MAIN CONTENTS

Chapter 6:

Sexually transmitted infections

contents

contents (continued)

1. Introduction

Sexually transmitted infections (STIs) have a profound impact on reproductive health. Although many different bacteria, viruses, and parasites can be transmitted through sexual contact, eight of them cause the greatest incidence of disease. Four are currently curable: syphilis, gonorrhoea, chlamydia, and trichomoniasis; while the others are viral infections that remain incurable: hepatitis B, herpes simplex virus (HSV or herpes), HIV, and human papillomavirus (HPV).

STIs directly impact sexual and reproductive health through stigmatization, infertility, cancers, and pregnancy complications, and can increase a person's risk of acquiring HIV. The goal of this chapter is to present details on preventing, diagnosing, and treating infections spread predominantly by sexual contact, including vaginal, anal, and oral sex, thereby mitigating the serious consequences of infection and disease.

1.1 Key terms, magnitude, and overview of STIs

The terms 'sexually transmitted infections' and 'sexually transmitted diseases' (STDs) are often used interchangeably, although they refer to two different conditions. 'Infections' may or may not lead to 'diseases', or disease complications and sequelae. Using STIs rather than STDs highlights that infections may exist and be transmissible without (or before) causing clinical manifestations. STIs are often asymptomatic (e.g. chlamydia, gonorrhoea, HPV), and some do not affect the genitals or reproductive tract directly (e.g. HIV, hepatitis B, hepatitis C).

'Reproductive tract infections' (RTIs) is an umbrella term for all infections of the reproductive tract. Not all STIs affect the reproductive tract and not all RTIs are sexually transmitted. STI refers to the *mode* of transmission, whereas RTI refers to the *site* where the infections develop.

RTIs include:

- STIs that affect the reproductive tract (e.g. gonorrhoea, chlamydia, syphilis, genital herpes simplex virus, trichomoniasis, chancroid, HPV).
- Endogenous RTIs that are caused by an overgrowth of micro-organisms normally found in the reproductive tract of healthy women and which are not sexually transmitted (e.g. bacterial vaginosis or vulvovaginal candidiasis, also known as yeast infections).
- Iatrogenic RTIs that can result from poor infection prevention and from medical procedures, such as intrauterine device (IUD) insertion, unsafe abortion, or other gynaecological/obstetric procedures (e.g. management of pregnancy complications, resulting in infection of the uterus, fallopian tubes, and other pelvic organs).

Acronyms

BV	bacterial vaginosis
GUD	genital ulcer disease
HBsAG	hepatitis B surface antigen
HBeAG	hepatitis B e antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSV	herpes simplex virus
IPPF	International Planned Parenthood Federation
IUD	intrauterine device
LGV	lymphogranuloma venereum
NAAT	nucleic acid amplification test
PCR	polymerase chain reaction
PID	pelvic inflammatory disease
POCT	point-of-care test
PrEP	pre-exposure prophylaxis
RDT	rapid diagnostic test
RPR	rapid plasma reagin
RST	rapid syphilis test
RTI	reproductive tract infection
STI	sexually transmitted infection
UTI	urinary tract infection
VVC	vulvovaginal candidiasis
WHO	World Health Organization

Urinary tract infections (UTIs) affect the bladder and urethra and can be caused by organisms that are sexually transmitted or by gastrointestinal bacteria (e.g. *E. coli* bacteria are the main cause of bladder infections).

STIs are a significant cause of global morbidity with large numbers of people acquiring new infections and living with existing infections, some of which can have life-threatening consequences. Worldwide, over 1 million new STIs are acquired every day.

1.1.1 Overview of STIs

Although there are more than 30 pathogens known to be transmitted through sexual contact, the vast majority of disease or illness linked to STIs is due to only eight, four of which are currently curable: ***Treponema pallidum* (syphilis), *Neisseria gonorrhoeae* (gonorrhoea), *Chlamydia trachomatis* (chlamydia), and *Trichomonas vaginalis* (trichomoniasis)**. These four can be treated with effective single-dose antibiotic regimens, although antimicrobial resistance has been increasing in STIs recently, especially in gonorrhoea. The four most common non-curable/viral STIs are **hepatitis B virus, genital herpes simplex virus (HSV type 2), HIV, and HPV**. Although incurable, these infections can be mitigated or modulated through treatment, and vaccinations exist for hepatitis B and for many types of HPV [1].*

Many STIs are asymptomatic or only have mild symptoms that may not be recognized easily, which increases the likelihood that complications develop and may have serious consequences in some cases. Sexual dysfunction, infertility, and psychological morbidity can also be a consequence of STIs, due to stigma and discrimination.

Gonococcal infections and **chlamydial infections** are often asymptomatic and are common in all people. Both infections can lead to severe complications in women, including pelvic inflammatory disease (PID), ectopic pregnancy, and infertility. In men, untreated urethral infection can lead to epididymitis, urethral stricture, and infertility. Lymphogranuloma venereum (LGV), caused by a more invasive serovar of *C. trachomatis*, is increasingly prevalent among men who have sex with men in some regions. Infants of individuals with gonococcal or chlamydial infection can develop neonatal conjunctivitis, which may lead to blindness if left untreated. Maternal chlamydial infection is also associated with preterm birth, low birth weight, and neonatal nasopharyngeal infection and pneumonia [2,3].

Primary syphilis often presents as a single, painless chancre, which may go unnoticed by clients. Untreated syphilis can progress to secondary syphilis, early and late latent (asymptomatic) syphilis, and tertiary syphilis (i.e. severe illness: neurosyphilis, cardiovascular syphilis, and gummatous syphilis). Vertical transmission of syphilis (congenital syphilis) is usually devastating to the fetus if maternal infection is not detected and treated early in pregnancy [4].

HPV infections are usually asymptomatic, and the vast majority clear up on their own within months to 2 years, although a small proportion persist. If the infections persist, several HPV types can cause cancers of the cervix, vulva, vagina, anus, penis, and oropharynx, as well as genital warts. Most significantly, HPV 16 and 18 cause approximately 70 per cent of cervical cancers and precancerous cervical lesions globally. Cervical cancer is the fourth most common cancer in women, with about 90 per cent of the new cases and deaths worldwide occurring in low- and middle-income countries in 2020 [5].

HIV is usually asymptomatic initially but reduces immune function if untreated so that individuals with HIV are increasingly susceptible to a wide range of infections, cancers, and other diseases. If undetected and untreated, HIV can also be transmitted perinatally during pregnancy, delivery, and breastfeeding. STIs that cause genital ulcers, such as syphilis, herpes, and chancroid, can also increase the risk of HIV acquisition (see *Chapter 7: HIV*).

Viral hepatitis attacks the liver and can cause both acute and chronic disease, although most people do not experience symptoms when newly infected. Viral hepatitis can also lead to death as a result of chronic liver disease and liver cancer, mostly caused by hepatitis B and C virus [6].

* Gardasil 9 vaccine protects against nine HPV types (HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58), while Cervarix protects against two HPV types and Gardasil against four HPV types.

1.2 IPPF position on STI management

- Comprehensive STI healthcare should be evidence-based, acceptable, accessible, affordable, and equitable, and should be offered as an integrated package of care with other sexual and reproductive healthcare for a person-centred approach.
- Screening, diagnosis, and treatment of STIs (including screening for STI risk), and HIV prevention and risk reduction counselling are essential components of comprehensive sexual and reproductive healthcare and in line with the International Planned Parenthood Federation's (IPPF) integrated service package (see *Chapter 1: Guiding principles and approaches).*
- STI management should be informed by national guidelines, or by World Health Organization (WHO) (see *Appendix 1*) and other relevant global guidance adapted to the local context.
- Correct and effective treatment of STIs, ideally given and taken on the same day, at the first contact between clients and healthcare providers, is important as it attempts to break the chain of transmission of the infection without delay.
- Tests that enable diagnosis and treatment in a single visit, known as rapid diagnostic tests (RDTs) or point-of-care tests (POCTs), are widely available for HIV and syphilis (separately or using a dual HIV/syphilis RDT). Use of these tests in the context of antenatal care is a priority, to help prevent perinatal transmission of both syphilis and HIV.
- Syndromic management is effective for some STIs and is recommended in settings without sufficient laboratory capacity or in the absence of diagnostic tests. Symptomatic clients should be managed in line with national STI management guidelines.
- All healthcare should be centred on a rights-based approach. Clients should never be coerced by anyone to obtain care and must give consent before receiving any STI healthcare.
- Inform clients requiring STI treatment that their sexual partner(s) should also be tested and/or treated and prepare these clients with practical advice on how to talk to their partner(s) about STIs (see *Section 2.5: Partner notification*).
- Periodic screening of populations most at risk for STIs is recommended, including youth (age range determined by local STI prevalence patterns), men who have sex with men, transgender people, sex workers, and people who use drugs.
- Clients should be referred for additional healthcare as required, including for prompt STI screening and treatment if not available at the facility where the client has presented. All STI healthcare should include follow-up visits to review treatment and provide further counselling and/or related care. All aspects of care should remain confidential.

1.3 Key competencies for healthcare providers

Know the local and national epidemiology of STIs: Providers need to be aware of the prevalence of STIs in their country or locality, as a basis for assessing the risk of STIs in their client population. Combining this information with an individual risk assessment during client history-taking will support effective STI management, especially where aetiological tests are not available (see *Section 3: Diagnostic tests*).

Keep up to date with clinical information and current guidance: Providers need to stay updated in their knowledge of STI presentations, screening/diagnostic methods, and treatment regimens, as well as STI prevention interventions; know the local and regional guidance (where available); and be aware of local changes relevant to particular infections and treatments, (e.g. reductions in antibiotic sensitivity/susceptibility). Emerging antimicrobial resistance in some STIs may affect recommended treatment, especially *N. gonorrhoeae* (the bacterium causing gonorrhoea).

Be able to provide non-judgmental and non-stigmatizing STI healthcare: Providers should aim to provide non-judgmental and confidential care and promote good sexual and reproductive health in a way that reduces the stigma associated with STIs, HIV, and unintended pregnancy. Many populations at higher risk of STIs (see *Box 1*) also face stigma and discrimination and

may not present for certain healthcare because they fear experiencing stigma or they may feel that care provision is not equipped to help them. Providers may also overlook populations at risk (such as people with disabilities), by presuming that they are not sexually active. Some clients may also not be able to afford treatment; they may avoid or delay accessing healthcare or mentioning STI symptoms due to stigma and shame; and/or they may have hectic lives and therefore cannot attend a clinic, finish a course of treatment, or return for follow-up.

Take all opportunities to provide STI information and care: Providers of sexual and reproductive healthcare should feel prepared to take the opportunity, whenever appropriate, to counsel clients on the benefits of STI screening and treatment and to support them in making informed choices. Information should be provided in a manner that is easily accessible and understandable and meets the needs of the client (pictorial, sign language, etc). Examples of potential opportunities include:

- During provision of contraceptive healthcare, and especially when potential STI symptoms are mentioned or found (e.g. inspect for symptoms when inserting an intrauterine device).
- During provision of a safe surgical abortion procedure or other gynaecological care requiring physical examination (e.g. cervical cancer screening).
- During antenatal care visits (e.g. strongly recommended to offer dual HIV and syphilis screening).
- During management of clients affected by sexual and gender-based violence and rape.

Be able to offer STI diagnosis and treatment: Screening or test methods that allow for a same day or same visit diagnosis are preferable to reduce loss to follow-up and support appropriate and efficient treatment for positive clients. Accurate and easy-to-use RDTs exist for HIV and syphilis (separate or as a combined 'dual' test), giving results within 20 minutes [7]. In the absence of accurate RDTs for other STIs, clinics will require supplies for taking samples, laboratory equipment (preferably on-site to expedite analysis), and training to provide a diagnosis. Where no laboratory facilities or RDTs are available to support aetiological diagnosis, access to STI treatment for symptomatic clients is still essential, therefore providers need to be skilled in syndromic management of STIs (see *Section 5*). The medications recommended by the facility's syndromic management protocol (based on national or regional guidance) should be widely available in adequate supply so that treatment is not delayed and loss to follow-up is minimized.

2. Comprehensive STI healthcare delivery

Effective STI management consists not only of antimicrobial therapy to cure and reduce infectiousness, but also comprehensive assessment and care of the person's sexual and reproductive health and that of their sexual partners.

The objectives of comprehensive STI healthcare delivery are to provide treatment, obtain cure, reduce infectiousness, reduce the risk of developing complications of STIs, reduce or prevent future risk-taking behaviour (including other bio-behavioural interventions, such as pre-exposure prophylaxis (PrEP) and voluntary medical male circumcision), and ensure that sexual partners are appropriately treated.

A full range of high-quality STI care should be provided within the continuum of sexual and reproductive healthcare. This requires that a client receives the following care, as relevant:

- medical and sexual history taken and noted
- correct diagnosis (whether syndromic or based on diagnostic tests)
- effective treatment
- health education and counselling about the infection and risk reduction
- advice on compliance with treatment
- promotion and/or provision of condoms (male or female)
- promotion and/or provision of PrEP

- promotion and/or provision of other preventive interventions, such as vaccines against hepatitis A and B, vaccines against HPV, where appropriate, and voluntary medical male circumcision
- encouragement to notify sexual partners
- clinical follow-up where appropriate

The specific STI care provided at the facility – and the specific population groups that may need extra attention (see *Box 1*) – will vary by country and region, depending on the local epidemiological and social context. The core package of healthcare offered needs to be regularly reviewed to ensure that, as new evidence emerges and new technologies and approaches are developed (e.g. use of internet messaging services for engagement), innovations are rapidly integrated and opportunities harnessed.

2.1 STI prevention

Prevention is the most important strategy to control STIs, including HIV infection.

Effective STI control requires ensuring access to high-quality and effective prevention healthcare, including ensuring access to vaccinations for hepatitis A, hepatitis B, and HPV, and promoting voluntary medical male circumcision where appropriate. Screening for asymptomatic STIs is important for early detection, prevention of serious consequences of infection, and preventing transmission of STIs. Inclusion of partner notification, testing, and/or treatment prevents reinfection.

It is also crucial that STI healthcare is non-stigmatizing and non-discriminatory, accessible for all, and integrated with other sexual and reproductive health or primary care services to maximize access, while ensuring privacy and confidentiality.

Healthcare providers have multiple roles to play in the prevention of STIs and their complications, as described in brief below.

- **Promote early use of clinic services** to treat STIs and prevent complications, emphasizing that many STIs are curable. Encourage health-seeking behaviour by teaching people how to recognize symptoms and when to seek care.

BOX 1: Specific populations most affected by STIs, including HIV

Countries should define the specific populations to focus on for STI healthcare, depending on the local contexts. These population groups may include:

- people most likely to have high numbers of sexual partners, e.g. sex workers and their clients
- men who have sex with men
- transgender people
- people with existing STI(s), including HIV
- adolescents and young people (ages 10–24)
- women
- people experiencing sexual and gender-based violence
- mobile populations
- children and young people living on the street
- prisoners
- people who use recreational drugs
- people affected by conflict and civil unrest

Source: WHO [8].

- **Promote safer sexual practices and condom use,** when counselling clients, including providing verbal and written information about STIs and key prevention messages (see *Box 2 – next page*), demonstrating correct male and female condom use, and discussing dual protection (against pregnancy and STIs, including HIV). Different condom sizes and types should be available, including female condoms, as well as condom-compatible lubricants. The use of lubricants helps prevent male condoms from breaking and slipping and can increase comfort and pleasure, particularly for anal sex. Explain that oil-based lubricants must not be used with latex condoms as they can degrade the latex, increasing the risk of condom breakage (for further information see *Chapter 7: HIV*).
- **Detect infections** that are not obvious. Ask about STI symptoms during history-taking when clients attend for any sexual and reproductive healthcare. Also look for signs of STIs when performing non-

STI examinations (e.g. cervical screening or IUD insertion). Offer screening for asymptomatic infections and periodic retesting/examination, when possible, especially if the client is assessed to be at high risk. Provide advice on how often a client should be tested depending on risk factors (e.g. for men who have sex with men, STI screening can be offered at 3–6-month intervals).

- **Prevent iatrogenic infection** by following universal precautions and strict instrument processing, using aseptic techniques, and by ruling out or treating cervical infection before performing transcervical procedures.
- **Manage symptomatic STIs** effectively by providing treatment, obtaining cure or reducing infectiousness, reducing the risk of developing complications of STIs, reducing or preventing future risk-taking behaviour, and ensuring that sexual partners are appropriately treated.
- **Counsel clients** on how to remain free from STIs after treatment by adopting safer sexual practices including biomedical interventions (see *Box 2*). Encourage clients to adhere to treatment, including ensuring partner notification and treatment, emphasizing that it is best if partners are treated simultaneously (see *Section 2.5: Partner notification*).
- **Recommend universal screening of pregnant individuals** for syphilis, HIV, and hepatitis B at first antenatal contact. For syphilis and HIV, use point-of-care RDTs (e.g. a dual RDT for both syphilis and HIV) and provide treatment to reduce vertical transmission risk to the fetus, which can be fatal.
- **Promote and provide vaccination against** hepatitis A and B and HPV infections, in accordance with local guidance. Hepatitis A and B vaccinations are often included in infant immunization programmes. Vaccines available for HPV are a bivalent vaccine that protects against HPV types 16 and 18, which cause 70 per cent of cervical cancer worldwide; a quadrivalent vaccine that protects against those as well as HPV types 6 and 11, which cause most anogenital warts; and a nonavalent vaccine that targets HPV types 6, 11, 16, and 18 as well as five additional high-risk oncogenic HPV types (31, 33, 45, 52, and 58), providing protection against anal, cervical, vaginal, and vulvar cancer as well as anogenital warts. HPV vaccines are intended to be given before the onset of sexual activity but are recommended regardless of onset of sexual activity in anyone aged up to 26 years. For adults aged between 26 and 45 years who are not vaccinated, some may still benefit from vaccination [9]. If available and licensed for use in the local context, healthcare providers should engage in shared decision-making regarding HPV vaccination (see *Chapter 8: Gynaecology and other reproductive healthcare*).
- **Promote voluntary medical male circumcision** for appropriate candidates to provide some protection against HIV (where prevalence is high, see *Chapter 7: HIV)* and other STIs, such as herpes and HPV.
- **Provide prophylaxis for ophthalmia neonatorum to all newborn babies** regardless of maternal symptoms or signs of gonorrhoea or chlamydia infection. Providers should check local treatment guidance.

BOX 2: Key counselling messages for the primary prevention of STIs, including HIV

Safer sexual activity and STI prevention can be achieved by adopting any combination of the following:

- be educated and aware about STIs and sexual health and well-being
- delay the age of sexual debut
- reduce the number of sexual partners
- engage in non-penetrative sex acts (e.g. mutual masturbation and rubbing)
- use condoms (male or female) consistently and correctly during penetrative sex acts (vaginal, oral, anal), along with condom-compatible lubricant
- get vaccinated against hepatitis A and B, and HPV
- use pre- and post-exposure prophylaxis (PrEP and PEP) for HIV, as needed (see *Chapter 7: HIV*)
- get screened or tested regularly when with new or multiple sexual partners
- seek immediate care in case of any symptoms of STIs

Source: Adapted from WHO [8] and WHO [10].

2.2 Counselling for clients attending STI healthcare

Counselling for STI testing should include information on the importance of testing, noting that STIs are common but that there is the potential to cure or control the infection, and emphasizing the benefits of preventing future complications, reducing or ending the possibility of transmission, and taking control of self-protection and protection of partner(s). Counselling should also include information on the importance of adhering to an STI treatment regimen and completing the course of medication (see *Section 2.4: Provision of STI treatment*). Counselling should encourage health-seeking behaviour whenever STI symptoms are noticed, especially if there has been any risk of exposure to STIs (e.g. new or multiple partners, condom breakage or non-use).

Information given should be client-centred, accessible, easy to understand, and sensitive to the client's individual circumstances. For example, the client may be starting a sexual relationship with a new partner, they may be living with HIV, or may be living with the threat of sexual and gender-based violence. Providers must also keep in mind that each client's needs are not static and will change over time.

Providers should emphasize that a positive diagnosis (either through syndromic management or aetiological testing) does not mean that someone is to 'blame'. Treatment of the partner, who is likely also to be infected, is essential if the client is to avoid being reinfected after their own treatment. This is an opportunity to discuss the benefits of partner notification and treating all parties at the same time to reduce the chances of treatment failure (see *Section 2.5: Partner notification*).

Joint counselling for couples on STI prevention can be explored as a possibility. Many clients will find it difficult to talk about the issue with their partner(s) and may appreciate support with communication.

For clients with a **positive** result, it is important to reassure them about confidentiality and provide support, if needed, on how to deal with stigma that may result from a positive diagnosis. Some clients may need further support or referrals, depending on their circumstances. Offer counselling on risk reduction to prevent future STIs by assessing current risks and barriers to safer sex and discuss a plan to reduce risk.

For clients with a **negative** result, offer counselling on risk reduction and how to stay 'negative' based on the client's individual circumstances, including safer sex messaging (see *Box 2*). Assess current risks and barriers to safer sex and discuss a plan to reduce risk.

All clients should be encouraged to ask questions, and to return (or call if the option is available and preferred by the client) if they have any further questions or concerns. They should also be offered written information (e.g. a relevant informative pamphlet), if available.

For HIV-related counselling and partner notification, see *Chapter 7: HIV*.

2.2.1 Mobile technology and STI care

The rapid expansion of internet access and mobile phones has created new opportunities to leverage mobile technologies to help reduce STI burden across diverse populations. Mobile technologies enable clients to be reached whenever and wherever they are and can be an important tool to augment in-person healthcare. Such tools can support a range of efforts including outreach and engagement of key populations, raise awareness of local healthcare, facilitate dissemination of educational contents, send reminders for follow-up, and increase access to STI screening and testing. A wide range of tools are available (e.g. phone or video calls, simple SMS or messaging apps, social media, and smartphone apps) (see *Table 1* – next page). A key consideration, however, needs to be given to proactively protecting privacy and confidentiality of participants, especially if phones are shared with others.

Key principles and considerations in using mHealth/eHealth for STI and HIV programmes:

- Conduct a needs assessment and ensure sufficient time for planning, piloting, and integration into workflows.
- Involve clients or the target population at all stages, which will help guide planning, promote feasibility, and support engagement/use and address digital literacy.

- Develop clear, actionable, and measurable goal(s) and outcomes for using the technology.
- Tailor digital content (posts, articles, videos) to the local population, and ensure language and messages used are not unintentionally stigmatizing.
- Ensure ethical conduct and use across mobile/internet-based platforms of technology.
- Have procedures to maintain the strictest confidentiality such as safeguarding data (e.g. list of mobile phone numbers of clients).
- Develop procedures to protect privacy (e.g. obtain the client's consent to contact them via SMS to prevent unintended disclosure of a client's health issue).
- Consider issues of sustainability and resources in planning and implementation.

TABLE 1: Examples of technological tools used to facilitate STI care

Technology platform	Use example
SMS – mobile phones	Reminders for appointments or for medication adherence
Social media (e.g. Instagram/ Facebook)	Posting educational and motivational digital content (graphics, short videos) about STI/HIV testing or how to access PEP/PrEP
WhatsApp	Connect clients to a peer outreach worker for ongoing support for HIV prevention
Private online groups (e.g. Messenger, WhatsApp, Facebook)	Develop a closed group of clients to create virtual peer support groups for clients living with HIV
WhatsApp provider group	Create a network of providers to support each other by sharing information, accessing experts who can answer questions in real-time, provide educational and informational updates for new guidelines
Dating apps/social media	Work with key population influencers and community stakeholders to reach people who are marginalized (e.g. men who have sex with men, transgender women, sex workers) to inform about safe and affirming healthcare
Multiple platforms	Distribute a link via social media and stakeholders to efficiently conduct a needs assessment of existing or potential new clients
Smartphone apps	Tailor and distribute custom apps to promote STI/HIV prevention and care

2.3 Client assessment

2.3.1 Sexual history and risk assessment

In the context of sexual and reproductive healthcare, the provider should start by asking about the client's general health followed by a full sexual and reproductive health history and initial sexual history screening questions (follow the steps described in *Chapter 2: Facility requirements and client history/examination*).

A. Risk assessment

For clients reporting more than one partner in the past year and for male clients who have sex with men, conduct a further risk assessment (see *Table 2* – next page).

Note that although these questions are brief, a sexual history will, in some situations, lead to a longer discussion of important sexual and reproductive health and related issues. *Table 2* provides additional questions that can be asked to further assess risk. The questions should be adapted/validated for the client/population/setting.

TABLE 2: Risk assessment: suggested additional questions to ask when sexual history screening indicates risk for STIs, including HIV

Partners	Do you know whether your partner has one or more other sexual partners? Do you know whether your partner has STI symptoms? In the past 3 months, have you had sex with a new partner, with someone you didn't know or had just met, or have you had multiple partners? Have you ever been coerced or pressured to have sex?
Practices	In the past 3 months, what kind of sex have you had: anal/vaginal/oral? (for men who have sex with men, ask about receptive anal sex, insertive anal sex, or both) Have you or any of your partners used alcohol or drugs when you had sex? Have you ever exchanged sex for drugs or money?
Past history of STIs	Have you ever had an STI? • If yes: which infection/disease (or what/where were the symptoms)? When did you have it? Were you and your partner(s) treated? Have you ever been tested for HIV? • If yes: how long ago was that test? What was the result?
Protection	What do you do to protect yourself from STIs, including HIV? When do you use this protection and with which partners? (for anal/vaginal/oral sex?) Have you been vaccinated against HPV, hepatitis A, or hepatitis B? Have you recently experienced condom breakage or slippage?

Source: Adapted from Altarum Institute [11].

B. Asking about clinical symptoms

After completing the risk assessment (section A), providers should ask the right questions about any clinical signs or symptoms to assess whether these are indicative of an STI or another pathology, even before proceeding to a clinical examination. These questions are summarized in *Box 3*.

BOX 3: Questions for clients about clinical symptoms

Questions to ask all clients on general symptoms	• Systemic symptoms such as fever, rash, joint or eye pain (can be related to complications of chlamydia and gonorrhoea). • For clients who have had anal intercourse, any pain, bleeding, or discharge from the anus or a change in bowel habit (indicate the need for further investigations). • Lumps in the groin (may indicate inguinal buboes or enlarged lymph nodes). • Urinating more often and pain in the urethra or the abdomen when passing urine (indicate the need for further investigations). • Soreness or itching on the external genitals or anus, any skin changes or ulcers (may indicate pubic lice, genital herpes, or genital warts).

Questions for clients who are women/have female genitalia	• Date of last menstrual period, any abnormal uterine bleeding, and use of contraception
	  ◦ It is important to confirm or exclude pregnancy, especially in the presence of pelvic pain and/or abnormal uterine bleeding (potential miscarriage or ectopic pregnancy, see *Chapter 8, Section 3. Management of common gynaecological conditions*), and to ensure that any current or planned medication is not contraindicated.
	  ◦ Perform a pregnancy test if required.
	  ◦ If the client is at risk of unintended pregnancy, offer contraceptive care, including emergency contraception if required, and discuss condom use.
	• Any bleeding after sex (may indicate cervicitis related to chlamydia).
	• Any abdominal or pelvic pain, or pain during sex (and location of pain).
	  ◦ Lower abdominal pain may indicate PID, most commonly caused by chlamydia, but also caused by gonorrhoea or other microorganisms (see *Chapter 8, Section 3. Management of common gynaecological conditions*). Presence of fever and deep dyspareunia increase the likelihood of having PID.
	• If there is any vaginal discharge, ask if this is different to normal (and to describe the colour/consistency/odour/amount). Different types of abnormal discharge may indicate an STI (e.g. chlamydia, gonorrhoea, trichomoniasis) or a non-sexually transmitted RTI (e.g. bacterial vaginosis, candidiasis).

Questions for clients who are men/have male genitalia	• Ask about the testicles: any changes in size or swelling, any pain
	  ◦ For sudden onset of severe pain, consider torsion as a possible diagnosis.
	  ◦ For swelling without pain, consider hydrocele (a harmless collection of fluid in the scrotum affecting one or both testicles) or varicocele (a swelling of the blood vessels in the testicles).
	• Ask if they urinate more often and if there is blood in the urine (indicate the need for further investigations).
	• If there is any discharge from the penis and its description (discharge may indicate an STI).

2.3.2 Clinical examination

Refer to *Chapter 2, Section 4: Physical examination* for guidance about physical examination. The additional information provided below is specifically for STI signs and symptoms.

Genital area:

- *All clients:* Inspect the external genitalia for any ulcers, rash, or warts.
- *Vaginal/cervical/ovarian examination:*
  - Speculum examination: Observe the amount, consistency, colour, and odour of vaginal discharge and the presence of ulcers or warts in the vagina or on the cervix. Suspect cervicitis secondary to STI if the cervix is friable (sensitive and prone to tearing, or bleeding on contact), or if there is mucopurulent discharge.
  - Bimanual examination: Check for lower abdominal pain (pelvic pain) and cervical motion tenderness (cervical excitation), which indicate acute infection.
- Testicular/penis examination:
  - Penis: Check or 'milk' the urethra (i.e. gently massage from the ventral part of the penis towards the meatus) for evidence of any reported discharge.
  - Scrotum and testicles: Check for scrotal swelling. Palpate the epididymis to assess for pain.

Groin areas:

- Check for inguinal swellings. If these are fluctuant and/or painful they are more likely to be buboes rather than enlarged lymph nodes.

Anal area:

- Check the peri-anal area of clients who may have receptive anal sex for ulcers, warts, discharge, bleeding, or other abnormalities as they may not be aware of their symptoms.
- Perform a rectal examination if there is mucopurulent discharge, mucosal oedema, or ulcers, and test for rectal chlamydia and gonorrhoea if resources are available.

Oral area:

- For clients who have oral sex, check for a sore throat and signs of oropharyngeal infection, and test for throat chlamydia and gonorrhoea if resources are available, especially among groups at high risk (e.g. men who have sex with men, sex workers).

Findings from the sexual history and the physical exam, in combination with local epidemiological information and national or facility-specific guidance, will guide in selecting the most appropriate aetiological test(s) as needed. Examinations also form part of syndromic management (see *Section 5*).

2.4 Provision of STI treatment

High-quality care and treatment for STIs must be available to people who need it at their first point of contact. For clients requiring treatment, whether based on syndromic, diagnostic, or self-administered tests (see *Sections 3 and 5*), it is critical for providers to have the appropriate medications available (see *Appendix 2: Recommended treatment options*) or to be able to refer clients to an accessible and affordable pharmacy.

Advise clients who require medical treatment:

- Take all medication as instructed, adhering to the regimen, even if symptoms disappear before the medication is finished. Explain that this helps to ensure that the treatment is effective and prevents the development of resistance to treatment.
- Not to have any sexual contact (vaginal, anal, or oral) until the treatment has been completed and symptoms have disappeared.
- Not to have any sexual contact until their partner(s) has also been treated (see *Section 2.5: Partner notification*). This may not apply to endogenous STIs. If that is not possible, condoms should be used. Provide condoms and lubricants to clients as needed.

Advise the client to return to the clinic:

- If they experience adverse effects of medication.
- If any symptoms have not resolved or have worsened.
- If they were not able to complete their treatment.
- If they think they may have been reinfected.

Encourage all clients to ask any questions they may have, and to return at any time if they have further questions or concerns. Routine follow-up is not essential. In addition to instructions for treatment, clients should be given verbal and written information and education as appropriate (see *Section 2.1: STI prevention*).

2.5 Partner notification

Once a client has been diagnosed with an STI and treatment has commenced, the provider should provide information, counselling, and support regarding notification of their sexual partner(s).

The purpose of notifying the client's sexual partner(s) is to treat those who are likely to have the same STI and to prevent the client from becoming reinfected after their treatment. Ideally, sexual partners of clients should be screened and treated as soon as possible.

The partner notification process can be challenging for several reasons:

- The concept of partner notification may be threatening to the client. It is essential to respect the client's wishes and to maintain their trust. It can help if the clinic has earned a reputation for maintaining confidentiality.
- Providers need to be sensitive to clients who may be more susceptive to adverse outcomes of disclosure, such as discrimination, violence, abandonment, or incarceration. These clients may need additional counselling.
- Many clients may find it difficult to discuss an STI diagnosis with their partner, especially those at risk of violence.
- The client's sexual partner(s) may not believe that they have an infection, especially if they have no symptoms, and may refuse to come for screening or treatment.
- Clients who have been diagnosed with vaginal discharge syndrome may not have an STI, but they may be given treatment for STIs in accordance with syndromic management (see *Section 5*). Providers need to discuss with the client whether to disclose this presumptive diagnosis and/or suggest treatment to their sexual partner(s).
- Some clients may not know the correct names and contact details of their sexual partner(s), and even if they do, some may be hard to locate.

It is critical that the provider does not force the client to decide and act against their will. The provider can give information about why partner notification and treatment are important but ultimately it is the client's choice whether to notify their partner(s).

Depending on the characteristics of the client and the circumstances of the case, providers can discuss and consider the following partner notification approaches with the client:

- **Client-led system of notification and referral:** Some clients may have the confidence to talk to their partner(s) directly and refer them for STI management. Ask these clients to bring or send in their partner(s) to the clinic. If possible, give them referral slips to hand to their sexual partner(s). Recommend an alternative clinic if that is more convenient for the partner.
- **Client-led system of treatment:** Some clients know that their partner will not attend for STI management, but they are willing to take the treatment to their partner to prevent delaying treatment. The client can be given information and sufficient medicines or prescriptions for their sexual partner(s) without requiring examination, to expedite the process. This is only possible where treatment is oral.
- **Provider-led system of notification:** Some clients may prefer that the healthcare provider contact their sexual partner(s) without naming them as the potential source of exposure. Ask these clients for the name(s) and address(es) of the partner(s), and try to contact them by telephone, post, or by visiting them at home, as needed, and recommend that they come for testing due to potential exposure to someone with an STI.
- **Combined approaches:** In many cases, more than one approach may be required. For instance, if a client offers to notify the sexual partner(s), the provider

may wait for a reasonable amount of time (about a week), then try another approach if the partner has not appeared for treatment.

Note: Providers also need to be aware of local or national regulations and protocols that may stipulate mandatory notification and reporting of particular STIs and should be open with the client about the implications, depending on the circumstances of the case.

2.6 Referral

Many providers see clients for STI care in primary care facilities and may not have immediate access to all tests or treatments. Each provider or facility should plan a referral pathway for clients who need to be seen or followed up elsewhere for STI testing and care, other sexual and reproductive healthcare, and other needs including mental health care.

It is generally recommended to refer clients in the following circumstances:

- There is an STI complication, such as suspected or confirmed PID, or a secondary infection for which close monitoring or appropriate management is not available on-site.
- There is doubt about a diagnosis, especially in clients who are acutely unwell, and there is a possibility that a non-STI-related condition may be the cause, such as ectopic pregnancy or acute appendicitis.
- Treatment has failed or the symptoms have failed to respond to the available treatment regimen (e.g. when there is persistent urethral discharge). In these cases, enhanced diagnostic services may be required to provide effective treatment and decrease the risk of antimicrobial resistance.
- Specialist treatment is required (e.g. for a pregnant client or a client with multiple medical comorbidities, or for surgical removal of more complicated anogenital warts).
- Further diagnostic tests or investigations are required.
- A client with chronic hepatitis B infection who could benefit from antivirals to slow disease progression, which are available at a specialist centre, or a hepatitis B client who is seriously ill with complications and requires higher-level care.
- A client requires any other sexual and reproductive healthcare that is not available at the facility.

Prevention and management of STIs within humanitarian settings

The prevalence of STIs including HIV can increase in emergencies if there is a lack of prevention, screening, and treatment healthcare. STIs can seriously impact sexual and reproductive health, and some can increase the risk of HIV acquisition.

In a crisis, and in low-resource settings, syndromic management of STIs is used (see *Section 5*). This involves managing cases based on clinical presentation (symptoms and signs) with reference to a decision-making flowchart, with use of on-site microscopy if available and appropriate. The additional resources needed for aetiological testing of STIs – and later returning the results to clients with provision of correct treatment – are not justified in emergencies.

Measures to reduce STI and HIV transmission must include the abundant availability and distribution of free condoms. Ensuring male and female condoms are available (lubricated, or with condom-compatible lubricants, as needed) in all appropriate locations (on- or off-site) from the earliest days of a humanitarian response is critical, since condoms offer the best protection from STIs, including HIV. In addition, post-exposure prophylaxis (PEP) for HIV and STIs should be provided to survivors of sexual violence. See *Chapter 11: Sexual and reproductive healthcare delivery in humanitarian settings* for full details of Minimum Initial Service Package objective 3 concerning prevention of transmission and reduction of morbidity and mortality due to HIV and other STIs in humanitarian settings.

3. Diagnostic tests

Accurate identification of asymptomatic and symptomatic STIs, as well as improvements in the sensitivity and specificity of the syndromic approach, all depend on the availability of diagnostic tests and a screening strategy. The different types of STI tests available are summarized in *Table 3*. Healthcare providers should be aware of which reliable, cost-effective, and high-quality diagnostic tests are appropriate and available locally and should procure and ensure an adequate stock of these tests.

Diagnostic tests, whether they are rapid POCTs or laboratory-based tests, should be provided after taking a full clinical and sexual history, and conducting further risk assessment and examination as appropriate (see *Section 2* and *Chapter 8: Gynaecology and other reproductive healthcare*).

For tests that require specimens using swabs (microscopy, culture, nucleic acid amplification test [NAAT]), these should be taken during the clinical examination indicated by sexual history, from the high vagina, cervix, throat, and/or anus. Swabs from the urethra (male and female) or vagina/cervix can also be taken if there is no access to urine-based testing for gonorrhoea/chlamydia. It should be noted that urine testing is preferred for males, but if not available, urethral swabs can be taken. Swab- rather than urine-based tests are recommended for females, if feasible, due to more sensitivity towards gonorrhoea infections (urine and swabs have similar high sensitivity for chlamydia [12]).

Testing for HIV, syphilis, and hepatitis requires blood/serological testing. Oral swab-based tests also exist for HIV.

Self-collection kits have the advantage of not needing a provider for collection. They can be carried out at home (and in some contexts posted directly to a laboratory), or simply used by the client in a private room/bathroom at the clinic after consultation, similar to the self-collection of urine samples. The effectiveness and thus wider availability of self-collection of urine samples and swabs for STI testing has increased the uptake of STI screening among clients while also reducing the workload of STI healthcare providers as it allows specimen collection without a pelvic examination or provider-collected urethral swab. Commonly self-collected swabs include vaginal, anorectal, and oropharyngeal. They can also be an additional resource to offer to clients who attend for screening or report symptoms but who do not give consent to be examined. Clients must receive clear instructions for the use of self-collection kits, using clear visual tools as appropriate.

Wherever possible, testing should be brought as close to the client as possible (POCTs) and allow for results during the same clinic visit (RDTs). This will maximize the rate of correct diagnosis and treatment received on the same day/visit, and minimize loss to follow-up, which is a risk when tests must be sent for laboratory analysis,

Recommendations on self-collection of samples for STI testing

Greater efforts are needed to expand STI testing globally, and self-collection of samples (SCS) is one way to facilitate this. SCS means that individuals take a specimen themselves, either at a healthcare facility or elsewhere, and send it to a laboratory for testing, and the laboratory returns the result to the individual. Follow-up in the case of positive test results requires linking the individual with the health system. In high-income countries, where laboratory facilities and healthcare are widely available, research shows that self-collected STI samples are as accurate as clinician-collected samples, and that SCS is feasible and acceptable in a variety of populations. SCS approaches can also potentially address some barriers that often prevent people from seeking STI testing from a healthcare provider or clinic, such as concerns about autonomy, inconvenience, stigma, and lack of privacy.

WHO recommendations:

- Self-collection of samples for *N. gonorrhoeae* and *C. trachomatis* should be made available as an additional approach to deliver STI testing.
- Self-collection of samples for *T. pallidum* (syphilis) and *T. vaginalis* may be considered as an additional approach to deliver STI testing.

Source: WHO [13].

delaying access to the results. POCTs/RDTs generally have lower sensitivity than laboratory-based tests but have the advantage that more clients will receive treatment and they incur no laboratory costs (including facilities, specialist equipment, and expertise). These tests can also be conducted by a range of healthcare professionals without laboratory training. Providers should be aware of the POCTs/RDTs that are available locally and regionally and make efforts to use them at their facilities where possible.

When aetiological tests are not available and when test results are not available immediately, providers need to apply a syndromic approach and make a clinical judgement when deciding whether and what treatment to provide. Syndromic management guidance is provided in *Section 5*, and key clinical and diagnostic information including on diagnostic tests is provided in *Section 4* for each infection. All information about provision of counselling and treatment is provided in *Section 2*. Details of recommended treatment regimens are outlined in *Appendix 2*.

TABLE 3: Types of diagnostic tests for STIs

Type of test	Description
Tests to detect the organism	
Microscopy	Wet preparation microscopy can be used to detect *C. albicans* (candidiasis), *T. vaginalis* (trichomoniasis), and bacterial vaginosis Gram stain can be used to observe the presence of intracellular diplococci to detect *N. gonorrhoeae* in men Immediate analysis and results can be provided while the client waits if equipment and expertise are available on-site
Culture	Culture can be used for *N. gonorrhoeae*, among others. Results can take several days, with the risk that clients waiting for results may be lost to follow-up Culture is also essential for *N. gonorrhoeae* to monitor antimicrobial resistance to inform treatment guidelines Transportation, sample collection, and storage must be rigorously controlled
Nucleic acid amplification tests (NAATs)	NAATs can be used for *C. trachomatis, N. gonorrhoeae, T. vaginalis,* and *M. genitalium* among others These tests use enzymatic methods to target the genetic material of the bacteria or virus then amplify it into billions of copies
Tests to detect the client's immune response to infection (antibodies)	
Enzyme-linked immunosorbent assays (ELISAs or EIAs) and direct fluorescence assays (DFAs)	Can be used to diagnose HIV These tests can have false-positive results, which may persist for some time after treatment but have the advantage in some cases that they can be provided as point-of-care tests (POCTs), potentially increasing the numbers of clients treated
Rapid diagnostic tests (RDTs), or POCTs	Available for syphilis and for HIV, or dual HIV/syphilis RDT Syphilis RDTs (also called rapid syphilis tests, or RSTs) test for the presence of treponemal antibodies, results available in 15 minutes. 85–98 per cent sensitive depending on the type of test Do not require access to specialized laboratory services

4. Common STIs, clinical features, and diagnostics

This section provides key information for the identification and diagnosis of infections by clinical features and diagnostic tests [14].

4.1 Curable bacterial STIs

4.1.1 Chlamydia trachomatis (chlamydia)

Chlamydia trachomatis causes chlamydia, the most common bacterial STI globally. Chlamydia includes a spectrum of diseases in a variety of sites (i.e. genital, ocular, lymph nodes, and bronchial). *C. trachomatis* can be transmitted through vaginal, anal, or oral sex. Many people infected with chlamydia will have no symptoms. Negative outcomes associated with untreated chlamydia infections include PID, ectopic pregnancy, tubal factor infertility, epididymitis, prostatitis, and others. Chlamydia can be easily treated and cured with antibiotics.

Clinical features and associated diseases

Women/female genitalia:

- Primary: Cervicitis, copious purulent discharge, friable cervix, dysuria, pelvic pain, cervical motion tenderness. Commonly asymptomatic.
- Sequelae: PID, endometritis, salpingitis, ectopic pregnancy, tubal factor infertility, preterm rupture of membranes, perihepatitis.

Men/male genitalia:

- Primary: Urethral discharge (urethritis), dysuria, testicular pain.
- Sequelae: Epididymitis, prostatitis, orchitis, infertility.

All sexes: Proctitis, pharyngitis, Reiter's syndrome. Asymptomatic infections are common.

Neonates: Conjunctivitis, chlamydial pneumonia.

Diagnostic tests

Diagnostic technologies for detection of chlamydia continue to advance. Due to the superior performance characteristics, NAATs are strongly recommended for diagnosis and screening of chlamydial infections. However, the choice of tests is dependent on the resources available and level of laboratory support.

- NAATs are the gold standard for chlamydia diagnosis, with higher sensitivity and specificity compared with other tests. They can also be used on urine samples. They are expensive.
- Rapid POCTs have lower sensitivity but may be useful in low-resource settings with a high prevalence of chlamydia, especially for community-based testing, and they enable the provision of immediate treatment.
- Culture has a suboptimal sensitivity and is not recommended for chlamydia diagnosis.
- Serology should only be used as a possible aid in the diagnosis and/or screening for complicated *C. trachomatis* infections, neonatal pneumonia, and LGV infections.

4.1.2 Lymphogranuloma venereum (LGV), caused by C. trachomatis L1–L3 serovars

LGV is found worldwide but is more prevalent in tropical and subtropical countries. LGV is caused by the distinct 'L' biovar of *C. trachomatis*, which contains serovars (L1, L2, L2a, L2b, L3) that are more invasive than those serovars responsible for the classical eye disease, trachoma (serovars A–C) and those causing non-gonococcal urethritis and associated infections of the genital tract (serovars D–K). Classically, LGV presents as a transient, herpetiform primary lesion of the external genitalia, but in many cases the lesion may pass unnoticed or manifest as an acute non-gonococcal urethritis in men or be completely asymptomatic in women as a result of primary infection of the cervix.

Clinical features and associated diseases

- All sexes: Inguinal lymphadenopathy (swelling/bubo) with or without an associated primary lesion (ulcer), proctitis. These symptoms are more commonly reported in men than women.
- In women, the perirectal and deep pelvic glands may become involved if the primary lesion is found on the

cervix, and the client may present with symptoms consistent with severe PID.

- Men who have sex with men (especially if they are living with HIV) may present with severe ulcerative proctitis or proctocolitis with rectal pain, blood-stained discharge, markedly abnormal anoscopy, fever, and lymphadenopathy.
- Complications: Perirectal abscesses, rectal strictures, fistulas, and chronic scarring. Chronic manifestations of the disease may result in blockage of the lymphatics draining the genitalia or rectum, causing oedema.

Diagnostic tests

NAATs or culture: The specimens of choice for both culture and NAATs for LGV include swabs taken directly from primary lesions (when present), urethral swabs, or first-catch urine specimens in men, endocervical swabs in women, and rectal swabs in men who have sex with men.

4.1.3 Neisseria gonorrhoeae (gonorrhoea)

N. gonorrhoeae causes gonorrhoea, the second most common bacterial STI globally. Gonorrhoea includes a spectrum of diseases in a variety of sites, including urogenital, pharyngeal, rectal, and conjunctival. *N. gonorrhoeae* is primarily transmitted through sexual contact (involving the anus, penis, vagina, mouth, or throat). Complications and sequelae associated with untreated *N. gonorrhoeae* infections include PID, ectopic pregnancy, infertility, penile oedema, epididymitis, and disseminated gonococcal infection. With antimicrobial resistant strains increasing, gonorrhoea is often treated with dual therapy of antibiotics.

Clinical features and associated diseases

Women/female genitalia:

- Uncomplicated gonorrhoea: Cervicitis with purulent discharge from cervical os and friable cervix, dysuria, lower abdominal tenderness. Commonly asymptomatic, particularly in the pharynx and rectum.
- Complicated gonorrhoea: Endometritis, salpingitis, Bartholin abscess, lymphangitis, tubo-ovarian abscess, ectopic pregnancy, infertility, preterm rupture of membranes, perihepatitis.

Men/male genitalia:

- Uncomplicated gonorrhoea: Urethral discharge (urethritis) which may be copious and purulent or scant and clear, dysuria. Can be asymptomatic, particularly in the pharynx and rectum.
- Complicated gonorrhoea: Penile oedema, Tyson's glands abscess, Cowper's glands abscess, seminal vesiculitis, epididymitis, orchitis, infertility (rare).

All sexes:

- Complicated gonorrhoea: Disseminated gonococcal infection.
- Rectum: Copious, purulent discharge, burning/stinging pain, tenesmus, blood in stools.
- Pharynx: Mild pharyngitis, mild sore throat, erythema.

Neonates: Ophthalmia neonatorum.

Diagnostic tests

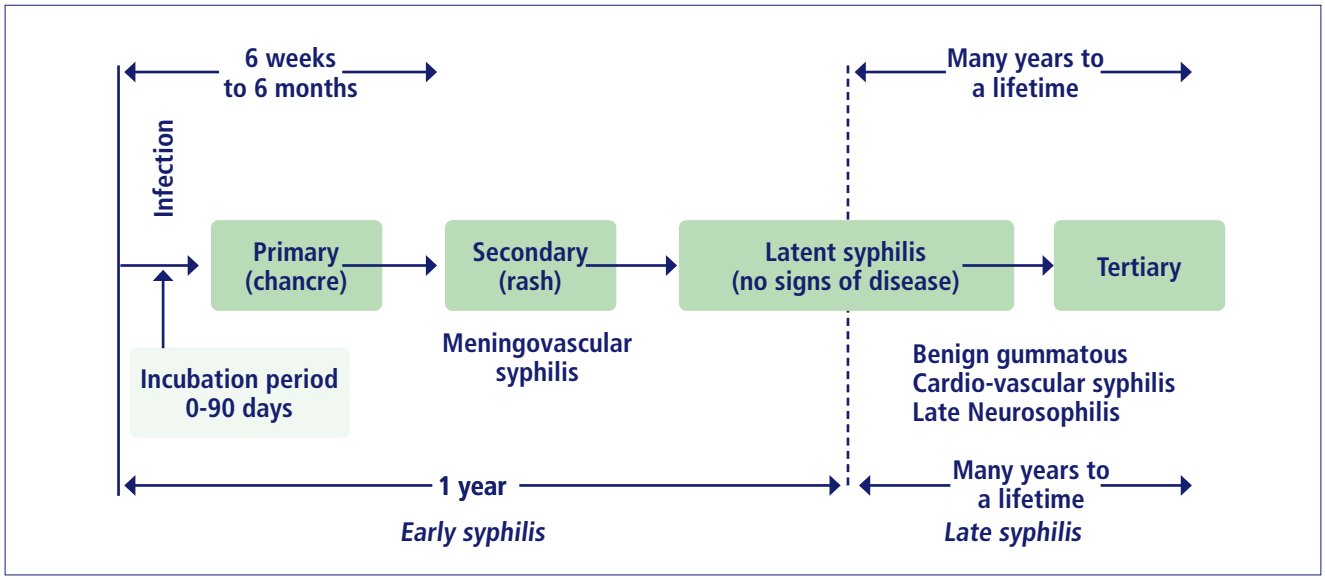
Laboratory procedures are needed for diagnosis, case finding, and test of cure. The diagnosis of gonorrhoea is established by identification of *N. gonorrhoeae* in genital or extra-genital secretions.

- NAATs are highly sensitive and specific diagnostic tests for gonorrhoea. They have superior sensitivity and specificity compared with culture, and can be conducted on urine, vulvovaginal, cervical, and urethral samples. NAATs can also be used on rectal and pharyngeal specimens but may have slightly lower sensitivity.
- Microscopy is sensitive and specific in symptomatic men with urethral discharge.
- Culture is sensitive and highly specific in optimized circumstances, inexpensive, and allows antimicrobial susceptibility testing.

4.1.4 Treponema pallidum (syphilis)

Syphilis, caused by the bacterium *T. pallidum*, is a chronic STI that continues to cause substantial morbidity and mortality. It is primarily transmitted through sexual contact when an open sore or 'chancre' is present during the early stages of infection, or transplacentally from a pregnant individual to the fetus. Untreated syphilis infections in pregnancy typically result in severe adverse pregnancy outcomes, such that universal screening for syphilis in pregnancy is recommended (see further information below). The course of untreated syphilis is shown in *Figure 1*. Tertiary syphilis, occurring many years after the initial infection, can cause significant damage, with manifestations classified as benign gummatous syphilis, cardiovascular syphilis, and neurosyphilis, which may coexist. The disease may progress significantly more rapidly in clients coinfected with HIV. Treatment for syphilis is highly effective and affordable with appropriate antibiotics.

FIGURE 1: The course of untreated syphilis: primary, secondary, latent, and tertiary stages



Source: Reproduced/translated with permission from Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus. Geneva: WHO; 2013.

Clinical features and associated diseases

All sexes:

- Primary: Primary chancre (typically a single, painless genital lesion), usually with bilateral inguinal lymphadenopathy (typically discrete and non-tender).
- Secondary: Evenly distributed, non-irritant skin rash that may be macular, papular, or papulo-squamous (often seen on the palms of the hands and soles of the feet). In warm, moist areas the rash may become enlarged to form condylomata lata, and on mucous surfaces form superficial grey-white serpiginous lesions known as 'snail-track ulcers'. There may also be generalized lymphadenopathy, fever, headache, and general malaise.
- Tertiary: Gummas (lesions) can occur in any organ of the body, but most frequently in skin, cartilage, and bone (benign gummatous syphilis), the walls of the aorta (cardiovascular syphilis), the cerebral vessels (meningovascular syphilis), or the brain and spinal cord (neurosyphilis).

Women/female genitalia: Spontaneous abortion, stillbirth, premature delivery.

Neonates: Stillbirth, congenital syphilis.

Diagnostic tests

Serological tests:

- *Treponemal tests:* The vast majority of commercially available POCTs or RDTs for syphilis, also known as RSTs. Other treponemal tests include FTA-Abs, *T. pallidum* haemagglutination assay, and *T. pallidum* passive particle agglutination assay.
- *Non-treponemal or reagin tests:* These include rapid plasma reagin (RPR) and Venereal Disease Research Laboratory (VDRL) tests.

Direct detection (using specimens obtained from skin lesions or tissues):

- Dark-field microscopy: The only POCT that is capable of establishing a direct diagnosis of syphilis in cases of adult primary or secondary or early congenital disease. The ideal specimen is a serous exudate from active lesions, free of red blood cells.
- Direct immunofluorescence, specifically the direct fluorescent antibody test: Specimen collection is the same as for dark-field microscopy. Both the specificity and sensitivity are superior to that of dark-field microscopy.
- NAATs: Several polymerase chain reaction (PCR) assays have been developed and successfully used to detect *T. pallidum*-specific DNA target sequences in primary and secondary lesions. They can be used to examine specimens from any lesion exudate, tissue, or body fluid, and the specimen can be fresh, frozen, or fixed and paraffin-embedded. They can also be applied to the diagnosis of congenital syphilis and also neurosyphilis.

Note on testing for congenital syphilis: Any skin and mucous membrane lesions present in the newborn of a seropositive individual should be examined by dark-field microscopy, direct immunofluorescence, or PCR for direct evidence of infection with *T. pallidum*. For information on serological testing in neonates, refer to the WHO laboratory manual [14].

Syphilis screening and treatment in pregnancy

Perinatal transmission of syphilis (congenital syphilis) is usually devastating to the fetus if maternal primary or secondary syphilis infection is not detected and treated sufficiently early in pregnancy, ideally before the second trimester. Latent (asymptomatic) syphilis infections in pregnancy also cause serious adverse pregnancy outcomes in more than half of cases.

WHO's recommendations and suggestions for syphilis screening and treatment in pregnant individuals are as follows [15]:

- *In all settings, regardless of local prevalence of syphilis:* Screen all pregnant individuals for syphilis at their first antenatal care visit.
- *In settings with low coverage of syphilis screening and treatment for pregnant individuals, high loss to follow-up of pregnant individuals, or limited laboratory capacity:* Use on-site tests (Strategies A, B and C, below) rather than the standard off-site laboratory-based screening and treatment strategy.
- *In settings with a low prevalence of syphilis (below 5 per cent):* Use a single on-site RST (also known as RDT or POCT) to screen pregnant individuals (Strategy A) rather than a single on-site RPR test (Strategy B).
- *In settings with a high prevalence of syphilis (5 per cent or greater):* Use an on-site RST and, if positive, provide a first dose of treatment and an RPR test, and then, if the RPR test is positive, provide treatment according to duration of syphilis (Strategy C).

Strategy A: Single on-site RST followed by treatment if positive

The on-site RST (treponemal test) can be provided as a single test and treatment can be given during the same visit based on the results. The RST does not distinguish between the presence of previously adequately treated syphilis and untreated syphilis. Therefore, pregnant individuals who test positive on the RST and are treated adequately for syphilis will likely still test positive on a subsequent RST (e.g. during a subsequent pregnancy). Pregnant individuals who tested positive on a previous

RST (e.g. during a previous pregnancy) could therefore be treated again for syphilis without repeating the RST if the risk of reinfection is considered high. Alternatively, a quantitative RPR test could be performed in these clients instead of an RST (i.e. to determine the titre).

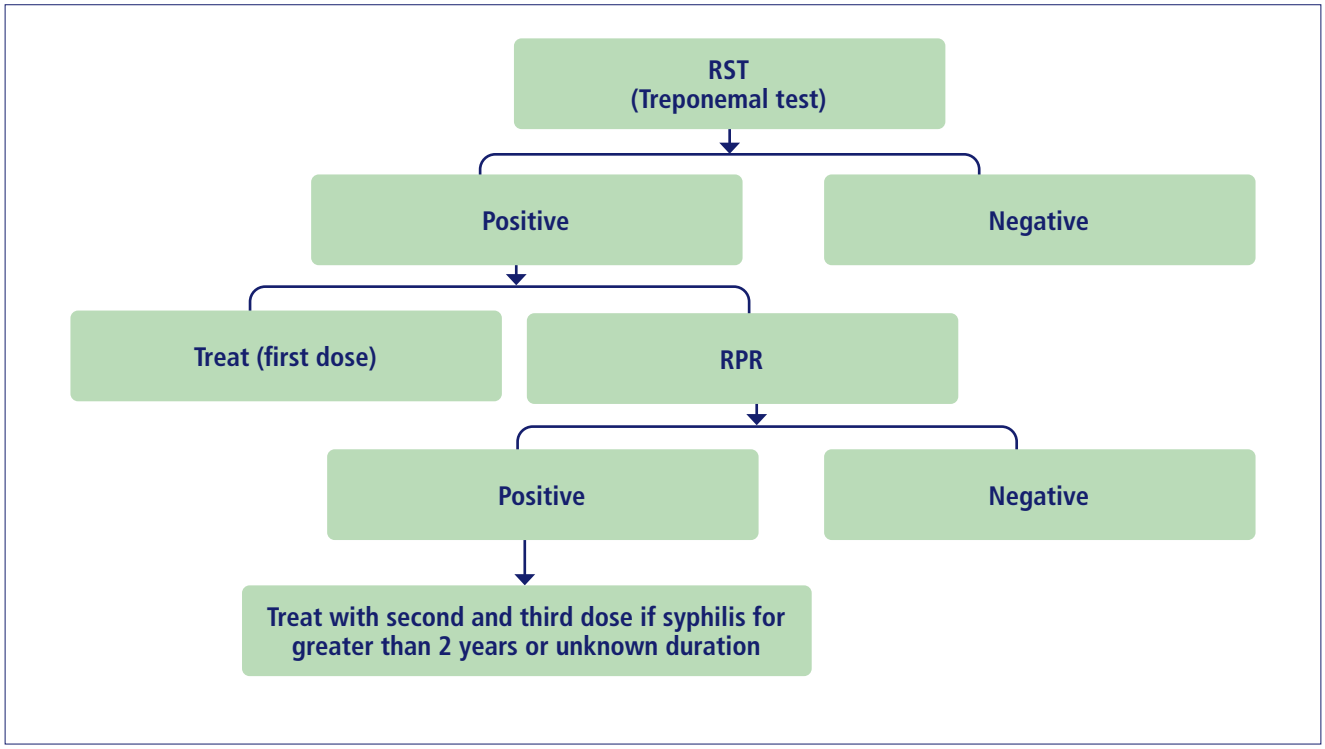
Strategy B: Single on-site RPR test followed by treatment if positive

The RPR test in this strategy is a single, on-site, rapid test, allowing treatment to be provided the same day. This means that (as with Strategy A), a pregnant client can receive testing and treatment during the same visit. If the RPR is negative, it can be repeated after approximately 1 month to obtain a correct (positive) diagnosis in cases where early syphilis was not yet detected on the first RPR test, since syphilis is only detectable by RPR approximately 1 month after the onset of the primary chancre. Provision of on-site RPR will require a rotator, blood centrifuge, and a refrigerator for reagents, and electricity to operate this equipment.

Strategy C: On-site RST followed (if positive) by first dose and RPR test (*Figure 2*)

An on-site RST is provided to the pregnant client first. If the result is seronegative, it can be interpreted as no syphilis infection and no treatment or further testing is given. If the on-site RST is positive, immediate treatment should be given to prevent adverse outcomes of pregnancy. An RPR test should then be done (on- or off-site, depending on available resources), and if this test is also positive then the client should be treated appropriately for syphilis according to the determined duration of their infection. If the RPR is negative, however, it can be repeated after approximately 1 month to obtain a correct (positive) diagnosis in cases where early syphilis was not yet detected on the first RPR test. This strategy may require the client to make two visits to the clinic if their first test was positive (i.e. to receive the results of the RPR test if it was not a rapid on-site test).

FIGURE 2: Flowchart to illustrate Strategy C



Source: WHO [15]: WHO guideline on syphilis screening and treatment for pregnant women. Geneva: WHO; 2017. Licence: CC BY-NC-SA 3.0 IGO.

4.1.5 Haemophilus ducreyi (chancroid)

Chancroid, caused by *Haemophilus ducreyi*, is transmitted exclusively by sexual contact with skin (except in rare instances of laboratory-acquired infection). The incubation time is 4–10 days. It is approximately seven times more common in men than women, and transmission is linked to high numbers of sexual partners. Chancroid was previously very common in certain parts of the world, but its prevalence has declined dramatically since the 1990s due to better access to antimicrobial agents, the roll-out of syndromic management, improved healthcare for sex workers, and sexual behavioural change in the era of HIV infection.

Clinical features and associated diseases

- All sexes: Painful, irregular genital ulcers with undermined edges (initially a tender papule, which ulcerates within 2 days) and multiple lesions may merge to form very large ulcers. This may be accompanied by unilateral painful inguinal lymphadenitis, which may lead to spontaneous rupture of suppurating lymph nodes (buboes), particularly if there has been a delay in seeking care or receiving the correct diagnosis.
- Atypical presentations of chancroid are common, and the disease can be easily confused with other genital ulcer diseases (GUDs), particularly genital herpes.
- Perianal chancroid may occur in men who have receptive sex with men and also among women who have engaged in penile–anal sex.

Diagnostic tests

- Culture of *H. ducreyi:* Technically demanding procedure with low yield outside of highly skilled laboratories used to working with the pathogen.
- NAATs: For diagnosis of chancroid.
- Antigen detection and nucleic acid probe technologies: Several research-based techniques have been described, including the use of monoclonal antibody-based antigen detection and DNA probes.
- Direct microscopy: Low sensitivity and low specificity.
- Serological assays: Those that are currently available are only useful for sero-epidemiological research purposes.

4.1.6 Klebsiella granulomatis (donovanosis, also known as granuloma inguinale)

Donovanosis is a chronic infection involving the skin, mucous membranes, and lymphatic system of the genitalia and perineal area. Its occurrence is limited to certain countries and regions, including Brazil, the Caribbean, India, Papua New Guinea, and southern Africa. Donovanosis is principally transmitted by sexual contact but has low infectivity. The incubation time varies from 1–12 weeks. Donovanosis may spread haematogenously to bones, joints, and the liver, and cutaneous lesions can also occur.

Clinical features

All sexes:

- Initially a subcutaneous nodular swelling erodes the skin surface (progressing slowly) to form a granulomatous genital ulcer with a well-defined border, which bleeds easily on contact, and which may become painful when a secondary bacterial infection develops, potentially contributing to necrotic debris in the ulcer.
- Ulcerative lesions may also occur in the inguinal and perianal areas and may spread to extragenital body sites. Genital and perianal lesions at various stages may resemble lesions formed by other conditions, such as syphilis, chancroid, carcinoma, and amoebiasis.
- New lesions may be formed by autoinoculation, and inguinal lymph nodes may become enlarged as a result of secondary infection (pseudobuboes).
- Donovanosis may spread haematogenously to bones, joints, and the liver.

Men/male genitalia: Urethral discharge (non-gonococcal urethritis).

Women/female genitalia: Cervicitis, endometritis, PID.

Diagnostic tests

- Microscopy: Visualization of Donovan bodies in stained smears obtained from clinical lesions (using a simple, rapid [1-minute] Giemsa method). Donovan bodies have also been identified from Papanicolaou (Pap) smears used in routine cervical cytology screening.
- Histopathology: Visualization of Donovan bodies in stained histological sections of tissue biopsies – may be helpful in the differential diagnosis between donovanosis and other conditions.
- NAATs: A research-based diagnostic PCR has been developed, which has been refined further into a colorimetric PCR test. However, these assays are not available in most countries for routine diagnostic purposes.

4.1.7 Mycoplasma genitalium (MG, also known as Mgen)

M. genitalium is a common cause of urethritis in men. In most settings, it is more common than *N. gonorrhoeae* but less common than *C. trachomatis.* In women, it can be found in the vagina, cervix, and endometrium and, like chlamydial and gonococcal infections, *M. genitalium* infections in women are commonly asymptomatic. *M. genitalium* should be suspected in cases of persistent or recurrent urethritis and may also be considered in persistent or recurrent cases of cervicitis and PID. Infection occurs through genital-to-genital or genital-to-rectal contact.

Clinical features

- *Men/male genitalia:* Urethral discharge (non-gonococcal urethritis).
- *Women/female genitalia:* Cervicitis, endometritis, PID.
- *All sexes*: May be asymptomatic, may cause proctitis.

Diagnostic tests

- NAAT from urine, urethral, anorectal, oropharyngeal, vaginal, or cervical swabs.
- Culture: Extremely slow (several months), challenging, and insensitive.
- Other: To date, no serological assays, antigen detection assays, or POCTs have proven useful for diagnosis of urogenital *M. genitalium* infections.

4.2 Curable protozoal STIs

4.2.1 Trichomonas vaginalis (trichomoniasis)

T. vaginalis is a motile, flagellated protozoan parasite that causes the STI trichomoniasis. Trichomoniasis is the most common curable STI worldwide. *T. vaginalis* is most commonly transmitted sexually through penis-to-vagina or vulva-to-vulva contact. Trichomoniasis is simple to cure with a single dose of appropriate antibiotics.

Clinical features

Women/female genitalia:

- Primary: Asymptomatic in at least 50 per cent of cases. Vaginosis with profuse, fulminant, purulent or frothy white to yellow discharge, dysuria, pelvic pain, itching.
- Sequelae: Adverse outcomes of pregnancy (e.g. low birthweight babies, preterm birth), increased risk of HIV transmission and acquisition.

Men/male genitalia:

- Primary: Asymptomatic in 70–80 per cent of cases. Urethral discharge (non-gonococcal urethritis), dysuria, testicular pain.
- Sequelae: Possible epididymitis and prostatitis.

Neonates: Low birthweight.

Diagnostic tests

Symptomatic trichomoniasis can be diagnosed using the syndromic approach based on:

- Odour, quality, and quantity of vaginal discharge (fulminate or frothy white discharge).
- Vaginal pH (usually >6.0).
- Possible presence of cervical friability (punctate cervical friability: 'strawberry cervix').

However, use of diagnostic testing is recommended due to the high proportion of asymptomatic cases:

- NAATs: Superior sensitivity relative to other diagnostic methods and very high specificity (as do other methods).
- Wet preparation (wet mount) microscopy: With this first-line diagnostic method, a positive result provides a definitive diagnosis with high specificity when correctly performed and interpreted (but sensitivity is low, except in symptomatic clients).
- Culture: Vaginal swabs, urethral swabs, and urine sediment from men are specimens licensed for culture. This method requires up to 5–7 days post-collection, and determination of positive results requires microscopy – this increases the sensitivity of the test beyond that of wet preparation microscopy, and specificity is also very high.
- Antigen detection: POCT for vaginal swab samples only. The latest generation of these tests has better sensitivity than microscopy and can provide results in approximately 30 minutes, and specificity is also very high.

4.3 Endogenous reproductive tract infections (not sexually transmitted)

4.3.1 Candida albicans (candidiasis)†

Both symptomatic and asymptomatic *C. albicans* infections are common in women. Predisposing factors for colonization and inflammation include changes in reproductive hormone levels associated with menstrual periods, pregnancy, and oral contraceptives; use of antibiotics; diabetes; and immunosuppression. Although sexual transmission of *C. albicans* may occur, the gastrointestinal tract has also been implicated as a source of infection. Men may acquire candidiasis from a sexual partner. They typically develop an allergic response to candidal antigen, although fulminant infection may be seen more frequently in clients with the predisposing factors.

Clinical features and associated diseases

- *Women/female genitalia:* Vulvovaginitis with an odourless, thick, white, curd-like ('cottage cheese') vaginal discharge, vulval and vaginal itching, burning sensation in the vulva, dysuria, and erythema of the labia and vulva. Also known as vulvovaginal candidiasis (VVC) or yeast infection.
- *Men/male genitalia:* Superficial infection of the glans penis. Can cause balanitis or balanoposthitis and rarely urethritis.

Diagnosis of VVC

- Clinical examination of symptoms (see above): In women with classic signs, it is often reasonable to give therapy on a presumptive clinical diagnosis without further confirmation (see *Section 5*).
- Microscopy: Detection of typical mycelia and yeast cells by wet mount or potassium hydroxide microscopy (which increases sensitivity) can be performed on-site and has a very high positive predictive value.
- Gram-stained smear and detection of budding yeast cells and pseudohyphae is preferred in some centres for the determination of candidiasis.

4.3.2 Bacterial vaginosis

Bacterial vaginosis (BV) is the most common cause of vaginal discharge, which is characteristically malodourous and is common among women of reproductive age as well as those who are post-menopausal. This syndrome is related to alterations in the vaginal ecology causing an increase in the local pH, resulting from a reduction in the protective hydrogen peroxide-producing lactobacilli and an increase in the numbers of various anaerobes, *such as Mycoplasma hominis* and *Gardnerella vaginalis*. It is an endogenous rather than a sexually transmitted infection, and symptomatic episodes have been linked to menstruation, presence of an IUD, and genital douching. Sexual activity is a risk factor for its acquisition (i.e. it is associated with an increased number of recent and lifetime partners, and having a new sexual partner).

† Vulvovaginal candidiasis is caused by the fungus *Candida albicans* in approximately 85 per cent of cases; *C. glabrata* is responsible for the remaining 15 per cent.

Clinical features

- Increased quantities of malodorous vaginal discharge.

Diagnostic tests

Diagnosis is based on the presence of at least three of the following four clinical criteria (Amsel criteria):

- homogenous white to grey adherent vaginal discharge
- vaginal fluid pH >4.5
- positive whiff/amine test (i.e. the release of a fishy amine odour from the vaginal fluid when mixed with 10 per cent potassium hydroxide solution)
- 'clue cells'‡ visible on microscopy

Diagnosis can also be achieved by assessment or scoring of bacteria in a Gram-stained vaginal smear.

4.4 Persistent viral infections (for HIV, see *Chapter 7*)

4.4.1 Genital herpes simplex virus (HSV)

Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) can both cause genital HSV infection, although HSV-1 is more typically associated with oral HSV infection than genital infection. Genital herpes is primarily transmitted by skin-to-skin contact. There is no cure for herpes. It is a life-long infection that periodically causes outbreaks of genital ulcers (or sores) and inflammation. Treatment is available to reduce symptoms and decrease the risk of transmission to a partner.

Clinical features and associated diseases

- *All sexes*: Anogenital vesicular lesions and ulcerations, genital pain and itching, dysuria, fever, headache, myalgias and malaise, cervicitis, tender inguinal and femoral lymphadenopathy.
- *Neonates*: Neonatal herpes can be transmitted vertically during vaginal delivery. This can result in disseminated infection, central nervous system involvement, and possibly neonatal death.

Primary infection/first clinical episode: Most initial infections are asymptomatic or atypical, and therefore undiagnosed. Only 10–25 per cent of primary infections give rise to the classical syndrome 4–7 days after sexual exposure. This includes bilateral clusters of erythematous papules, vesicles, or ulcerations on the external genitalia, in the perianal region, or on the buttocks. Clients present with genital pain and itching and 80 per cent of women also report dysuria. Constitutional symptoms, such as fever, headache, myalgias, and malaise are common. Cervicitis and tender inguinal and femoral lymphadenopathy frequently accompany initial infections. Over a period of 2–3 weeks, new lesions appear and existing lesions progress to vesicles and pustules and then coalesce into ulcers before crusting over and healing. Atypical presentations of infections due to HSV-2 may include small erosions and fissures, as well as dysuria or urethritis without lesions [16].

Recurrent episodes: Recurrences are often preceded by prodromal symptoms (including tingling, paresthesia, and pain), are characterized by fewer lesions than the first episode, and are usually present unilaterally and without systemic symptoms. Pain is less severe during recurrences, and the lesions heal in 5–10 days without antiviral treatment. Immunocompromised clients, including those with HIV, generally have more frequent recurrences with more severe symptoms [16].

Diagnostic tests

Genital herpes is often diagnosed clinically; however, laboratory diagnosis is necessary to differentiate between HSV-1 and HSV-2, to diagnose other causes of genital ulceration (e.g. other STIs that cause painful genital ulcer, such as syphilis), and to detect non-infectious causes (e.g. Crohn's disease). The choice of test and how to interpret the results are important considerations.

‡ Clue cells are "squamous epithelial cells covered with many small coccobacillary organisms, giving a stippled, granular aspect; the edges of these epithelial cells are not clearly defined, owing to the large number of bacteria present and the apparent disintegration of the cells" [14].

Direct diagnosis from clinical specimens (material from lesions)

- Direct examination of specimens and cytological examination using conventional staining procedures: Low sensitivity and specificity for diagnosis of herpes virus infection.
- Viral antigen detection: Viral antigen in material from mucocutaneous lesions can be detected using direct immunofluorescence, immunoperoxidase staining, or enzyme-linked immunosorbent assay (ELISA). Rapid POCTs for HSV antigen detection are commercially available.
- Viral culture: HSV isolation in cell culture has been the cornerstone of HSV diagnosis, but it is feasible only in specialized laboratories at high cost and is resource intensive. It has high specificity but lower diagnostic sensitivity than NAATs.
- NAATs: NAATs are the most sensitive test currently available to detect HSV in genital samples. They are up to four times more sensitive, less dependent on collection and transportation conditions, and more rapid than viral culture. Strict validation of in-house PCRs or commercially available NAATs in individual settings is important.

Indirect serological methods

- Serological testing is recommended as an aid to diagnosis of genital herpes in clients with recurrent genital symptoms, atypical lesions, or with healing lesions and negative HSV cultures.
- Rapid POCTs exist for detection of HSV-2-specific antibodies, using capillary blood from a finger stick (or serum). These tests have good sensitivity and specificity and can provide results while the client waits; however, they are expensive compared with ELISA-based methods.

Serological testing for HSV is not routinely recommended in asymptomatic clients, but is indicated in the following groups:

- History of recurrent or atypical genital disease when direct virus detection methods have been negative.
- First-episode genital herpes, where differentiating between primary and established infection guides counselling and management.
- Sexual partners of clients with genital herpes, where concerns are raised about transmission.

HSV serology and pregnancy:

- Testing of asymptomatic pregnant individuals is not routinely recommended but is indicated when there is a history of genital herpes in the partner.
- HSV-1 and/or HSV-2 seronegative clients should be counselled about strategies to prevent a new infection with either virus type during pregnancy.

4.4.2 HPV types 6 and 11 (anogenital warts, also known as condylomata acuminata)

Transmission of genital HPV generally occurs readily via skin-to-skin genital contact. There are more than 200 different HPV types, of which 40 are known specifically to infect the anogenital mucosa of humans. While most people never develop symptoms and most HPV infections go away by themselves, HPV can cause genital warts and certain types of cancer. HPV types frequently detected in the anogenital tract are subdivided into low-risk and high-risk types, based on their relative risk for the rare complication of neoplasia.[§] Low-risk HPV types are typically found in low-grade intraepithelial lesions (non-precancerous lesions), as well as anogenital warts. HPV types 6 and 11 account for 85–90 per cent of anogenital warts. Anogenital warts are benign exophytic, papular, or flat growths that may occur anywhere in the anogenital area. They are extremely common, particularly in young people commencing sexual activity. In rare cases, lesions may cause problems owing to size and obstruction, but the most common problems are cosmetic and psychosocial. Lesions tend to recur after treatment. Acquisition of HPV types 6 and 11 can be effectively prevented by administration of HPV vaccination.

§ The high-risk HPVs are found in low- and high-grade lesions, as well as cancers of the cervix and other anogenital sites (vulva, vagina, anus, penis). Collectively, HPV 16 and 18 are responsible for approximately 70 per cent of all cervical cancer cases worldwide. For information about cervical cancer and precancer, and HPV vaccination, refer to *Chapter 8: Gynaecology and other reproductive healthcare*.

Clinical features

- *Men/male genitalia:* Penile and anal warts.
- *Women/female genitalia*: Vulval, anal, and cervical warts.

Diagnostic tests

- Clinical diagnosis.

4.4.3 Hepatitis B virus

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is a major global health problem and can cause both acute and chronic disease. The virus is most commonly transmitted perinatally, as well as through contact with blood (e.g. needlestick injury, tattooing, piercing, menstrual blood) or other infected body fluids (e.g. saliva, vaginal and seminal fluids). Sexual transmission of hepatitis B is most likely in unvaccinated men who have sex with men and in heterosexual individuals with multiple sexual partners or contact with sex workers. Chronic hepatitis B infection is defined as persistence of hepatitis B surface antigen for 6 months or more, and it can lead to liver cirrhosis and primary liver cancer, which can be fatal. Hepatitis B can be prevented by a vaccine that is 98–100 per cent effective. WHO recommends that all people are immunized against hepatitis B as infants [6].

Clinical features and associated diseases

Acute hepatitis B infection:

- When newly infected, most people do not experience any symptoms, while others have acute illness with symptoms lasting several weeks: yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting, and abdominal pain.
- A small subset of people with acute hepatitis can develop acute liver failure, which can be fatal.

Chronic hepatitis B infection:

- 20–30 per cent of those who develop chronic hepatitis B infection experience major complications, i.e. cirrhosis (scarring of the liver) or hepatocellular carcinoma (liver cancer).

Diagnostic tests

- The WHO 2017 testing guidelines [17] recommend the use of a single quality-assured serological in vitro diagnostic test to detect hepatitis B surface antigen (HBsAG) (to screen for HBV exposure). This test can be an RDT or a laboratory-based enzyme immunoassay (EIA), chemiluminescence immunoassay (CLIA), or electrochemiluminescence immunoassay (ECLIA). RDTs used should meet minimum performance standards and be delivered at the point of care to improve access and linkage to care and treatment.
- Nucleic acid testing technologies are typically used to detect the presence of the virus; determine if the infection is active and if the individual would benefit from antiviral treatment; determine when antiviral treatment should be discontinued (due to non-response or resistance); or to confirm effective suppression (HBV).
- Acute HBV infection is characterized by the presence of HBsAg and immunoglobulin M (IgM) antibody to the core antigen, HBcAg. During the initial phase of infection, individuals are also seropositive for hepatitis B e antigen (HBeAg). HBeAg is usually a marker of high levels of replication of the virus. The presence of HBeAg indicates that the blood and body fluids of the infected individual are highly infectious.
- Chronic infection is characterized by the persistence of HBsAg for at least 6 months (with or without concurrent HBeAg). Persistence of HBsAg is the principal marker of risk for developing chronic liver disease and liver cancer (hepatocellular carcinoma) later in life.
- Recent data caution on the need to test for HBV infection and consider antiviral therapy prior to starting direct-acting antiviral therapy in HBV/HCV

coinfected clients because of a potential risk of HBV reactivation and worsening of liver disease.

- Non-invasive assessment of liver disease stage at baseline and during follow-up: Aspartate aminotransferase (AST)-to-platelet ratio index (APRI) is recommended as the preferred non-invasive test to assess for the presence of cirrhosis (APRI score >2 in adults) in resource-limited settings. Transient elastography (e.g. FibroScan) or FibroTest may be the preferred non-invasive tests in settings where they are available and cost is not a major constraint [18].

Notes:

- It is not possible, on clinical grounds, to differentiate hepatitis B from hepatitis caused by other viral agents, hence laboratory confirmation of the diagnosis is essential.
- Many people are diagnosed only when they already have advanced liver disease. Among the long-term complications of HBV infections, cirrhosis and hepatocellular carcinoma cause a large disease burden. Liver cancer progresses rapidly, and since treatment options are limited, the outcome is generally poor. In low-income settings, most people with liver cancer die within months of diagnosis.
- WHO recommends that all blood donations be tested for hepatitis B to ensure blood safety and avoid accidental transmission to people who receive blood products.
- Refer to the full WHO guidelines for information on who (and how) to test for chronic infection, and further details on diagnostic tests [17].

4.4.4 Hepatitis C virus

The hepatitis C virus (HCV) can cause both acute and chronic hepatitis (liver disease), ranging in severity from a mild illness lasting a few weeks, to a serious, life-long illness. Hepatitis C is a major cause of liver cancer. HCV is a bloodborne virus, most commonly transmitted through sharing injecting equipment for drug use; reuse or inadequate sterilization of medical equipment, especially syringes and needles in healthcare settings; transfusion of unscreened blood and blood products; during pregnancy from the pregnant individual to the fetus; and sexual practices that lead to exposure to blood (e.g. among men who have sex with men, particularly those with HIV infection or those taking PrEP against HIV infection). Although it is less common, HCV can be transmitted sexually as well as perinatally. The incubation period for hepatitis C ranges from 2 weeks to 6 months. Most deaths from chronic hepatitis C are caused by liver cirrhosis and primary liver cancer. Research into a vaccine against HCV is ongoing. Antiviral medicines can cure more than 95 per cent of people with hepatitis C infection, thereby reducing the risk of death, but access to diagnosis and treatment is low [17,19].

Clinical features and associated diseases

- Initial infection: Approximately 80 per cent of people do not exhibit any symptoms. Those who are acutely symptomatic may exhibit fever, fatigue, decreased appetite, nausea, vomiting, abdominal pain, dark urine, grey-coloured faeces, joint pain, and jaundice (yellowing of skin and the whites of the eyes).
- Long-term sequelae: Chronic, life-long liver disease, liver cirrhosis, and hepatocellular carcinoma (primary liver cancer).

Diagnostic tests

- WHO's 2017 guidelines [17] recommend the use of a single quality-assured serological in vitro diagnostic test to detect HCV antibody (to screen for HCV exposure). This test could be an RDT or a laboratory-based enzyme immunoassay (EIA), chemiluminescence immunoassay (CLIA), or electrochemiluminescence immunoassay (ECLIA). RDTs used should meet minimum performance standards and be delivered at the point of care to improve access and linkage to care and treatment.
- If the test is positive for anti-HCV antibodies, a nucleic acid test for HCV ribonucleic acid (RNA) is needed to confirm chronic infection (about 30 per cent of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment, but they will still test positive for anti-HCV antibodies). Nucleic

acid tests are also used to determine when antiviral treatment should be discontinued (due to non-response or resistance) and to confirm virological cure (HCV).

- Recent data caution on the need to test for HBV infection and consider antiviral therapy prior to starting direct-acting antiviral therapy in HBV/HCV coinfected clients because of a potential risk of HBV reactivation and worsening of liver disease.

Notes:

- Clients diagnosed with chronic HCV infection should have an assessment of the degree of liver damage (fibrosis and cirrhosis) by liver biopsy or through a variety of non-invasive tests.
- The degree of liver damage is used to guide treatment decisions and management of the disease.
- WHO recommends treatment with pan-genotypic direct-acting antivirals for persons over age 12. Treatment can cure most people after 12–24 weeks of therapy, depending on the absence or presence of cirrhosis.
- Because new HCV infections are usually asymptomatic, few people are diagnosed when the infection is recent. In those people who go on to develop chronic HCV infection, the infection is also often undiagnosed because it remains asymptomatic until decades after infection when symptoms develop secondary to serious liver damage.
- Refer to the full WHO guidelines for information on who (and how) to test for chronic infection, and further details on diagnostic tests [17].

4.5 Emerging infections that are potentially sexually transmissible

Other infectious pathogens are emerging as being potentially sexually transmissible, including Ebola and Zika viruses. Healthcare providers have a role to play in providing appropriate counselling for safer sex practices and advising clients on the need for testing and to avoid travel to affected regions and unprotected sex with those returning from these areas. Other viruses of note include human T-lymphotropic virus type 1 (HTLV-1).

Ebola virus disease is a rare but severe and often fatal illness, with death rates during outbreaks ranging from 25 per cent to 90 per cent. It is generally transmitted through contact with infected animals or with bodily fluids of infected humans or contact with items contaminated with such bodily fluids. WHO states that: "Sexual transmission of the Ebola virus, from males to females, is a strong possibility, but has not yet been proven. Less probable, but theoretically possible, is female to male transmission. More surveillance data and research are needed on the risks of sexual transmission, and particularly on the prevalence of viable and transmissible virus in semen over time" [20].

WHO's interim advice is that, until their semen has twice tested negative for Ebola virus (with one week between RT-PCR tests), or until 12 months have passed since the onset of symptoms, male Ebola virus disease survivors should abstain from all types of sex or practice safer sex with correct and consistent condom use. All Ebola survivors and their sexual partners should thus receive appropriate counselling and be provided with condoms, and males should be offered monthly testing starting at 3 months after disease onset [20].

Zika virus infection during pregnancy can cause congenital abnormalities, including microcephaly, and is also associated with preterm birth and miscarriage (see *Chapter 9: Maternal health*). Most Zika virus infections are asymptomatic, but it can cause generally mild symptoms for up to 1 week, including fever, rash, conjunctivitis, muscle and joint pain, malaise, or headache. Zika virus is primarily transmitted through bites from infected mosquitos from the *Aedes* genus, but it can also be transmitted through sex. WHO states that: "sexual transmission of Zika virus is much more likely from men to women than from women to men, and same-sex transmission, from man to man, has only been documented once" [21].

Advice for the prevention of sexual transmission of Zika virus needs to consider the current and projected rates of mosquito-borne transmission of Zika virus in geographic areas. In areas with no mosquito-borne transmission, sexual transmission from returning

travellers is one of the main routes of Zika virus transmission. WHO has issued detailed guidelines for the prevention of sexual transmission of Zika virus, which include the following:

- People living in areas with ongoing Zika virus transmission AND people travelling to or returning from areas with ongoing Zika virus transmission, and their sexual partners, particularly pregnant individuals, should be informed about the risk of sexual transmission of Zika as well as the risk of vertical transmission to the fetus during pregnancy, and should have access to a full range of contraceptive healthcare, including emergency contraception, to support an informed choice about preventing pregnancy.
- They should also be aware of the potential risk of sexual transmission of Zika virus after known or presumptive infection (3 months for men, 2 months for women) and advised to use condoms correctly and consistently or abstain from sex to prevent sexual transmission, especially during pregnancy [21].

Human T-lymphotropic virus type 1 (HTLV-1) can cause adult T-cell leukaemia/lymphoma (ATL) and a progressive nervous system condition known as HTLV-1-associated myelopathy or tropical spastic paraparesis (HAM/TSP). HTLV-1 is transmitted primarily through infected bodily fluids including blood, breast milk, and semen. Risk factors include unprotected sex, injecting drugs, and transplantation of tissue, blood, and blood products [22].

5. Syndromic management

Syndromic management is widely used to manage people with symptoms of STIs. In most resource-limited settings, syndromic management flow charts are still the standard of care where laboratory diagnosis is not available or, where it is available, getting results takes several days. Although the STI syndromic approach has some shortcomings, it remains an essential component of managing people with symptoms of STIs. Given the existence of RDTs, the syndromic approach can be strengthened by integrating them where possible.

The symptoms and signs documented during history-taking and physical examination can be grouped together into syndromes. Syndromic management provides treatment for the pathogen(s) most commonly responsible for causing the syndrome(s). In some cases, the syndrome may be attributable to more than one possible infection. This approach is mostly used in settings where aetiological tests and laboratory diagnosis are not available to manage clients reporting symptoms or in whom suspicious clinical signs are noted on exam.

For effective syndromic management, providers should know the local disease patterns, antimicrobial susceptibilities, and the appropriate treatment based on national guidance. Flow charts for syndromic management of STIs (see *Appendix 3*) can give clear step-by-step instructions culminating in one or more effective treatment regimens, based on the symptoms, signs, and/or risk factors, with the determination of the most likely infection/pathogen based on the epidemiology of the country, region, or population.

STI risk assessment is particularly important for syndromic management of abnormal vaginal discharge, which can also be caused by non-sexually transmitted (endogenous) RTIs (see *Section 4.3*). For any client with lower abdominal pain or scrotal swelling, the need for emergency surgery must be ruled out, and an early follow-up visit arranged if uncertain.

Although the STI syndromic approach has some shortcomings, it remains an essential component of managing people with symptoms of STIs [23].

Treatment according to national STI/RTI treatment guidelines should start as soon as possible once a syndromic diagnosis has been made. Wherever possible, single-dose oral treatment is recommended to ensure compliance and cure (or suppression for viral STIs). For details per infection/organism, including clinical features and diagnosis, see *Section 4.3*; for treatment information see *Appendix 2*.

5.1 Urethral discharge syndrome

Urethral discharge from the penis is commonly caused by *N. gonorrhoeae* and/or *C. trachomatis* and/or non-gonococcal and non-chlamydial pathogens, such as *M. genitalium* and *T. vaginalis*. Clients with urethritis (inflammation of the urethra) often present with urethral discharge with or without dysuria (pain on urination). Occasionally, dysuria or itching at the tip of the urethra may be the only symptoms. Urethral discharge may range in quantity and in character from being clear to purulent. Distinguishing between discharge caused by gonorrhoea, chlamydia, or any other cause of urethritis is not clinically possible.

Without laboratory diagnosis, treatment of a client with urethral discharge from the penis should adequately cover both gonorrhoea (*N. gonorrhoeae*) and chlamydia (*C.* trachomatis) as these cannot be distinguished from each other by symptoms, clinical presentation, or incubation period (usually shorter for gonorrhoea, 3–7 days versus chlamydia, 5–21 days). Dual infections of gonorrhoea and chlamydia are generally not uncommon. If microscopy is available, the presence of intracellular diplococci on a Gram-stained smear can provide a presumptive diagnosis of gonorrhoea, while their absence means that treatment only for chlamydia can be considered. See *Appendix 3, Figure 1* for management of urethral discharge from the penis.

Persistent or recurrent symptoms of urethritis may result from drug resistance, poor compliance with the treatment regimen, or reinfection. If able to exclude reinfection by taking a thorough sexual history, additional treatment for *T. vaginalis* and *M. genitalium* may be considered. See *Appendix 3, Figure 2* for management of persistent or recurrent urethral discharge from the penis.

Possible diagnoses/pathogens: *N. gonorrhoeae, C. trachomatis, T. vaginalis, M. genitalium* (in cases of persistent urethral discharge, *T. vaginalis* and *M. genitalium* should be suspected).

Recommended treatment

Treat for uncomplicated **gonorrhoea**

PLUS

Treat for **chlamydia**

Special note: Use local guidelines where available to choose the appropriate treatment, especially for gonorrhoea, which is increasingly drug resistant. See *Appendix 2* for recommended treatment options.

5.2 Genital ulcer disease syndrome

The causative pathogens for GUD vary in different regions and may change over time. The five most common STI causes of GUD are genital HSV, syphilis (*T. pallidum*), chancroid (*H. ducreyi*), donovanosis (*K. granulomatis*), and lymphogranuloma venereum (LGV, caused by *C. trachomatis,* L1–L3 serovars). GUD can also be non-STI related (infectious e.g. bacterial skin infections, fungi) or non-infectious aetiologies (e.g. fixed drug eruption, Behçet syndrome, sexual trauma, psoriasis), and distinguishing this from STI-related causes is a major challenge. A client with genital ulcers may also have more than one disease, and clinical manifestations and patterns of GUD may be further altered in the presence of HIV infection. Clinical differential diagnosis may not be accurate, particularly in settings where several aetiological causes are prevalent. The STI causes of GUD have changed over time: chancroid has decreased and herpes and syphilis have increased. Clients with ulcers should be treated for all locally relevant causes.

GUD is of particular concern due to its epidemiological synergy with HIV. People with GUD, such as HSV, are much more likely to become infected with HIV if exposed, and people with both HIV and genital ulcers are more likely to transmit HIV to others [16].

Both an inexpensive rapid dual HIV/syphilis blood test and a single rapid test for syphilis (including

self-administered) are currently available. These are accurate and easy to use with minimal training [7]. These RDTs for syphilis should be used where available. They provide results in 10–20 minutes and can be performed in any setting because they do not require refrigerated storage or laboratory equipment. The sensitivity of the RDTs ranges from 85–98 per cent and the specificity from 93–98 per cent, compared with the *T. pallidum* haemagglutination assay and *T. pallidum* passive particle agglutination assay as reference standards [4]. Laboratory-assisted differential diagnosis is rarely helpful for other causes of GUD. See *Appendix 3, Figure 3* for management of genital ulcer disease including anorectal ulcers.

Possible diagnoses/pathogens: Genital herpes simplex virus (HSV-2, and less often HSV-1), *T. pallidum*, *H. ducreyi*, *K. granulomatis*, *C. trachomatis* serovars L1–L3.

Recommended treatment

Treat for **syphilis**

PLUS

Treat for **genital herpes (HSV)**

PLUS

Treat for **chancroid**, only in geographic settings where cases are reported or emerging

Special notes: Those with suspected HSV need to be advised to keep the affected area clean and dry and should be counselled that there is no definitive cure – although suppressive (antiviral) therapy can control recurrent attacks – along with education about the natural history of HSV-2 infection and the importance of treatment compliance [24].

Syndromic management should include treatment for syphilis, unless the person has been treated for syphilis within the past 3 months, and treatment for herpes.

For people with recurrent ulcers that are too frequent (such as 4–6 episodes or more a year) or with severe symptoms or causing distress, suppressive therapy may be proposed and preferred to episodic treatment. People receiving suppressive therapy may be assessed after 1 year and asked whether they want to continue or to change to episodic therapy. Note that recurrence rates may revert to the period before suppressive therapy started, and clients need to be aware of that.

For people living with HIV and immunosuppressed individuals, dose adjustments are recommended for valaciclovir and famciclovir, but not for acyclovir:

- For recurrent episodes, valaciclovir 500 mg is recommended for 5 days instead of 3 days, and famciclovir is recommended at a dose of 500 mg twice daily for 5 days instead of 250 mg.
- For suppressive therapy, valaciclovir is recommended at 500 mg twice daily instead of once daily, and famciclovir at 500 mg twice daily instead of 250 mg twice daily.

People who report allergies to penicillin should be treated with the effective alternatives for syphilis, which include doxycycline and erythromycin.

5.3 Vaginal discharge syndrome

Vulvovaginal symptoms are one of the most common reasons for attending a health facility. The symptoms include a vaginal discharge perceived by the client to be abnormal, vulval irritation, or itching. Other conditions may include vulvovaginal growths, such as warts and cancer, especially of the cervix.

The symptom of vaginal discharge is highly indicative of vaginitis caused by a vaginal infection, but may also, less commonly, be due to cervicitis caused by a cervical infection. Vaginitis may be caused by trichomoniasis (*T. vaginalis*), bacterial vaginosis (BV), and/or vulvovaginal candidiasis (VVC, caused by *Candida* species, usually *C. albicans*). Trichomoniasis is an STI caused by a flagellated protozoan. It is most often asymptomatic, but some will have a yellow-green, foul-smelling vaginal discharge and vulval itching. BV and VVC are both endogenous RTIs, and both can be asymptomatic. In symptomatic cases, BV is associated with a fishy-smelling, thin, grey-white discharge, while VVC is associated with vulval itching and soreness, and a white, odourless, curdy discharge. Cervicitis can be caused by gonorrhoea (*N. gonorrhoeae*) and/or chlamydia (*C. trachomatis*), and *M. genitalium*, but most

cases are asymptomatic such that only a minority of clients presenting with vaginal discharge syndrome have cervical infections.

The most applicable approach to managing clients presenting with vaginal discharge depends on the diagnostic capacity and expertise within a healthcare delivery point. See *Appendix 3, Figure 4* for a flowchart to help determine which management options to implement for vaginal discharge.

If available, laboratory testing should be used to diagnose clients with vaginal discharge for STIs such as *N. gonorrhoeae* and/or *C. trachomatis*. In the absence of such testing, the syndromic approach for management of vaginal discharge can preferably be based on, where possible, speculum examination for signs of cervical infection, or alternatively on the presence of vaginal discharge, or STI risk assessment if speculum examination is not feasible. Microscopy is accurate for the diagnosis of vaginal infection, if already available. However, setting up microscopy examination and resources required may outweigh just providing treatment for vaginal infection. Knowledge about the local prevalence of trichomoniasis, gonorrhoea, and chlamydia is also useful in deciding syndromic management for clients presenting with vaginal discharge.

Where speculum examination is possible, VVC can often be diagnosed clinically. If a microscope is also available, the presence of motile trichomonads in a wet preparation (wet mount) confirms *T. vaginalis* infection, clue cells suggest BV, and budding yeasts or pseudohyphae confirm the presence of *Candida* species, usually *C. albicans*. The use of Gram staining using vaginal discharge samples is recommended in addition, where possible. In the absence of microscopy, all clients presenting with vaginal discharge should receive treatment for both trichomoniasis and BV, and sexual partners should also be treated for trichomoniasis, unless sexual transmission can be ruled out during history. Clients with vaginal discharge and a positive risk assessment for STIs (and positive signs on pelvic examination if available, i.e. abdominal tenderness and cervical motion tenderness) should also be treated for gonorrhoea and chlamydia. See *Appendix 3, Figure 5* for the management of vaginal discharge.

Possible diagnoses/pathogens: Cervical infections (*N. gonorrhoeae, C. trachomatis, M. genitalium*) and/or vaginal infections (*T. vaginalis, C. albicans*, BV).

Recommended treatment for vaginal infection

Treat for **bacterial vaginosis** and **trichomoniasis**

PLUS

Treat for **yeast infection** if curd-like white discharge, vulvovaginal redness, and itching are present

Recommended treatment for cervical infection

Treat for uncomplicated **gonorrhoea**

PLUS

Treat for **chlamydia**

Special notes:

- A healthy person may have a variable amount of clear and white vaginal discharge (physiological discharge). This discharge usually increases before and after menstruation and becomes more watery in the middle of the menstrual cycle. It also increases during pregnancy, while taking oral contraceptive pills, and when an IUD is in place.
- Treatment of sexual partners of clients with BV has not been demonstrated to be of benefit. It is recommended that predisposing factors such as the use of antiseptic/antibiotic vaginal preparations or vaginal douching be reduced or eliminated.
- Predisposing and underlying factors for VVC include the use of antibiotics, the use of antiseptic/antibiotic vaginal preparations or vaginal douching, uncontrolled diabetes mellitus, immunosuppression, and corticosteroid use [24].
- BV and *T. vaginalis* may be treated simultaneously with the same medicine, metronidazole. Similarly, in the treatment of cervicitis, some medicines, such as doxycycline and azithromycin, can simultaneously treat *C. trachomatis* and *M. genitalium*.

5.4 Lower abdominal pain

This symptom often indicates the presence of PID, referring to infection of the upper part of the female reproductive tract (i.e. the uterus, fallopian tubes, and ovaries). Lower abdominal pain may be accompanied by dyspareunia, dysuria, dysmenorrhoea, abnormal vaginal discharge, bleeding, fever, and sometimes nausea and vomiting. Clients with this syndrome (with PID) may have endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis.

PID is usually caused by an STI, most commonly chlamydia (*C. trachomatis*), but also gonorrhoea (*N. gonorrhoeae*) and *M. genitalium,* but it can also be an endogenous condition caused by organisms in the normal vaginal flora (anaerobic bacteria). PID can also be iatrogenic, following recent instrumentation of the uterus or trauma to the cervix caused by, for example, abortion or insertion of an IUD. PID can cause irreversible damage to the fallopian tubes, leading to tubal infertility, ectopic pregnancy, and/or chronic pelvic pain (for further information on gynaecological issues, see *Chapter 8: Gynaecology and other reproductive healthcare*).

The diagnosis of PID can be made clinically, especially in sexually active clients, based on a speculum and bimanual exam, with findings of lower abdominal tenderness (usually bilateral), often with cervical motion tenderness, adnexal tenderness or uterine tenderness, sometimes accompanied by vaginal/cervical discharge and/or fever. Laparoscopy is helpful when it is available. There is no need to delay treatment for PID by waiting for laboratory test results, but it is important to rule out ectopic pregnancy, appendicitis, and other conditions (see special notes below). See *Appendix 3, Figure 6* for management of lower abdominal pain.

Possible diagnoses/pathogens: *N. gonorrhoeae, C. trachomatis*, *M. genitalium*, anaerobic bacteria.

Recommended treatment for PID

Treat for uncomplicated **gonorrhoea**

PLUS

Treat for **chlamydia**

PLUS

Treat for **anaerobic infections**

Special notes:

- Caution the use of analgesics to avoid masking pain that may indicate need for abdominal surgery.
- If a client with an IUD presents with PID, discuss, and consider removing the device, especially if the symptoms have not resolved with treatment within 72 hours.
- Hospitalization of individuals with acute PID should be seriously considered under the following circumstances:
  - the diagnosis is uncertain
  - surgical emergencies, such as appendicitis and ectopic pregnancy cannot be ruled out
  - a pelvic abscess is suspected
  - severe illness precludes management on an outpatient basis
  - the person is pregnant
  - the person is unable to follow or tolerate an outpatient regimen
  - the person has failed to respond to outpatient therapy
- Inpatient clients should be clinically monitored during admission and be reviewed 24–48 hours after starting intravenous antibiotics therapy.

5.5. Anorectal discharge

Anorectal STIs can be acquired through receptive anal sex but may also be due to contiguous spread from a genital infection. Anorectal STIs are relatively common among men who have sex with men, female sex workers, transgender people, and people who have anal sex.

Anorectal STIs are frequently asymptomatic but can lead to proctitis (inflammation of the distal 10–12 cm of the rectum), which is not always symptomatic. Acute proctitis can present with pain/discomfort, inflammation, cramping/tenesmus, mucopurulent anal discharge, anorectal bleeding, constipation, sensation of rectal fullness or of incomplete defecation. Chronic proctitis due to LGV can present with a history of mucus-streaking of the stool, constipation, and feeling of incomplete defecation.

Proctitis is most often caused by anorectal gonorrhoea (*N. gonorrhoeae*), chlamydia (*C. trachomatis*), but can also be caused by LGV, HSV, syphilis (*T. pallidum*) and *M. genitalium*. HPV infection, meanwhile, can cause benign anogenital warts (*condylomata acuminata*, caused by HPV types 6 and 11) and anal cancer and precancerous lesions (especially HPV type 16) [25].

Anoscopic examination may reveal the presence of mucopus in the rectum, rectal mucosal oedema, and contact bleeding in clients with gonococcal and chlamydial proctitis. In syphilis-, herpes- and LGV-related proctitis, rectal ulceration can be seen. Granulomatous inflammatory masses may also be seen in LGV. Differential diagnosis can include other gastrointestinal infections of the rectum and colon (proctocolitis) including *Shigella*, *Campylobacter*, *Salmonella,* cytomegalovirus, and amoebiasis, as well as neoplastic lesions, perineal abscesses, and chronic conditions such as ulcerative colitis or Crohn's disease. See *Appendix 3, Figure 7* for management of anorectal discharge.

Possible organisms: *N. gonorrhoeae, C. trachomatis,* including LGV (*C. trachomatis* serovars L1, L2), HSV-1, HSV-2, *T. pallidum*, *M. genitalium*, HPV various types.

Recommended treatment

Treat for **gonorrhoea**

PLUS

Treat for **chlamydia**

PLUS

Treat for **herpes (HSV)** if there is anorectal pain

Special notes:

Anorectal infections often go unrecognized and untreated, not only because they can be asymptomatic, but also due to a combination of low levels of clinical suspicion and stigmatization of anal sex.

If ulcerations are seen, treatment should also follow the flow chart for genital ulcers and consider managing the person for syphilis and/or LGV.

5.6 Other common syndromes

5.6.1 Scrotal swelling

Epididymitis (inflammation of the epididymis) usually presents as unilateral testicular pain and swelling with acute onset, often with tenderness of the epididymis and vas deferens. Occasionally, there could be erythema and oedema of the overlying scrotal skin. The adjacent testis is also often inflamed (orchitis) giving rise to epididymo-orchitis.

Epididymitis is commonly caused by gonorrhoea (*N. gonorrhoeae*) or chlamydia (*C. trachomatis*) and should be suspected in clients at high risk for STI infection. Epididymitis can also be a complication of a bacterial urinary tract infection, and can be caused by tuberculosis, filariasis, and infections due to *Escherichia coli*, *Klebsiella* spp., or *Pseudomonas aeruginosa*. If quick and effective treatment is not given, fibrous scarring and destruction of testicular tissue may lead to infertility.

Other possible diagnosis: hydrocele, hernia, varicocele, trauma, tumour, and testicular torsion. In young people, testicular torsion should be suspected when onset of scrotal pain is sudden. *Testicular torsion is a surgical emergency that needs urgent referral and treatment*.

Possible pathogens: *N. gonorrhoeae*, *C. trachomatis.*

Special note: Use local guidelines where available to choose the appropriate treatment, especially for gonorrhoea, which is increasingly drug resistant.

Supportive therapy: Bed rest, antipyretics and analgesics, and scrotal support until local inflammation and fever subside.

5.6.2 Inguinal bubo

Inguinal and femoral buboes are localized enlargements of the lymph nodes (buboes) in the groin (inguinal) area, which are painful and may be fluctuant. They are a common feature of chancroid (*H. ducreyi*) and LGV (*C. trachomatis* serovars L1, L2, and L3). Occasionally, the bubo might have ruptured and pus may be present. Enlarged lymph nodes that are not acutely inflamed (e.g. painless adenopathy due to syphilis) are not buboes.

Non-sexually transmitted local and systemic infections can also cause swelling in the groin area and need to be considered in the differential diagnosis (e.g. inguinal hernia, infections of the lower limb, HIV infection with generalized lymphadenopathy, filariasis, tuberculosis lymphadenopathy, and plague).

Possible diagnoses/pathogens: *H. ducreyi*, *C. trachomatis* serovars L1, L2, and L3.

Special notes:

- Caution is needed in pregnant individuals. Select an appropriate treatment regimen.
- Fluctuant lymph nodes should be aspirated through healthy skin. Incision and drainage or excision of nodes may delay healing and should not be attempted.
- Where there is doubt and/or treatment failure, referral for diagnostic biopsy is advisable.

Table 4 lists the possible aetiologies of the common STI syndromes discussed in Section 5.

TABLE 4: Common STI syndromes and aetiologies

STI syndrome	Possible STI aetiologies
Urethral discharge	*N. gonorrhoeae, C. trachomatis, T. vaginalis, M. genitalium*
Genital ulcer disease	*T. pallidum, H. ducreyi,* HSV, *K. granulomatis, C. trachomatis* (LGV strains L1–L3)
Vaginal discharge	Cervical infections (*N. gonorrhoeae, C. trachomatis, M. genitalium*) and vaginal infections (*T. vaginalis, C. albicans,* bacterial vaginosis)
Lower abdominal pain	Cervical infections (*N. gonorrhoeae, C. trachomatis, M. genitalium*), vaginal infections (*T. vaginalis, C. albicans,* bacterial vaginosis), and anaerobic infections
Anorectal discharge	*N. gonorrhoeae, C. trachomatis,* (LGV strains L1–L3)
Scrotal swelling	*N. gonorrhoeae, C. trachomatis, T. vaginalis, M. genitalium*
Inguinal bubo	*H. ducreyi, C. trachomatis* (LGV strains L1–L3)

6. References

[1] World Health Organization. Sexually transmitted infections (STIs). Key facts. November 2021. Available at: https://www.who.int/en/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis). Accessed 22 April 2022.

[2] World Health Organization. WHO guidelines for the treatment of *Neisseria gonorrhoeae*. Geneva: WHO; 2016. Available at: https://apps.who.int/iris/bitstream/handle/10665/246114/9789241549691-eng.pdf. Accessed 22 April 2022.

[3] World Health Organization. WHO guidelines for the treatment of *Chlamydia trachomatis*. Geneva: WHO; 2016. Available at: https://apps.who.int/iris/bitstream/handle/10665/246165/9789241549714-eng.pdf. Accessed 22 April 2022.

[4] World Health Organization. WHO guidelines for the treatment of *Treponema pallidum* (syphilis). Geneva: WHO; 2016. Available at: https://www.who.int/publications-detail-redirect/9789241549714. Accessed 22 April 2022.

[5] World Health Organization [website]. Cervical cancer. Key facts. February 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer. Accessed 23 March 2022.

[6] World Health Organization [website]. Hepatitis B. Key facts. June 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. Accessed 20 June 2022.

[7] World Health Organization. Sexually transmitted infections. Evidence Brief. Geneva: WHO; 2019. Available at: https://apps.who.int/iris/bitstream/handle/10665/329888/WHO-RHR-19.22-eng.pdf. Accessed 2 November 2021.

[8] World Health Organization. Global health sector strategy on sexually transmitted infections 2016–2021. Geneva: WHO; 2016. Available at: https://apps.who.int/iris/handle/10665/246296. Accessed 22 April 2022.

[9] Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2019;68(32):698–702.

[10] World Health Organization. Training modules for the syndromic management of sexually transmitted infections, second edition. Geneva: WHO; 2007. Available at: https://apps.who.int/iris/bitstream/handle/10665/43275/9241593407_mod1_eng.pdf. Accessed 2 April 2020.

[11] Altarum Institute. Sexual Health and Your Patients: A Provider's Guide. Washington, DC: Altarum Institute; 2016. Updated 2020. https://nationalcoalitionforsexualhealth.org/tools/for-healthcare-providers/asset/Asking-Essential-Sexual-Health-Questions.pdf. Accessed 20 March 2020.

[12] Johnson RE, Newhall WJ, Papp JR, et al. Screening tests to detect Chlamydia trachomatis and Neisseria gonorrhoeae infections—2002. *MMWR Recomm Rep*. 2002;51(RR-15):1–38.

[13] World Health Organization. WHO guideline on self-care interventions for health and well-being, 2022 revision. Geneva: WHO; 2022. Available at: https://www.who.int/publications/i/item/9789240052192. Accessed 11 July 2022.

[14] World Health Organization. Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus. Geneva: WHO; 2013. Available at: https://apps.who.int/iris/handle/10665/85343. Accessed 22 April 2022.

[15] World Health Organization. WHO guideline on syphilis screening and treatment for pregnant women. Geneva: WHO; 2017. Available at: https://www.who.int/publications/i/item/9789241550093. Accessed 22 April 2022.

[16] World Health Organization. WHO guidelines for the treatment of *Genital Herpes Simplex Virus*. Geneva: WHO; 2016. Available at: https://www.who.int/reproductivehealth/publications/rtis/genital-HSV-treatment-guidelines/en/. Accessed 12 March 2020.

[17] World Health Organization. Guidelines on hepatitis B and C testing. Geneva: WHO; 2017. Available at: https://www.who.int/publications/i/item/9789241549981. Accessed 31 March 2020.

[18] World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: WHO; 2015. Available at: https://www.who.int/publications/i/item/9789241549059. Accessed 31 March 2020.

[19] World Health Organization [website]. Hepatitis C. Key facts. June 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c. Accessed 20 June 2022.

[20] World Health Organization Regional Office for Africa [website]. Frequently asked questions on Ebola virus disease vaccine. Available at: https://www.afro.who.int/health-topics/ebola-virus-disease/faq-vaccine. Accessed 24 March 2022.

[21] World Health Organization. WHO guidelines for the prevention of sexual transmission of Zika virus: executive summary. Geneva: WHO; 2019. Available at: https://apps.who.int/iris/bitstream/handle/10665/311026/WHO-RHR-19.4-eng.pdf. Accessed 2 April 2020.

[22] World Health Organization. Human T-lymphotropic virus type 1. Key facts. March 2021. Available at: https://www.who.int/news-room/fact-sheets/detail/human-t-lymphotropic-virus-type-1. Accessed 2 November 2021.

[23] World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Available at: https://www.who.int/publications/i/item/9789240024168. Accessed 19 July 2021.

[24] World Health Organization. Regional Office for South-East Asia. Management of sexually transmitted infections: regional guidelines. WHO; 2011. Available at: https://apps.who.int/iris/handle/10665/205471. Accessed 22 April 2022.

[25] Wieland U, Kreuter A. The importance of HPV16 in anal cancer prevention. *Lancet.* 2018;18(2):131–132.

6.1 Resources

International Planned Parenthood Federation. IMAP Statement on Zika virus and sexual and reproductive health. March 2016. Available at: https://www.ippf.org/sites/default/files/ippf_imap_zika_web.pdf

Mayaud P, McCartney D, Mabey D. Sexually Transmitted Infections (Part 3, Section D). In: ET Ryan, DR Hill, T Solomon, NE Aronson, TP Endy, editors. Hunter's Tropical Medicine and Emerging Infectious Diseases. Tenth edition. Elsevier Inc; 2020.

National LGBT Health Education Center. Taking Routine Histories of Sexual Health: A System-Wide Approach for Health Centers. November 2015. Available at: http://www.lgbthealtheducation.org/wp-content/uploads/COM-827-sexual-history_toolkit_2015.pdf

Toskin I, Blondeel K, Peeling RW, Deal C, Kiarie J. Advancing point of care diagnostics for the control and prevention of STIs: the way forward. *Sex Transm Infect.* 2017;93(S4):S81–S88.

World Health Organization. Sexually transmitted and other reproductive tract infections: a guide to essential practice. Geneva: WHO; 2005. Available at: https://www.who.int/publications/i/item/9241592656

World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018. Available at: https://www.who.int/publications/i/item/9789241550345

7. Appendices

Appendix 1: List of WHO guidance on STI management

Specific WHO guidance on STI management is provided in the following key documents:

- WHO guidelines for the treatment of *Neisseria gonorrhoeae*. 2016. Available at: https://apps.who.int/iris/bitstream/handle/10665/246114/9789241549691-eng.pdf
- WHO guidelines for the treatment of *Treponema pallidum* (syphilis). 2016. Available at: https://www.who.int/publications/i/item/9789241549714
- WHO guidelines for the treatment of *Genital Herpes Simplex Virus*. 2016. Available at: https://www.who.int/publications/i/item/978924154987
- WHO guidelines for the treatment of *Chlamydia trachomatis*. 2016. Available at: https://apps.who.int/iris/bitstream/handle/10665/246165/9789241549714-eng.pdf
- WHO guideline on syphilis screening and treatment for pregnant women. 2017. Available at: https://www.who.int/publications/i/item/9789241550093
- Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. 2015. Available at: https://www.who.int/publications/i/item/9789241549059
- Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. 2018. Available at: https://www.who.int/publications/i/item/9789241550345
- Guidelines for the management of symptomatic sexually transmitted infections. 2021. Available at: https://www.who.int/publications/i/item/9789240024168

Appendix 2: Recommended treatment options

Recommended treatment options for urethral discharge syndrome

• Therapy for uncomplicated *Neisseria gonorrhoeae*
Plus
• Therapy for *Chlamydia trachomatis*

Infections covered	First choice	Effective substitutes
In settings in which local antimicrobial resistance data are not available, the WHO STI guideline suggests dual therapy for gonorrhoea.		
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose Plus **Azithromycin 1 gram,** orally, single dose	**Cefixime 400 mg**, orally, single dose Plus **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg**, orally, twice daily for seven days (to be given only if gonorrhoea therapy did not include azithromycin)	**Azithromycin 1 gram**, orally, single dose **or** **Erythromycin 500 mg**, orally, 4 times a day for 7 days **or** **Ofloxacin 200–400 mg**, orally, twice a day for 7 days. (to be given only if gonorrhoea therapy did not include azithromycin)
In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, single therapy may be given.		
N. gonorrhoeae	**Ceftriaxone 250 mg**, intramuscularly, single dose	**Cefixime 400 mg**, orally, single dose **or** **Spectinomycin 2 grams**, intramuscularly, single dose (availability makes this antibiotic impractical)
Additional therapeutic options for recurrent or persistent infections		
T. vaginalis	**Metronidazole 2 grams**, orally, single doses	**Metronidazole 400 or 500 mg**, twice daily for 7 days
M. genitalium	**Azithromycin 500 mg**, orally on day 1, **250 mg** daily on days 2–5	

[a] Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and *M. genitalium* and reduced susceptibility of *N. gonorrhoeae* to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Recommended treatment options for vaginal discharge syndrome

A. Treatment options for vaginal infections

• Therapy for bacterial vaginosis and trichomoniasis
Plus
• Therapy for yeast infection if curd-like white discharge, vulvovaginal redness and itching are present

Infections covered	First-line options	Effective substitutes	*Note:* In pregnancy, metronidazole should, ideally, be avoided in the first trimester
Bacterial vaginosis	**Metronidazole 400 mg or 500 mg**, orally, twice daily for 7 days	**Clindamycin 300 mg**, orally, twice daily for 7 days **or** Metronidazole 2 grams, orally, single dose	**Metronidazole 200 mg or 250 mg**, orally, 3 times a day for 7 days **or** **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days **or** **Clindamycin 300 mg**, orally, twice daily for 7 days
T. vaginalis	**Metronidazole 2 grams**, orally, in a single dose **or** **Metronidazole 400 mg or 500 mg**, orally, twice daily for 7 days	**Tinidazole 2 grams** orally, single dose **or** **Tinidazole 500 mg** orally, twice daily for 5 days	**Metronidazole 200 mg or 250 mg**, orally, 3 times a day for 7 days **or** **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days
***C. albicans* (yeast infection)**	**Miconazole vaginal pessaries, 200 mg** inserted at night for 3 nights **or** **Clotrimazole vaginal tablet, 100 mg**, inserted at night for 7 nights	**Fluconazole 150 mg (or 200mg)**, orally, single dose **OR** **Nystatin, 200,000-unit vaginal tablet**, inserted at night for 7 nights	**Miconazole 200 mg vaginal pessaries** inserted once daily for 3 days **or** **Clotrimazole vaginal tablet 100 mg** inserted at night for 7 days **or** **Nystatin pessaries 200,000 units**, inserted at night for 7 nights

People taking metronidazole should be cautioned to avoid alcohol. Use of metronidazole in the first trimester of pregnancy is not recommended unless the benefits outweigh the potential hazards.

B. Treatment options for cervical infection

• Therapy for uncomplicated *N. gonorrhoeae*
Plus
• Therapy for *C. trachomatis*

Infections covered	First choice (choose one from each cell below)	Effective substitutes	Options for pregnant women or during breastfeeding
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhoea.			
N. gonorrhoeae[a]	**Ceftriaxone 250 mg, intramuscularly, single dose plus Azithromycin 1 gram, orally, single dose**	**Cefixime 400 mg, orally, single dose plus Azithromycin 1 gram, orally, single dose**	**Ceftriaxone 250 mg, intramuscularly, single dose plus Azithromycin 1 gram, orally, single dose or Cefixime 400 mg, orally, single dose plus Azithromycin 1 gram, orally, single dose**
C. trachomatis	**Doxycycline 100 mg, orally, twice daily for 7 days (to be given only if gonorrhoea therapy did not include azithromycin)**	**Azithromycin 1 gram, orally, single dose or Erythromycin 500 mg, orally, 4 times a day for 7 days or Ofloxacin 200–400 mg, orally, twice daily for 7 days (to be given only if gonorrhoea therapy did not include azithromycin)**	**Erythromycin 500 mg, orally, 4 times a day for 7 days or Azithromycin 1 gram, orally, single dose (to be given only if gonorrhoea therapy did not include azithromycin)**
M. genitalium	**Azithromycin 500 gram,** orally day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)		**Azithromycin 500 gram,** orally, day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)

[a] Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and *M. genitalium* and reduced susceptibility of *N. gonorrhoeae* to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Treatment options for pelvic inflammatory disease

• Therapy for uncomplicated *N. gonorrhoeae*
Plus
• Therapy for *C. trachomatis*
Plus
• Therapy for anaerobic infections

Infections covered	First choice	Effective substitutes
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhoea.		
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose plus **Azithromycin 1 gram**, orally, single dose	**Cefixime 400 mg**, orally, single dose plus **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg**, orally, twice daily for 14 days	**Erythromycin 500 mg**, four times daily for 14 days (to be given only if gonorrhoea therapy did not include azithromycin)
In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, single therapy may be given as below.		
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose	**Cefixime 400 mg**, orally, single dose
The treatment for anaerobes must be included in either treatment option above.		
Anaerobes	**Metronidazole 400 mg or 500 mg**, orally, twice daily for 14 days	

[a] Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and reduced susceptibility to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Recommended treatment options for genital ulcer disease

• Multiple-dose therapy for herpes simplex virus infection
plus
• Single-dose long-acting penicillin therapy or multi-dose therapy of alternatives

Infections covered	First-line options	Effective substitutes	For pregnant and breastfeeding women and people younger than 16 years
Genital herpes	**Primary infection** **Acyclovir 400 mg**, orally, 3 times a day for 10 days **or** **Acyclovir 200 mg**, orally, 5 times a day for 10 days	**Primary infection** **Valaciclovir 500 mg**, twice a day for 10 days **or** **Famciclovir 250 mg**, orally, 3 times a day for 10 days	**Primary infection** Use acyclovir only when the benefit outweighs the risk. The dosage is the same as for primary infection in non-pregnancy.
	Recurrent infection – episodic therapy **Acyclovir 400 mg**, orally, 3 times a day for 5 days **or** **Acyclovir 800 mg**, orally, twice daily for 5 days **or** **Acyclovir 800 mg**, 3 times a day for 2 days	**Recurrent infection – episodic therapy** **Valaciclovir 500 mg**, twice daily for 5 days **or** **Famciclovir 250 mg**, orally, twice daily for 5 days	**Recurrent infection – episodic therapy** **Acyclovir 400 mg**, orally, 3 times a day for 5 days **or** **Acyclovir 800 mg**, orally, twice daily for 5 days **or** **Acyclovir 800 mg**, 3 times a day, for 2 days
	Suppressive therapy for recurrent herpes[a] **Acyclovir 400 mg**, orally, twice daily **or** **Valaciclovir 500 mg**, once daily	**Suppressive therapy for recurrences**[a] **Famciclovir 250 mg**, orally, twice daily	**Suppressive therapy for recurrent herpes**[a] **Acyclovir 400 mg**, orally, twice daily **or** **Valaciclovir 500 mg**, once daily
Syphilis (early) (treatment for primary, secondary and early latent [less than two years since infection] syphilis)	**Benzathine penicillin 2.4 million units**, intramuscularly in a single dose	**Doxycycline 100 mg**, orally, twice a day for 14 days **or** **Erythromycin 500 mg**, 4 times a day for 14 days	**Benzathine penicillin 2.4 million units**, intramuscularly in a single dose **or** **Erythromycin 500 mg**, orally, 4 times a day for 14 days[b]

continued

continued

Syphilis (late) (treatment for late latent and tertiary syphilis)	**Benzathine penicillin 2.4 million units** by intramuscular injection, once weekly for 3 consecutive weeks	**Procaine penicillin 1.2 million units** by intramuscular injection, once daily for 20 consecutive days **or** **Doxycycline 100 mg**, orally, twice daily for 30 days	**Erythromycin 500mg** orally, 4 times a day for 30 days[b]

[a] Suppressive therapy for recurrent herpes is recommended for individuals with 4–6 or more recurrent episodes per year, severe symptoms or episodes that cause distress. Increased dosages or duration of treatment are required for people living with HIV (*27*).

[b] Although erythromycin is used to treat pregnant women, it does not cross the placental barrier completely and the fetus is not treated. The newborn infant therefore needs treatment soon after delivery.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Treatment options for people with anorectal discharge

Recommended treatment regimens for anorectal infections		
Infections covered	**Recommended choice**	**Effective substitutes**
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose **plus** **Azithromycin 1 gram**, orally, single dose	**Cefixime 400 mg**, orally, single dose **plus** **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg** orally, twice daily, for 7 days **or** **Doxycycline for 21 days** (to cover rectal lymphogranuloma venereum) if suspected or confirmed on NAAT (to be given only if dual therapy did not include azithromycin)	**Erythromycin 500 mg**, orally, 4 times a day for 14 days (to be given only if dual therapy did not include azithromycin)
Syphilis (if ulcer present)	**Benzathine penicillin 2.4 million units** intramuscularly, single dose People with a positive syphilis test and no ulcer: administer the same dose at weekly intervals for a total of three doses	**Doxycycline 100 mg** orally, twice daily for 14 days **Erythromycin 500 mg** 4 times a day, orally, for 14 days Extend treatment to 30 days if syphilis serology is positive

continued

continued

Genital herpes	Recurrent infection: **Acyclovir 400 mg**, orally, 3 times a day for 5 days **or** **Acyclovir 800 mg**, orally, 3 times a day for 2 days **or** **Acyclovir 800 mg**, orally, 2 times a day for 5 days	**Recurrent infection:** **Valaciclovir 500 mg**, twice daily for 3 days
	Primary genital herpes: **Acyclovir 400 mg**, orally, 3 times a day for 10 days **or** **Acyclovir 200 mg**, 5 times a day for 10 days	**Primary genital herpes:** **Valaciclovir 500 mg**, orally, twice daily for 10 days
	Suppressive therapy for recurrent herpes **Acyclovir 400 mg**, orally, twice daily **or** **Valaciclovir 500 mg**, once daily For duration, see the genital ulcer disease section	**Suppressive therapy for recurrences** **Famciclovir 250 mg**, orally, twice daily **(Famciclovir 500 mg**, twice daily for people living with HIV or immunocompromised**)**

a Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and reduced susceptibility to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Treatment for genital warts caused by human papillomavirus (HPV) types 6 and 11

No one treatment is completely satisfactory. Local treatment can remove the warts, but they may recur. This should be explained to the client before commencing therapy. Note that management of vaginal and/or cervical warts, urethral meatal warts, and anal warts should be undertaken in a higher-level or specialist facility.

Chemical methods

a. Podophyllin 25 per cent in compound tincture of benzoin, to be applied *by the healthcare provider* carefully to the warts, avoiding normal tissue. The client should be instructed to wash the podophyllin off after 4–6 hours. Treatment is repeated once a week. If warts persist after 6–8 applications, refer the client to a higher facility.

b. Podophyllotoxin 0.5 per cent solution/gel could be applied *by the client* using a cotton swab to visible genital warts twice a day for 3 days, followed by 4 days of no therapy. This cycle may be repeated, as necessary, for up to 4–5 cycles. The total volume of podophyllin/podophyllotoxin should be limited to 0.5 ml per day and the total wart area treated should not be more than 10 cm^2.

c. Trichloroacetic acid (TCA) 80–90 per cent can be applied *by the healthcare provider* carefully to the warts, avoiding normal tissue, followed by powdering of the treated area with talc or sodium bicarbonate to remove excess acid. Repeat application at weekly intervals. TCA causes immediate chemical cauterization. It is not absorbed systemically and therefore can be safely used in pregnancy.

- If the warts persist after 2 months of treatment with podophyllin, podophyllotoxin, or TCA, refer the client to a higher-level facility for further management.

d. Imiquimod 5 per cent cream can be applied *by the client* with a finger/cotton swab at bedtime, left on overnight, 3 times a week on every other day for as long as 16 weeks. The treated area should be washed with soap and water 6–10 hours after application.

Important: The use of podophyllin/podophyllotoxin is contraindicated during pregnancy and lactation. The safety of imiquimod during pregnancy has not been established.

Physical methods (may not be feasible at the primary healthcare level)

a. Cryotherapy can be given with liquid nitrogen, solid carbon dioxide, or a cryoprobe. Repeat applications every 1–2 weeks. Cryotherapy is non-toxic, does not require anaesthesia and, if carried out properly, does not result in scarring.

b. Electrosurgery

c. Surgical removal

Source: World Health Organization. Regional Office for South-East Asia. Management of sexually transmitted infections: regional guidelines. WHO; 2011. Available at: https://apps.who.int/iris/handle/10665/205471. Accessed 31 March 2020.

Treatment for hepatitis B virus (HBV)

Acute hepatitis B:

- There is no specific treatment, but care can help to maintain comfort and adequate nutritional balance, including replacement of fluids lost from vomiting and diarrhoea.
- Avoid unnecessary medications. Acetaminophen/paracetamol and medication against vomiting should not be given [1].

Chronic hepatitis B (persistence of hepatitis B surface antigen [HBsAg] for 6 months or more):

- Only a proportion (10–40 per cent depending on setting and eligibility criteria) of people with chronic hepatitis B infection will require treatment. Treatment for chronic hepatitis B must be continued for life in most people who start it (cure/clearance of HBsAg is rare). The treatment suppresses the virus and can slow the progression of cirrhosis, reduce incidence of liver cancer, and improve long-term survival. For information on who to treat and who not to treat among people with chronic hepatitis B, monitoring treatment, and when to stop treatment, refer to the full WHO guidelines [2].
- In high-income countries, surgery and chemotherapy can prolong life for up to a few years. Liver transplantation is sometimes used in people with cirrhosis in high-income countries, with varying success.

First-line antiviral therapies for chronic hepatitis B

- In all adults, adolescents, and children aged 12 years or older in whom antiviral therapy is indicated, the nucleos(t)ide analogues (NAs) that have a high barrier to drug resistance (tenofovir or entecavir) are recommended. Entecavir is recommended in children aged 2–11 years.
- NAs with a low barrier to resistance (lamivudine, adefovir, or telbivudine) can lead to drug resistance and are not recommended.

For HBV/HIV-coinfected people (adults/adolescents/children), please check the recommended antiretroviral therapy regimen.

Second-line antiviral therapies for the management of treatment failure

- In people with confirmed or suspected antiviral resistance (i.e. history of prior exposure or primary non-response) to lamivudine, entecavir, adefovir, or telbivudine, a switch to tenofovir is recommended.

Prevention of perinatal HBV transmission using antiviral therapy

- In HBV-monoinfected pregnant individuals, the indications for treatment are the same as for other adults, and tenofovir is recommended. No recommendation was made on the routine use of antiviral therapy to prevent perinatal HBV transmission.

For HIV-infected pregnant and breastfeeding individuals, check the recommended antiretroviral therapy regimen.

References

[1] World Health Organization. Hepatitis B. Key facts. June 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. Accessed 20 June 2022.

[2] World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: WHO; 2015. Available at: https://www.who.int/publications/i/item/9789241549059. Accessed 31 March 2020.

Treatment for hepatitis C virus (HCV)

WHO recommends offering treatment to all individuals diagnosed with HCV infection who are 12 years of age or older, irrespective of disease stage, as described below.

In adults (aged 18 years and older) with chronic HCV infection, the following pangenotypic direct-acting antiviral regimens can be used:

- For adults without cirrhosis:
  - sofosbuvir/velpatasvir 12 weeks
  - sofosbuvir/daclatasvir 12 weeks
  - glecaprevir/pibrentasvir 8 weeks
- For adults with compensated cirrhosis:
  - sofosbuvir/velpatasvir 12 weeks
  - glecaprevir/pibrentasvir 12 weeks
  - sofosbuvir/daclatasvir 24 weeks
  - sofosbuvir/daclatasvir 12 weeks

In adolescents aged 12–17 years or weighing at least 35 kg with chronic HCV infection:

- sofosbuvir/ledipasvir for 12 weeks in genotypes 1, 4, 5, and 6
- sofosbuvir/ribavirin for 12 weeks in genotype 2
- sofosbuvir/ribavirin for 24 weeks in genotype 3

In children younger than 12 years with chronic HCV infection, WHO recommends:

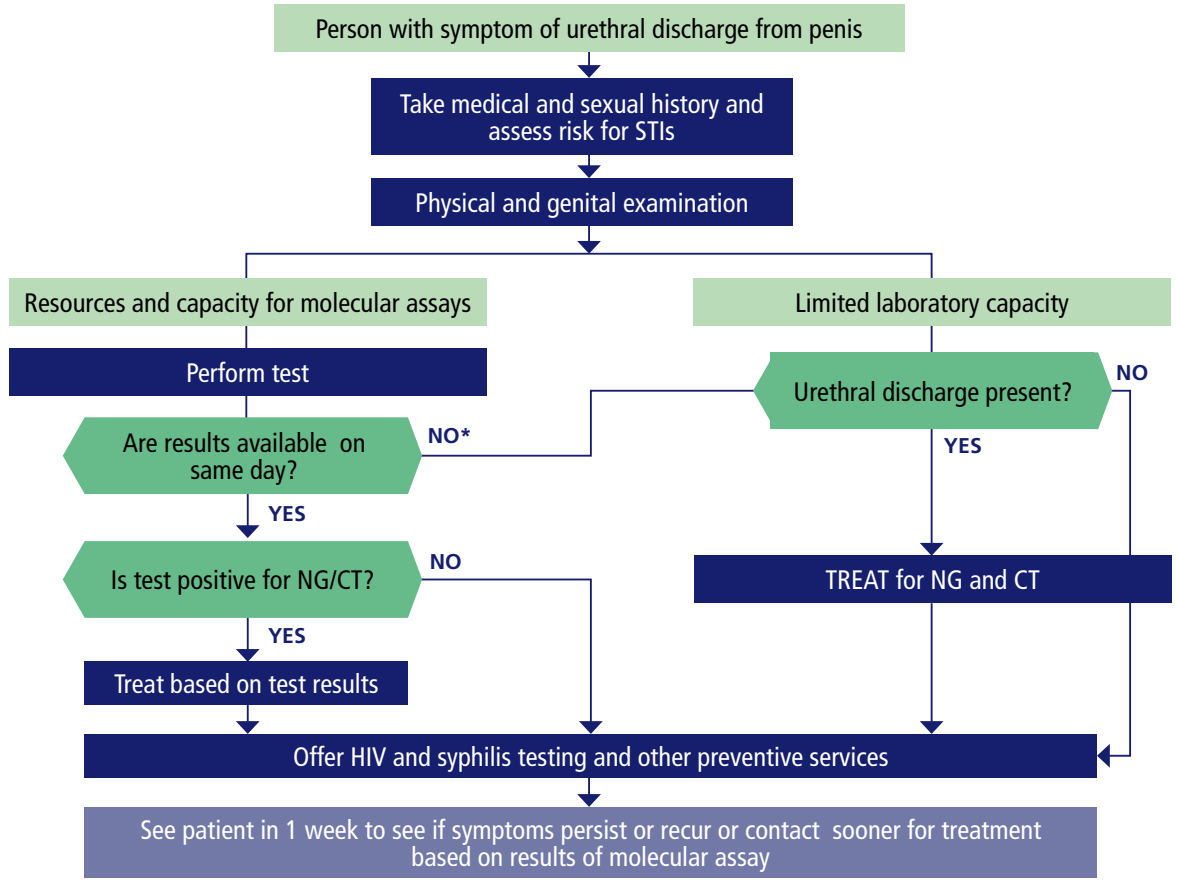
- deferring treatment until 12 years of age (conditional recommendation, very low quality of evidence)
- treatment with interferon-based regimens should no longer be used

For further information on clinical considerations, including coinfections, refer to the source guidelines.

Source: World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018. CC BY-NC-SA 3.0 IGO. Available at: https://www.who.int/publications/i/item/9789241550345. Accessed 31 March 2020.

Appendix 3: Syndromic management flowcharts

Figure 1: Management of urethral discharge from the penis

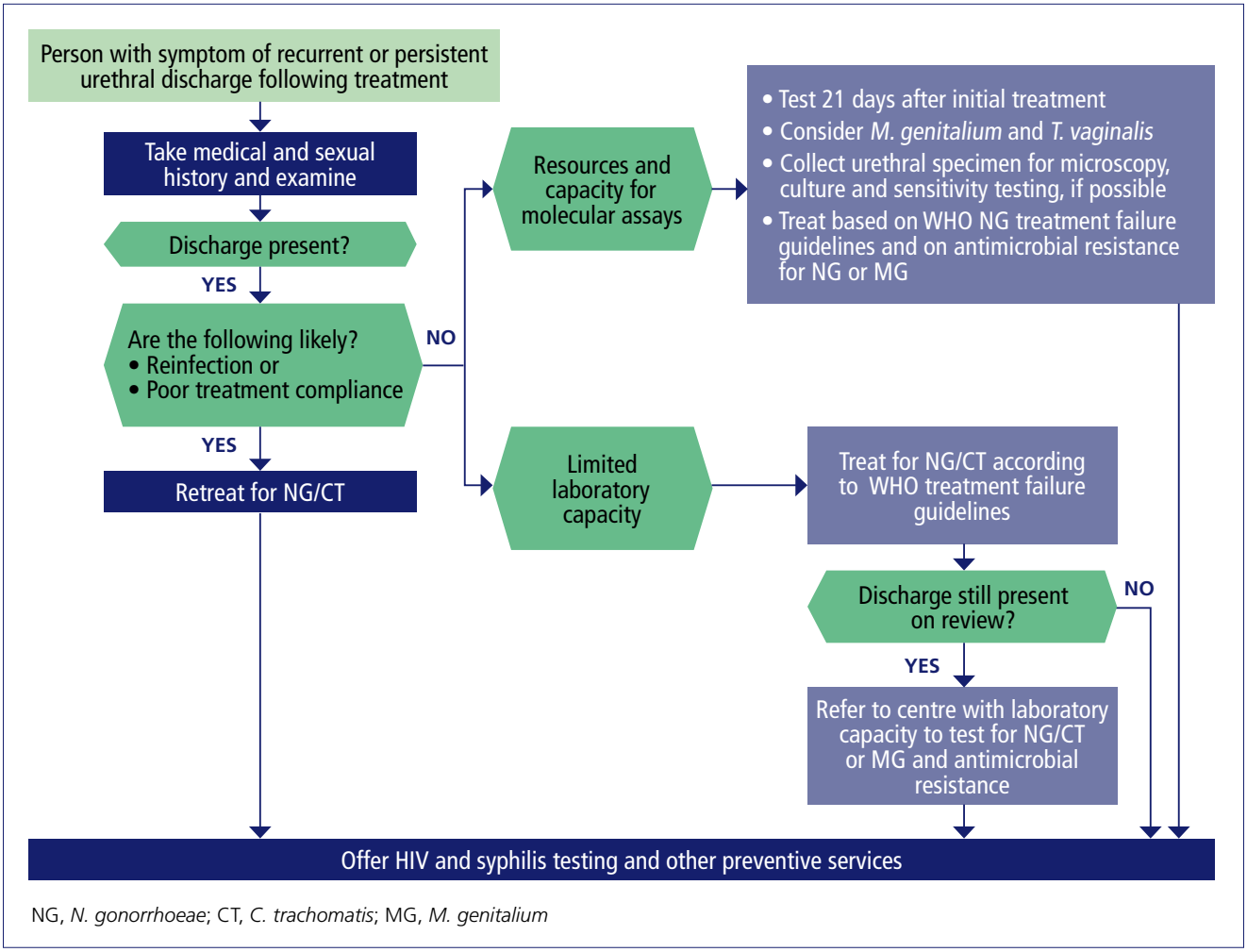


NG, *N. gonorrhoeae*; CT, *C. trachomatis*

* If molecular assay was performed and results were not available on same day, revise the syndromic treatment initially provided according to the test results when available

If test is negative but urethral discharge is present, treat for non-gonococcal/non-chlamydial urethritis (such as *M. genitalium*, *T. vaginalis* or herpes simplex virus)

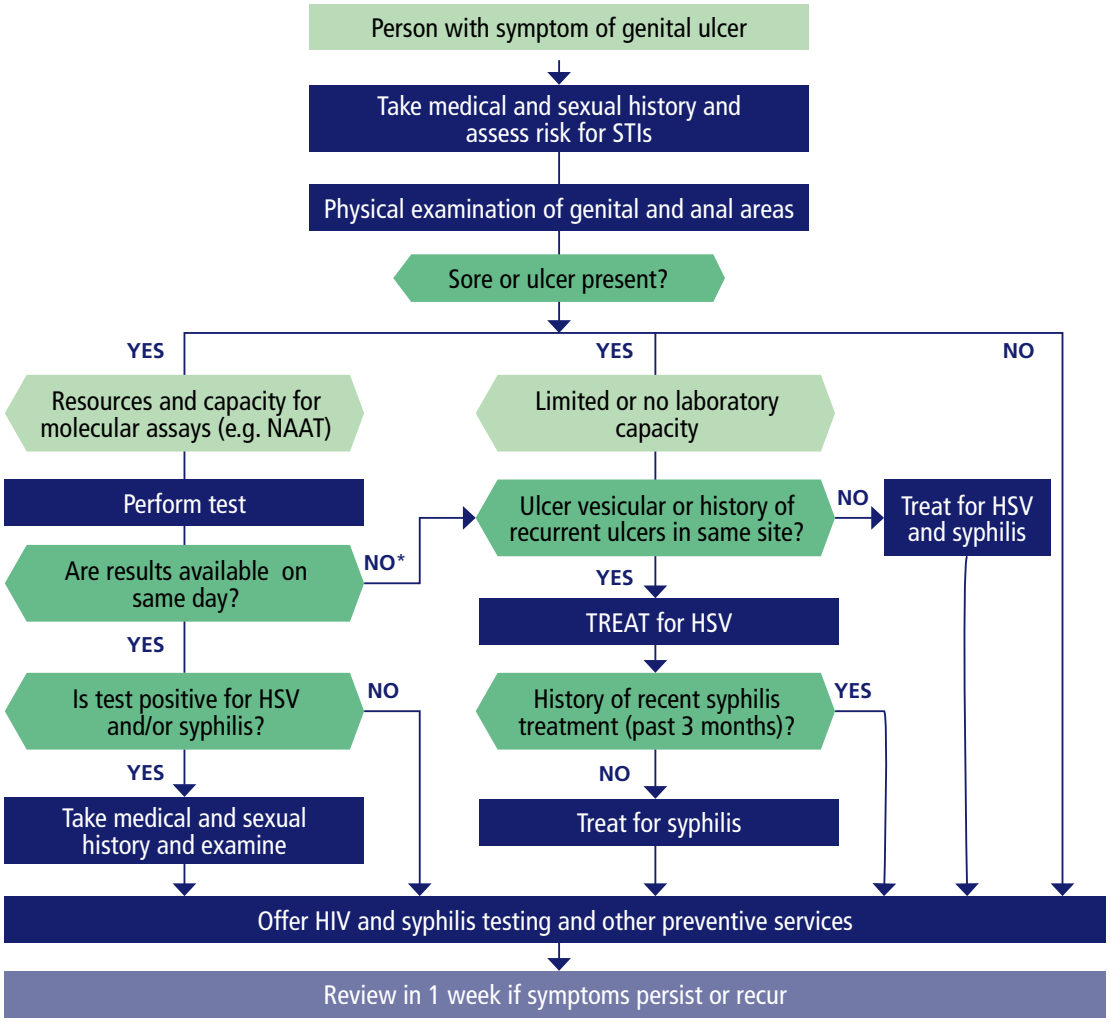
Figure 2: Management of persistent or recurrent urethral discharge from the penis



NG, *N. gonorrhoeae*; CT, *C. trachomatis*; MG, *M. genitalium*

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Figure 3: Management of genital ulcer disease including anorectal ulcers

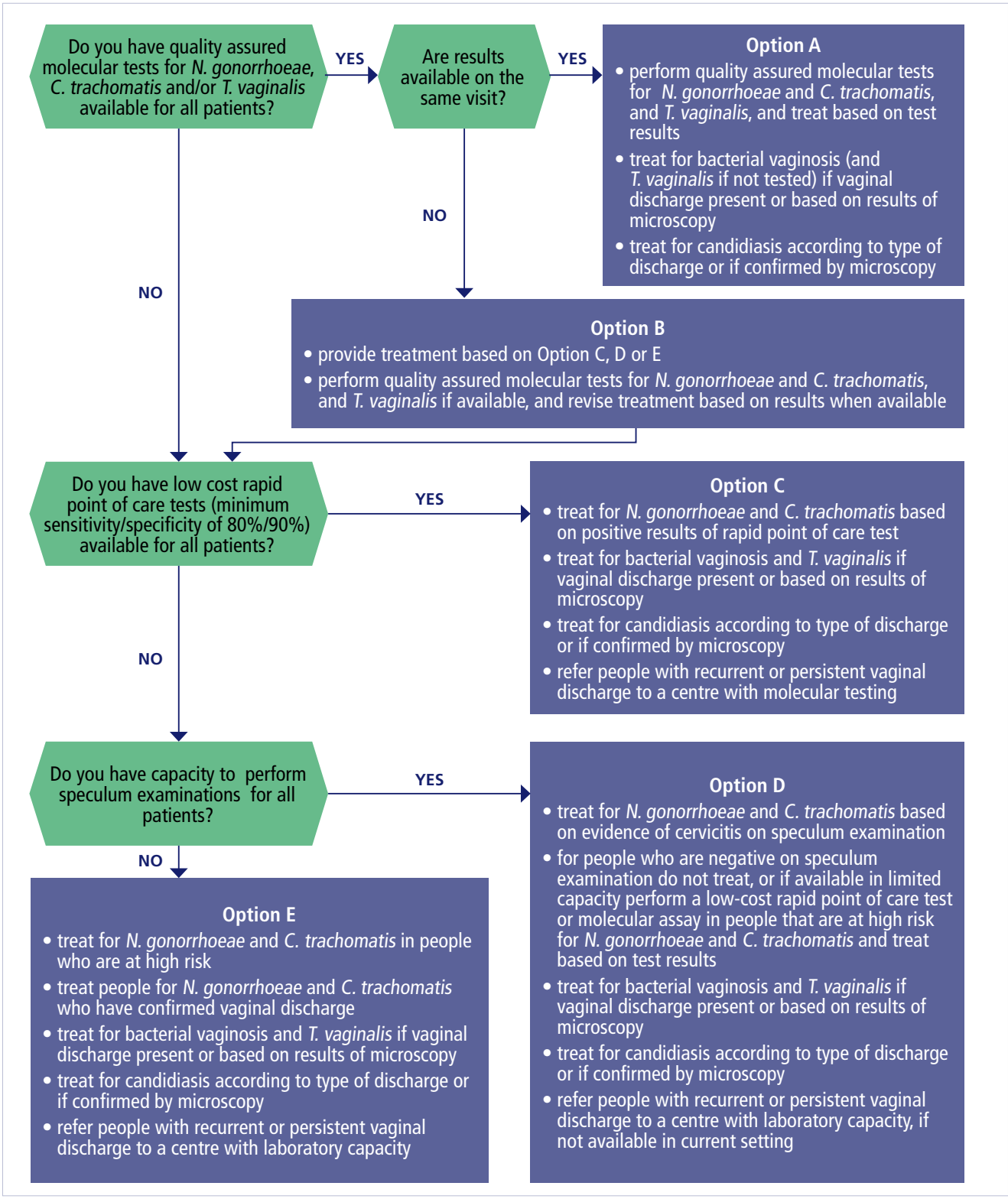


HSV, herpes simplex virus

* If molecular assay was performed and results were not available on same day, revise the syndromic treatment initially provided according to the test results when available

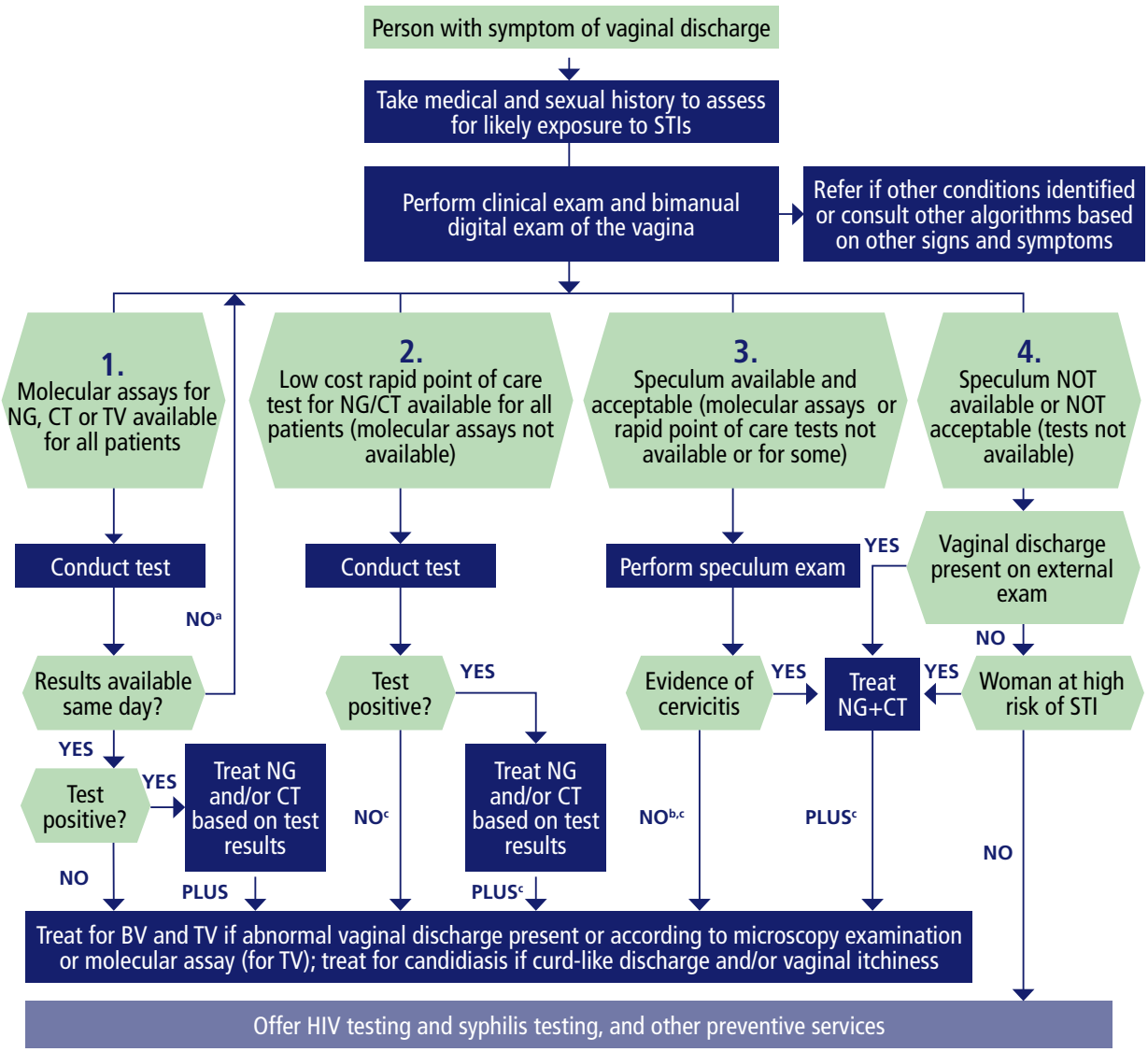
Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Figure 4: Flowchart to determine which management options to implement at a service delivery point for vaginal discharge



Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Figure 5: Management of vaginal discharge



NG, *N. gonorrhoeae*; CT, *Chlamydia trachomatis*; TV, *Trichomonas vaginalis*; BV, *bacterial vaginosis*

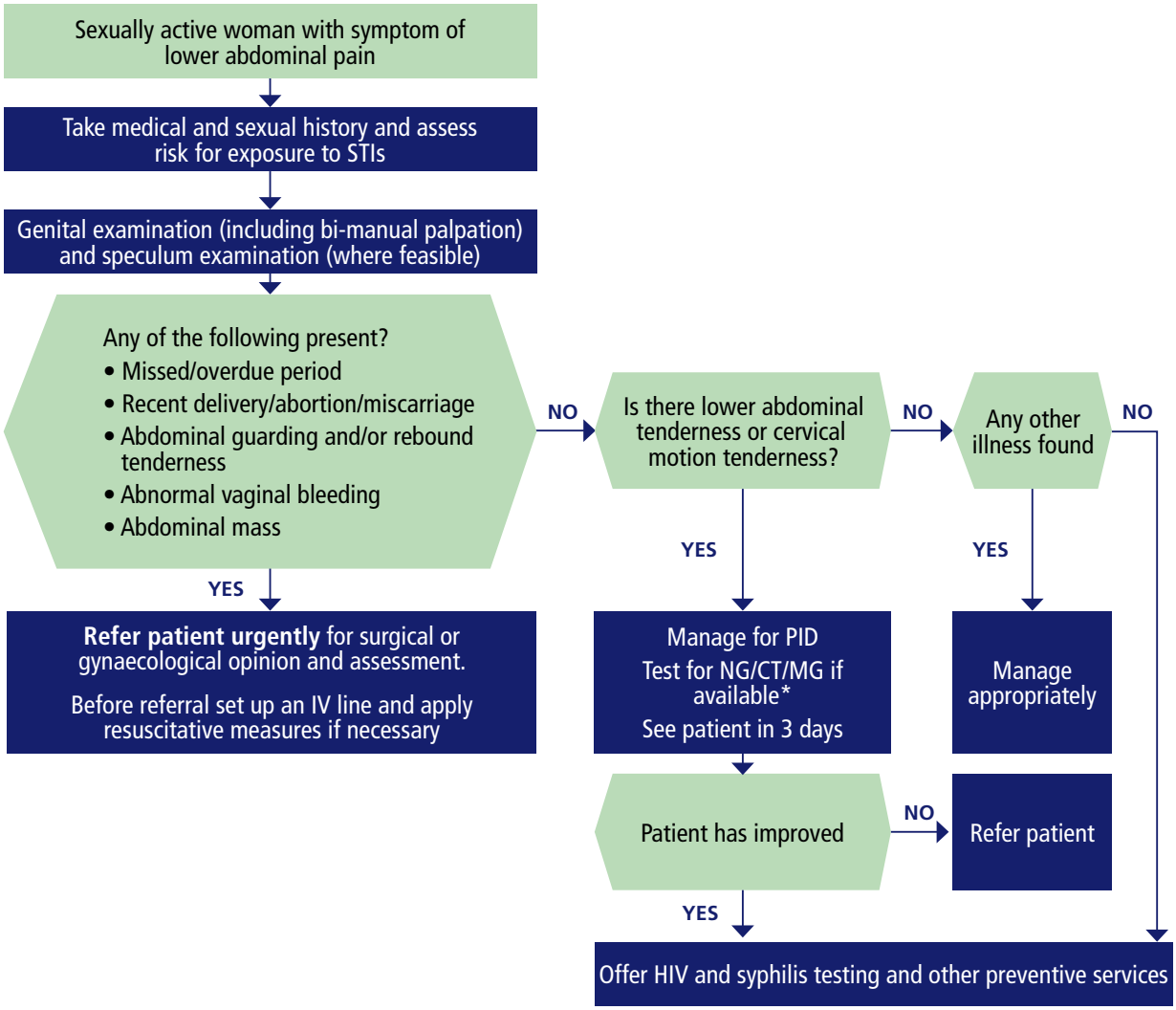
a If molecular assay was performed and results were not available on same day, revise the syndromic treatment initially provided according to the test results when available

b Perform rapid point of care test or molecular assay if available to confirm NG/CT and treat if positive; if negative do not treat and ask woman to return if symptoms recur

c If woman complains of recurrent or persistent discharge refer to a centre with laboratory capacity

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Figure 6: Management of lower abdominal pain

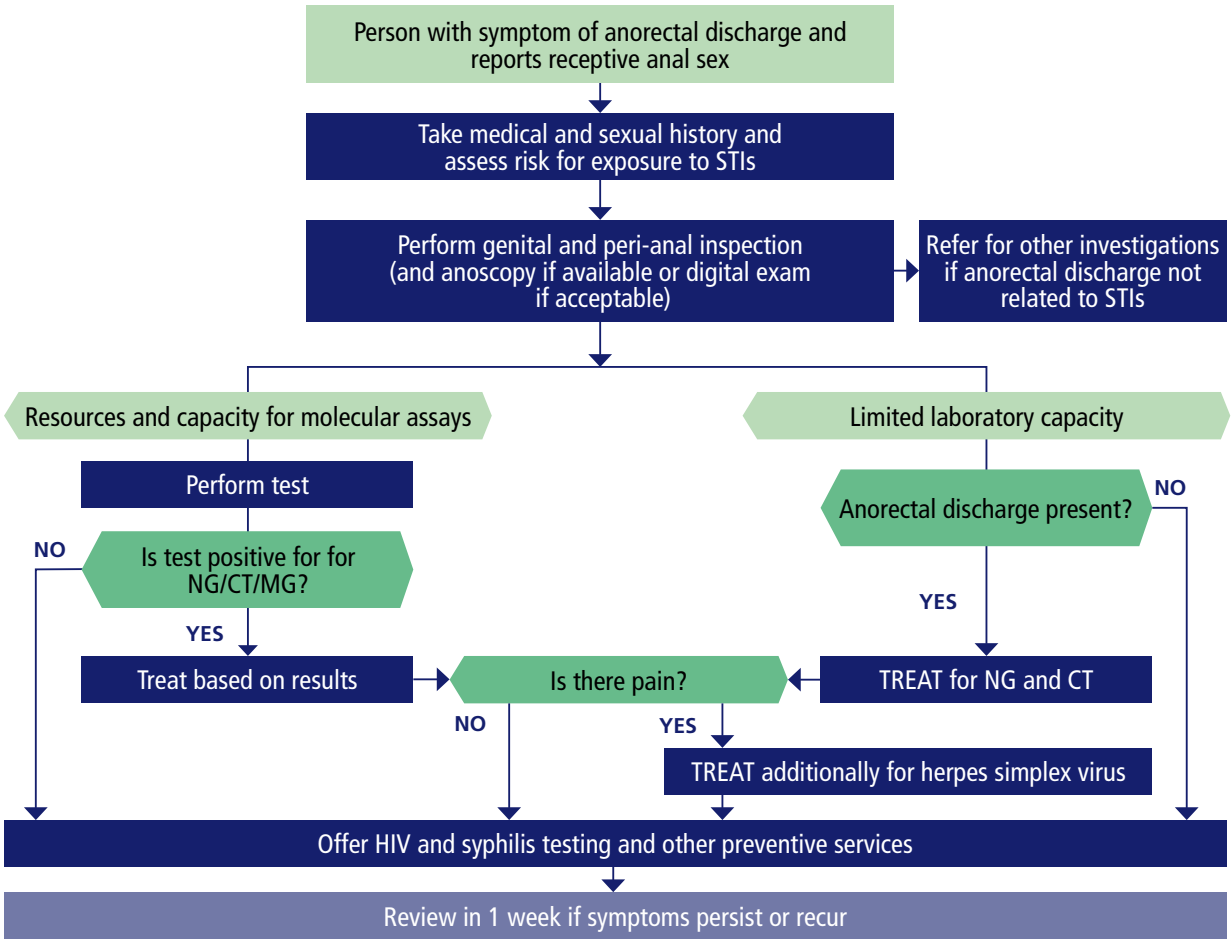


*to support partner notification

NG, *N. gonorrhoeae*; CT, *C. trachomatis*; MG, *M. genitalium*

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Figure 7: Management of anorectal discharge



NG, *N. gonorrhoeae*; CT, *C. trachomatis*; MG, *M. genitalium*

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.