to two weeks of commencing antibiotic therapy
- Regardless of whether disease symptoms are present, sex partners of patients with chancroid should be examined and treated if they had sexual contact with the patient during the 10 days preceding the patient's symptom onset

v. Follow–up

- Patients should be re-examined 3-7 days after initiation of therapy
- If treatment is successful, ulcers improve symptomatically within 3 days and substantial re-epithelization occurs within 7 days after onset of therapy
- The time required for complete healing is related to the size of the ulcer; large ulcers may require more than 2 weeks
- Healing can be slower for uncircumcised men who have ulcers under the foreskin

Treatment failure:

- Investigate for possible co-infections with *T. pallidum* or HSV
- Determine possible resistance by isolation of *H.ducreyi* and susceptibility testing.
- Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and may require frequent needle aspiration (or drainage).
- Men who are uncircumcised and persons with HIV infection do not respond as well to treatment.

Complications (mostly in men)

- Phimosis
- Scarring
- Rectal or urogenital fistulas from suppurative buboes

References:

1. Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, Reno H, Zenilman JM, Bolan GA. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021 Jul 23;70(4):1-187
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4.14 LYMPHOGRANULOMA VENEREUM

Aetiology

- It is caused by *C. trachomatis* serovars L1-L3
- The L2b serovar has been responsible for the lesions in the MSM communities
- Most have associated HIV infection
- In contrast to serovars A-K, which remain confined to the mucosa, serovar L strains are invasive and can disseminate via underlying connective tissue and spread to regional lymph nodes

Incubation period

3 to 30 days

Clinical presentation

1. Primary stage:

- A small painless papule or pustule that erode to form a small herpetiform ulcer that heals within a week (may go undetected)
- Urethral, vaginal, cervical or rectal mucopurulent discharge is occasionally seen (depending on the inoculation site)
- Proctitis (symptoms: rectal pain, anorectal bleeding, mucoid and/or hemopurulent rectal discharge, tenesmus, constipation)

Proctitis in MSM

- Proctitis is the main presenting symptoms of infection in the LGV epidemic among MSM
- Haemopurulent discharge, severe anorectal pain, tenesmus, rectal bleeding and constipation are common presenting features
- Anoscopic examination: shows haemorrhagic proctitis, purulent oedema and distal granular proctitis, mucosal ulceration and tumourous mass
- Not accompanied by inguino-femoral lymphadenopathy
- 25% are asymptomatic
- Genital infections among MSM are rare; the ratio of genital vs. anorectal LGV infections is 1 in 15
- Proctitis can mimic chronic inflammatory bowel diseases like Crohn's disease, both clinically and in the histopathological features

2. Secondary stage:

- Inguinal stage happens 2-6 weeks after onset of primary lesion
- Painful inguino-femoral lymphadenopathy.
- Typically presents with unilateral enlargement, inflammation, suppuration, and abscess known as "buboes", rupturing in a third of cases.

- The typical ‘groove sign’ [enlargement of the inguinal nodes above, and the femoral nodes below the inguinal ligament (Poupart’s ligament)] is seen in 15-20% of cases.
- Intra-abdominal or retroperitoneal lymphadenopathy may occur causing low back pain and/or abdominal pain.
- Fever, chills, malaise, arthritis, pneumonitis, perihepatitis or abnormal hepatic enzymes (systemic spread)

3. Tertiary stage:

- Often called ‘anogenitorectal syndrome’, present mostly in women
- Chronic proctocolitis is followed by peri-rectal abscesses, fistulas, strictures and stenosis of the rectum, possibly leading to ‘lymphorrhoids’ (haemorrhoid-like swellings of obstructed rectal lymphatic tissue)
- Chronic progressive lymphangitis leads to chronic oedema and sclerosing fibrosis. Complications include lymphoedema of the genitalia (elephantiasis, “saxophone penis”), esthiomene (chronic ulcerative disease of vulva leading to disfiguring fibrosis and scarring) and frozen pelvis syndrome

Investigations

Diagnosis is based on clinical suspicion, epidemiological information, and the exclusion of other aetiologies of genital or rectal ulcers, inguinal lymphadenopathy, or proctocolitis. Special attention should be given to MSM’s and HIV patients.

Molecular test

Detection of *Chlamydia trachomatis* by NAAT using genital or extragenital specimens should be sent for LGV-specific strain *Chlamydia trachomatis* for confirmation

Management

i. Pharmacological treatment

Preferred	**Alternative**
Doxycycline 100mg PO q12h for 21 days	Azithromycin 1g PO weekly for 3 weeks OR Erythromycin ethylsuccinate 800mg PO q6h for 21 days
Note: *Doxycycline is contraindicated in pregnancy.* *Complete treatment of patients with LGV includes appropriate antimicrobial coverage and drainage of infected buboes.* *Longer courses of therapy might be required in the setting of fistulas, buboes, and other forms of severe disease.* *If an alternative treatment regimen is given or pregnant, consider TOC 4 weeks after completion of treatment.*	

ii. Surgical treatment

- Needle aspiration of fluctuant buboes through healthy overlying skin may be required for pain relief and prevention of ulcer formation. Repeat visits may be required.
- Surgical incision of buboes is not recommended due to potential complications such as chronic sinus formation.
- Some of the late complications of the third stage of LGV may require surgical repair.

iii. Epidemiological treatment

Sex partner/s that have had contact with the patient within the past 60 days should be evaluated and treated if symptomatic. If no symptoms are present, they should be treated for exposure as empirically as follows:

- Doxycycline 100 mg PO b.d for 7 days

iv. Follow–up

- Patients should be followed up until their signs and symptoms have resolved (within 3-6 weeks)
- In anorectal disease, symptoms should resolve within 1-2 weeks of commencing antibiotic therapy
- In inguinal disease, symptoms might persist for many weeks and follow-up visits should be implemented
- Patients should abstain from any sexual contact until they have completed therapy

All persons who have been treated for LGV should be retested for chlamydia approximately 3 months after treatment. If retesting at 3 months is not possible, providers should retest at the patient's next visit for medical care within a 12-month period after initial treatment.

Complications

- Soiling
- Pain
- Constipation
- Mega colon
- Sexually acquired reactive arthritis
- Aseptic cardiac involvement
- Meningitis
- Ocular inflammatory disease
- Pneumonitis
- (Peri) hepatitis

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1. Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, Reno H, Zenilman JM, Bolan GA. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021 Jul 23;70(4):1-187
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4.15 GRANULOMA INGUINALE (DONOVANOSIS)

Aetiology

*Klebsiella granulomatis (*formerly known as *Calymmatobacterium granulomatis*)

Epidemiology

Sporadic cases have been described in India, South Africa and South America. Although granuloma inguinale was previously endemic in Australia, it is now extremely rare.

Incubation period

2-4 weeks (up to 50 days) - controversial and not well established

Clinical presentation

Present initially as a single or multiple painless, slowly progressive nodules or papules on the genitals or perineum which later ulcerates. The usual sites of infection in men are the prepuce, coronal sulcus, frenulum and glans penis and in women, the labia minora and fourchette.

Four types of donovanosis are classically described:

- Granulomatous ulcer: non-tender, fleshy, exuberant, single or multiple, beefy red ulcers that bleed readily when touched
- Hypertrophic or verrucous ulcer: ulcer or growth with a raised irregular edge, sometimes with a walnut appearance
- Necrotic ulcer: deep foul-smelling ulcer causing tissue destruction
- Sclerotic: extensive fibrous and scar tissue

Usually there is no lymphadenopathy. Genitals are affected in 90% of cases and the inguinal area in 10%. It may form pseudo buboes (subcutaneous granulomas) in the inguinal area.

Extragenital infection can occur with infection extension to the pelvis, or it can disseminate to intra-abdominal organs, bones, or the mouth.

Investigations:

- **Tissue biopsy for HPE**
  Donovan bodies showing chronic inflammation with infiltration of plasma cells and polymorphonuclear leucocytes using Wright or Giemsa stain.

- **Molecular test**
  Confirmed detection of *Klebsiella granulomatis* DNA

Management

i. Pharmacological treatment

Preferred	Alternative
Azithromycin 1g PO weekly or 500mg q24h Duration of treatment: at least 3 weeks or until all lesions have completely healed	Doxycycline 100mg PO q12h OR Trimethoprim/sulfamethoxazole 160/800mg PO q12h OR Erythromycin ethylsuccinate 800mg PO q6h Duration of treatment: at least 3 weeks or until all lesions have completely healed
Note: *Doxycycline is contraindicated in pregnancy*	

The addition of another antibiotic as an adjunct treatment can be considered if the above regimens do not give a satisfactory response after a few days.

Treatment of pregnant or lactating mothers and children

- Macrolide regimen (erythromycin or azithromycin) is recommended for pregnant and lactating women.
- Children can be treated with azithromycin 20mg/kg once daily.
- Infants born to mothers with untreated genital lesions are at risk of infection and a course of prophylactic antibiotics should be considered, the recommended regimen is azithromycin 20mg/kg once daily for 3 days.

Contact tracing

Sexual partners within the 60 days before onset of the patient's symptoms must be screened and offered therapy.

Follow-up

Weekly until ulcers have healed. After treatment and complete healing of the lesions, the patient must be followed up for at least one year, every two or three months. Relapse can occur 6-18 months after apparently effective therapy.

Complications

- Haemorrhage
- Genital lymphoedema or elephantiasis
- Genital mutilation and cicatrisation
- Squamous cell carcinoma
- Scar adhesion of the scrotum to the penis
- Destruction of the penis body
- Stenosis of the urethral, vaginal and anal orifices

References

1. Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, Reno H, Zenilman JM, Bolan GA. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021 Jul 23;70(4):1-187
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APPENDIX 1

Table: Sensitivity and Specificity of laboratory tests for Syphilis as appendix

APPENDIX 2

DISEASE NOTIFICATION

Reporting or notifying of infectious diseases is mandated by the Prevention and Control of Infectious Disease Act 342, 1988. Currently, 31 infectious disease conditions are required to be notified by law including the four STIs; chancroid, gonorrhoea, HIV and syphilis. All private and public health facilities must notify these STI cases by telephone/fax/e-notification to the nearest district health office. Failure to notify is liable to be compounded under the above act. Any delay in notification will increase the risk of transmission. Notified cases will be followed up by the health authorities for verification and preventive measures. The district health authorities are responsible for determining that the cases meet the surveillance case definitions before they register the cases (Reference from Case Definitions for Infectious Diseases in Malaysia; Ministry of Health Malaysia, 2017).

CHANCROID (ICD 10: A51) Pg.14

- **Case Definition**

  Clinical case definition:
  A sexually transmitted disease characterized by one or more painful genital ulcers with/without regional lymphadenopathy.

- **Laboratory criteria for diagnosis:**

  Isolation of *Haemophilus ducreyi*, a fastidious gram-negative coccobacillus bacteria.

- **Case Classification:**

  (i) Confirmed:
  A clinically compatible case that is laboratory confirmed by the isolation of *H. ducreyi.*

  OR

  (ii) Probable/Suspected:
  Clinical compatible case with the exclusion presence of
  - Primary syphilis by dark-field examination of exudates or by serological test for syphilis performed at least 7 days after onset of ulcer.
  - Herpes genitalis (painful grouped erosions/ vesicles).

- **Types of Surveillance:**

  Mandatory National Notification of Infectious Diseases under the Infectious Disease Prevention and Control Act 342, 1988.

- **When to notify:**
  All confirmed case is mandatory to be notified to the nearest District Health Office within a week (7 days) of diagnosis.

- **How to notify:**
  Notification should be done via an e-notification system or through submission of the notification form to the nearest District Health Office.

GONOCOCCAL INFECTIONS (ICD 10: A 54.9) Pg. 29

- **Case Definition**

  Clinical case definition:
  A sexually transmitted infection commonly manifested by urethritis, cervicitis, or salphingitis. Infection may be asymptomatic.

- **Laboratory criteria for diagnosis:**

  - Isolation of Neisseria gonorrhoeae, also known as gonococcus or
  - Observation of Gram-negative diplococci bacteria in gram stain from a clinical specimen obtained by urethral swabs in males or from the endocervical area in females.

- **Case Classification:**

  Confirmed:
  A case that is laboratory confirmed.

- **Types of Surveillance:**

  Mandatory National Notification of Infectious Diseases under the Infectious Disease Prevention and Control Act 342, 1988.

- **When to notify:**

  Only confirmed cases are mandatory to be notified to the nearest District Health Office within a week (7 days) of diagnosis.

- **How to notify:**

  Notification should be done via an e-notification system or by phone to the nearest District Health Office. It is then followed by submission of the notification form.

- **References Laboratory:**

  National Public Health Laboratories (NPHL) conduct sentinel surveillance for gonococcal antimicrobial drug resistance.

HIV INFECTION (ICD 10: B24) Pg. 37

- **Case Definition:**

1. In adults, adolescents or children aged ≥ 18 months, a reportable case of HIV infection must meet at least one of the following criteria:

a. Laboratory criteria

Detection of antibody to HIV virus

Reactive result on a screening test for HIV antibody (rapid or laboratory-based enzyme immunoassay), and followed by a positive result on a confirmatory test for HIV antibody (rapid or laboratory-based enzyme immunoassay) relying on different antigens or different operating characteristics.

Detection of HIV virus (viral antigen)

Positive result or report of detectable quantity on any of the following HIV virology (non-antibody) tests:
• HIV nucleic acid (DNA or RNA) detection.
• HIV p24 antigen test including neutralization assay,
• HIV isolation (viral culture)

b. Clinical or other criteria (if the above laboratory criteria are not met)

Conditions that meet the criteria included in the case definition for AIDS.

2. In a child aged < 18 months, a reportable case of HIV infection must meet at least one of the following criteria:

a. Laboratory criteria

Definitive

Positive result or report of detectable quantity on any of the following HIV virology (non-antibody) tests:
• HIV nucleic acid (DNA or RNA) detection
• HIV p24 antigen test including neutralization assay
• HIV isolation (viral culture)
confirmed by a second virological test obtained from a separate determination taken more than six weeks after birth.

OR

Presumptive

A child who does not meet the criteria for definitive HIV infection but who has a positive result on only one specimen (excluding cord blood) using the above HIV virology (non-antibody) tests.

- **Case Classification:**

  Not applicable.

- **Types of Surveillance:**

  Mandatory National Notification of Infectious Diseases under the Infectious Disease Prevention and Control Act 342, 1988.

- **When to notify:**

  Only confirmed cases should be notified are mandatory to be notified to the nearest District Health Office within a week (7 days) of diagnosis.

- **How to notify:**

  Notification should be done via an e-notification system or by phone to the nearest District Health Office. It is then followed by submission of the notification form.

SYPHILIS (ICD 10: A51.0, A51.4, A53.0, A52.3, A50.9) Pg. 76

- **Case Definition**

1. Acquired

a. Primary Syphilis (ICD 10: A51.0)

- **Clinical case definition:**

  Characteristic lesion is the chancre (solitary, painless indurated ulcer), but atypical primary lesions may occur

- **Laboratory criteria for diagnosis:**

  - Demonstration of T. pallidum in clinical specimens by dark field microscopy or
  - Serology.

b. Secondary Syphilis (ICD 10: A51.4)

- **Clinical case definition:**

  The clinical manifestations of secondary syphilis result from hematogenous dissemination of the infection and are protean: condyloma lata (papulosquamous eruption), hands and feet lesions, macular rash, diffuse lymphadenopathy, headache, myalgia, arthralgia, pharyngitis, hepatosplenomegaly, alopecia, and malaise. The primary chancre may still be present.

- **Laboratory criteria for diagnosis:**

- Demonstration of T. pallidum in clinical specimens by dark field microscopy or
- Serology.

c. Latent Syphilis (ICD 10: A53.0)

- **Clinical case definition:**

  A stage of asymptomatic infection due to T. pallidum. Latent syphilis is subdivided into early latent syphilis when duration of infection is less than 24 months and late latent syphilis after 24 months from the initial infection.

  (i) Presence of one or more of the following criteria indicates early latent syphilis:
  - A non-reactive serology test for syphilis or a non-treponemal titre that has dropped fourfold within the past 24 months
  - A history of symptoms consistent with primary or secondary syphilis without a history of subsequent treatment in the past 24 months.

- A history of sexual exposure to a partner with confirmed or presumptive primary or secondary syphilis or presumptive early latent syphilis and no history of treatment in the past 24 months.
- Reactive non-treponemal and treponemal tests from an individual whose only possible exposure occurred within the preceding 24 months.

(ii) Late latent syphilis cases are those without the above criteria.

- **Laboratory criteria for diagnosis:**

- Demonstration of T. pallidum in clinical specimens by dark field microscopy or
- Serology.

d. Neurosyphilis (A52.3)

- **Clinical case definition:**
  Evidence of central nervous system (CNS) infection with T. pallidum.

- **Laboratory criteria for diagnosis:**
  A reactive serologic test for syphilis and reactive VDRL in cerebrospinal fluid (CSF).

2. Congenital Syphilis (A50.9)

- **Clinical case definition:**

  - A condition caused by an infection in utero with Treponema pallidum. A wide spectrum of severity exists, from inapparent infection to severe cases that are clinically apparent at birth.
  - An infant or child (aged less than 2 years) may have signs such as rash, snuffles, hepatosplenomegaly, condyloma lata, jaundice (nonviral hepatitis), pseudoparalysis, anemia, or edema (nephrotic syndrome and/or malnutrition).
  - An older child may have stigmata (e.g., interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinson teeth, saddle nose, rhagades, or Clutton's joints).

- **Laboratory criteria for diagnosis:**

  Demonstration of Treponema pallidum by:
  - Darkfield microscopy of lesions, body fluids, or neonatal nasal discharge; or
  - Polymerase chain reaction (PCR) or other equivalent direct molecular methods of lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material; or
  - Immunohistochemistry (IHC), or special stains (e.g., silver staining) of specimens from lesions, placenta, umbilical cord, or autopsy material.

- **Case classification:**

(i) Probable:

A condition affecting an infant whose mother had untreated or inadequately treated* syphilis at delivery, regardless of signs in the infant;
OR,
An infant or child who has a reactive non-treponemal test for syphilis (Venereal Disease Research Laboratory (VDRL), rapid plasma reagin (RPR) or equivalent serologic methods) AND any one of the following:

- Any evidence of congenital syphilis on physical examination (see Clinical description).
- Any evidence of congenital syphilis on radiographs of long bones (e.g.osteochondritis, diaphyseal osteomyelitis, periostitis).
- Serum RPR titre that is at least '4-fold higher' than their mother's.
- A reactive cerebrospinal fluid (CSF) Venereal Disease Research Laboratory (VDRL) test.
- In a non-traumatic lumbar puncture, an elevated CSF leukocyte (white blood cell, WBC) count or protein (without other cause), suggested parameters for abnormal CSF WBC and protein values:
  - During the first 30 days of life, a CSF WBC count of >15 WBC/mm3 or a CSF protein >120 mg/dl is abnormal.
  - After the first 30 days of life, a CSF WBC count of >5 WBC/mm3 or a CSF protein >40 mg/dl, regardless of CSF serology. (The treating clinician should be consulted to interpret the CSF values for the specific patient).

* Adequate maternal treatment is defined as at least one injection of 2.4 million units of intramuscular Benzathine Benzylpenicillin at least 30 days before delivery.

(ii) Confirmed:

A case that is laboratory confirmed (see Laboratory criteria for diagnosis).

(iii) Syphilitic stillbirth:

A foetal death occurs after a 20-week gestation or in which the foetus weighs greater than 500g and the mother had untreated or inadequately treated* syphilis at delivery.

- **Types of Surveillance:**

  Mandatory National Notification of Infectious Diseases under the Infectious Disease Prevention and Control Act 342, 1988.

- **When to notify:**

  (i) Acquired Syphilis
  Only confirmed cases should be notified. The clinical staging of cases can be mentioned in the notification form

  (ii) Congenital syphilis
  All probable, confirmed and syphilitic stillbirths should be notified.

  Both acquired and congenital syphilis cases are mandatory to be notified to the nearest District Health Office within a week (7 days) of diagnosis.

- **How to notify:**

  Notification should be done via an e-notification system or through submission of the notification form to the nearest District Health Office.

  These case definitions have been referred from the Centers for Disease Control, (CDC) US, Atlanta, 2018 and Global guidance on criteria for the elimination of mother-to-child transmission of HIV and Syphilis by the World Health Organization (WHO), 2017. They were updated in the Ministry of Health surveillance system in 2020.

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