

GUIDELINES

FOR THE MANAGEMENT OF

SEXUALLY TRANSMITTED INFECTIONS



World Health Organization



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Note on terminology

The World Health Organization recommends that the term sexually transmitted disease (STD) be replaced by the term sexually transmitted infection (STI). The term sexually transmitted infection has been adopted since 1999 as it better incorporates asymptomatic infections. In addition, the term has been adopted by a wide range of scientific societies and publications.

Reproductive tract infections encompass three main groups of infection, particularly in women, and sometimes in men. These groups are endogenous infections in the female genital tract (e.g. candidiasis and bacterial vaginosis), iatrogenic infections that may be acquired through non-sterile medical, personal or cultural practices, and some classical STIs. As endogenous infections are not primarily sexually transmitted, clinical and public health actions as recommended for STIs may not apply to them. Given the current state of knowledge and understanding of these non-sexually transmitted infections, treatment of partners is not recommended as routine public health practice. Reassurance and patient education are critical with regard to the nature of these infections.



PREFACE

Sexually transmitted infections (STIs) are among the most common causes of illness in the world and have far-reaching health, social and economic consequences for many countries.

The emergence and spread of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) have had a major impact on the management and control of STIs. At the same time, resistance of several sexually transmitted pathogens to antimicrobial agents has increased, adding to therapeutic problems.

In 1991, WHO published recommendations for the comprehensive management of patients with STIs within the broader context of control, prevention and care programmes for STI and HIV infection. WHO convened an Advisory Group Meeting on Sexually Transmitted Diseases Treatment in May 1999 to review and update treatment recommendations in the light of recent developments (see Annex 1).

In November 2001, an expert consultation on improving the management of STIs was convened by WHO in Geneva (see Annex 2). The consultation focused on the syndromes of genital ulcers and vaginal discharge. The former because of the observed increase of herpes simplex virus type 2 (HSV2) as the main cause of genital ulcers in developing countries, and the latter for its continued complexity and controversy as an entry point for managing cervical gonococcal and chlamydial infections. Recommendations from the consultation have led to the revisions included in this publication, covering the two areas of syndromic management of genital ulcer disease and vaginal discharge.



1. INTRODUCTION

1.1. BACKGROUND

Sexually transmitted infections (STIs) remain a public health problem of major significance in most parts of the world. The incidence of acute STIs is believed to be high in many countries. Failure to diagnose and treat STIs at an early stage may result in serious complications and sequelae, including infertility, fetal wastage, ectopic pregnancy, anogenital cancer and premature death, as well as neonatal and infant infections. The individual and national expenditure on STI care can be substantial.

The appearance of HIV and AIDS has focused greater attention on the control of STIs. There is a strong correlation between the spread of conventional STIs and HIV transmission, and both ulcerative and non-ulcerative STIs have been found to increase the risk of sexual transmission of HIV.

The emergence and spread of HIV infection and AIDS have also complicated the management and control of some other STIs. For example, owing to HIV-related immunosuppression, the treatment of chancroid has become increasingly difficult in areas with a high prevalence of HIV infection.

Antimicrobial resistance of several sexually transmitted pathogens is increasing, rendering some regimen ineffective. New agents, such as third-generation cephalosporins and fluoroquinolones, capable of treating infections with resistant strains, are available but remain expensive. However, their initial high cost must be weighed against the costs of inadequate therapy, including complications, relapse and further transmission of infection.

1.2. RATIONALE FOR STANDARDIZED TREATMENT RECOMMENDATIONS

Effective management of STIs is one of the cornerstones of STI control, as it prevents the development of complications and sequelae, decreases the spread of those



infections in the community and offers a unique opportunity for targeted education about HIV prevention.

Appropriate treatment of STIs at the first contact between patients and health care providers is, therefore, an important public health measure. In the case of adolescent¹ patients, there is the potential to influence future sexual behaviour and treatment-seeking practices at a critical stage of development.

2

INTRODUCTION

It is strongly recommended that countries establish and use national standardized treatment protocols for STIs. These can help to ensure that all patients receive adequate treatment at all levels of health care services. The protocols can also facilitate the training and supervision of health care providers and can help to reduce the risk of development of resistance to antimicrobials. Finally, having a standardized list of antimicrobial agents can also facilitate drug procurement.

It is anticipated that the recommendations contained in this document will help countries to develop standardized protocols adapted to local epidemiological and antimicrobial sensitivity patterns. It is recommended that national guidelines for the effective management of STIs be developed in close consultation with local STI and public health experts.

1.3. CASE MANAGEMENT

STI case management is the care of a person with an STI-related syndrome or with a positive test for one or more STIs. The components of case management include: history taking, clinical examination, correct diagnosis, early and effective treatment, advice on sexual behaviour, promotion and/or provision of condoms, partner notification and treatment, case reporting and clinical follow-up as appropriate. Thus, effective case management consists not only of antimicrobial therapy to obtain cure and reduce infectivity, but also comprehensive consideration and care of the patient's reproductive health.

¹ WHO has defined adolescents as persons in the 10-19 years age group, while youth has been defined as the 15-24 years age group. "Young people" is a combination of these two overlapping groups covering the range 10-24 years (*A picture of health? A review and annotated bibliography of the health of young people in developing countries*. Geneva, World Health Organization, 1995 [WHO/FHE/ADH/95.4]).



1.4. SYNDROMIC MANAGEMENT

Etiological diagnosis of STIs is problematic for health care providers in many settings. It places constraints on their time and resources, increases costs and reduces access to treatment. In addition, the sensitivity and specificity of commercially available tests can vary significantly, affecting negatively the reliability of laboratory testing for STI diagnosis. Where laboratory facilities are available they must be staffed by suitably qualified personnel with adequate training to perform technically demanding procedures, and the establishment of external quality control must be made mandatory.

Many health care facilities in developing countries lack the equipment and trained personnel required for etiological diagnosis of STIs. To overcome this problem, a syndrome-based approach to the management of STI patients has been developed and promoted in a large number of countries in the developing world. The syndromic management approach is based on the identification of consistent groups of symptoms and easily recognized signs (syndromes), and the provision of treatment that will deal with the majority of, or the most serious, organisms responsible for producing a syndrome. WHO has developed a simplified tool (a flowchart or algorithm) to guide health workers in the implementation of syndromic management of STIs.

Syndromic management for urethral discharge in men, and genital ulcers in men and women, has proved to be both valid and feasible. It has resulted in adequate treatment of large numbers of infected people, and is inexpensive, simple and very cost-effective. However, recent data have indicated that herpes simplex virus type 2 (HSV2) is fast becoming the commonest cause of genital ulcer disease (GUD) in developing countries. This may negatively affect the treatment outcome of GUD if antiviral therapy is not appropriately instituted.

WHO's simplified generic tool includes flowcharts for women with symptoms of vaginal discharge and/or lower abdominal pain. While the flowcharts for abdominal pain are quite satisfactory, those for vaginal discharge have limitations, particularly in the management of cervical (gonococcal and chlamydial) infections. In general, but especially in low-prevalence settings and in adolescent females, endogenous vaginitis rather than an STI is the main cause of vaginal discharge. Attempts made to increase the sensitivity and specificity of the vaginal discharge



flowchart for the diagnosis of cervical infection, by introducing an appropriate, situation-specific risk assessment, have not been successful. Some of the risk assessment questions based on demographics, such as age and marital status, tend to classify too many adolescents as being at risk of cervical infection. Therefore, there is a need to identify the main STI risk factors for adolescents in the local population and tailor the risk assessment accordingly. For adolescents in particular it may be preferable to base the risk factors on sexual behaviour patterns.

Further details on recommendations for treatment using a syndrome-based approach are given in section 2.

1.5. RISK FACTORS FOR STI-RELATED CERVICITIS

The flowcharts currently available for the management of cervical infection, referred to in section 1.4, are therefore far from ideal. Initially, it was thought that the finding of vaginal discharge would be indicative of both vaginal and cervical infection. However, it has become clear that while vaginal discharge is indicative of the presence of vaginal infection, it is poorly predictive of cervical infection (gonococcal and/or chlamydial), particularly in adolescent females.

Some clinical signs seem to be more frequently associated with the presence of cervical infection. In the published literature, clinical observations that have consistently been found to be associated with cervical infection are the presence of cervical mucopus, cervical erosions, cervical friability and bleeding between menses or during sexual intercourse.

A number of demographic and behavioural risk factors have also been frequently associated with cervical infection. Some of those, which in some settings have been found to be predictive of cervical infection, are: being less than 21 years old (25 in some places); being unmarried; having more than one sexual partner in the previous three months; having a new partner in the previous three months; having a current partner with an STI; recent use of condoms by the partner. Such risk factors are, however, usually specific for the population group for which they have been identified and validated, and cannot easily be extrapolated to other populations or to other locations. Most researchers have suggested that it is important to obtain more than one demographic risk factor in any particular patient.



Adding these signs and a risk assessment to the vaginal discharge flowchart does increase its specificity and, therefore, its positive predictive value, although the latter remains low especially when the flowchart is applied to populations with relatively low rates of infection.

1.6. SELECTION OF DRUGS

Antimicrobial resistance of several sexually transmitted pathogens has been increasing in many parts of the world and this has rendered some low-cost regimen ineffective. Recommendations to use more effective drugs frequently raise concerns about cost and possible misuse.

A two-tier drug policy with the provision of less effective drugs at the peripheral health care level and the most effective and usually more expensive drugs only at a referral level may result in an unacceptable rate of treatment failures, complications and referrals, and may erode confidence in health services. This approach is not recommended. The drugs used for STI treatment in all health care facilities should have an efficacy of at least 95%. Criteria for the selection of drugs are listed in the box below.

Criteria for the selection of STI drugs

Drugs selected for treating STI should meet the following criteria:

- high efficacy (at least 95%)
- low cost
- acceptable toxicity and tolerance
- organism resistance unlikely to develop or likely to be delayed
- single dose
- oral administration
- not contraindicated for pregnant or lactating women.

Appropriate drugs should be included in the national essential drugs list and in choosing drugs, consideration should be given to the capabilities and experience of health personnel.



2. TREATMENT OF STI-ASSOCIATED SYNDROMES

This section discusses the management of the most common clinical syndromes caused by sexually transmitted agents. Flowcharts for the management of each syndrome are provided.

For all these conditions (except vaginitis) the sexual partner(s) of patients should also be examined for STIs and promptly treated for the same condition(s) as the index patient.

Successful management of STIs requires members of staff to be respectful of patients and not to be judgemental. Clinical examination must take place in appropriate surroundings where privacy can be ensured and confidentiality guaranteed. When dealing with adolescents, the health care provider should be reassuring, experienced and conversant with the changes in anatomy and physiology associated with the different maturation stages, e.g. the menarche in girls or nocturnal emissions in boys. In some situations, health care workers require training to overcome their own sensitivities and to be able to address the issues associated with sexuality and STIs in an open and constructive manner.

2.1. URETHRAL DISCHARGE

Male patients complaining of urethral discharge and/or dysuria should be examined for evidence of discharge. If none is seen, the urethra should be gently massaged from the ventral part of the penis towards the meatus.

If microscopy is available, examination of the urethral smear may show an increased number of polymorphonuclear leukocytes and a Gram stain may demonstrate the presence of gonococci. In the male, more than 5 polymorphonuclear leukocytes per high power field (x 1000) are indicative of urethritis.



The major pathogens causing urethral discharge are *Neisseria gonorrhoeae* (*N. gonorrhoeae*) and *Chlamydia trachomatis* (*C. trachomatis*). In the syndromic management, treatment of a patient with urethral discharge should adequately cover these two organisms. Where reliable laboratory facilities are available, a distinction can be made between the two organisms and specific treatment instituted.

Recommended syndromic treatment

- therapy for uncomplicated gonorrhoea (for details see section 3.1)
- PLUS**
- therapy for chlamydia (for details see section 3.2)

Note

- Patients should be advised to return if symptoms persist 7 days after start of therapy.

AT A GLANCE

Urethral Discharge

For details, see sections 3.1 and 3.2

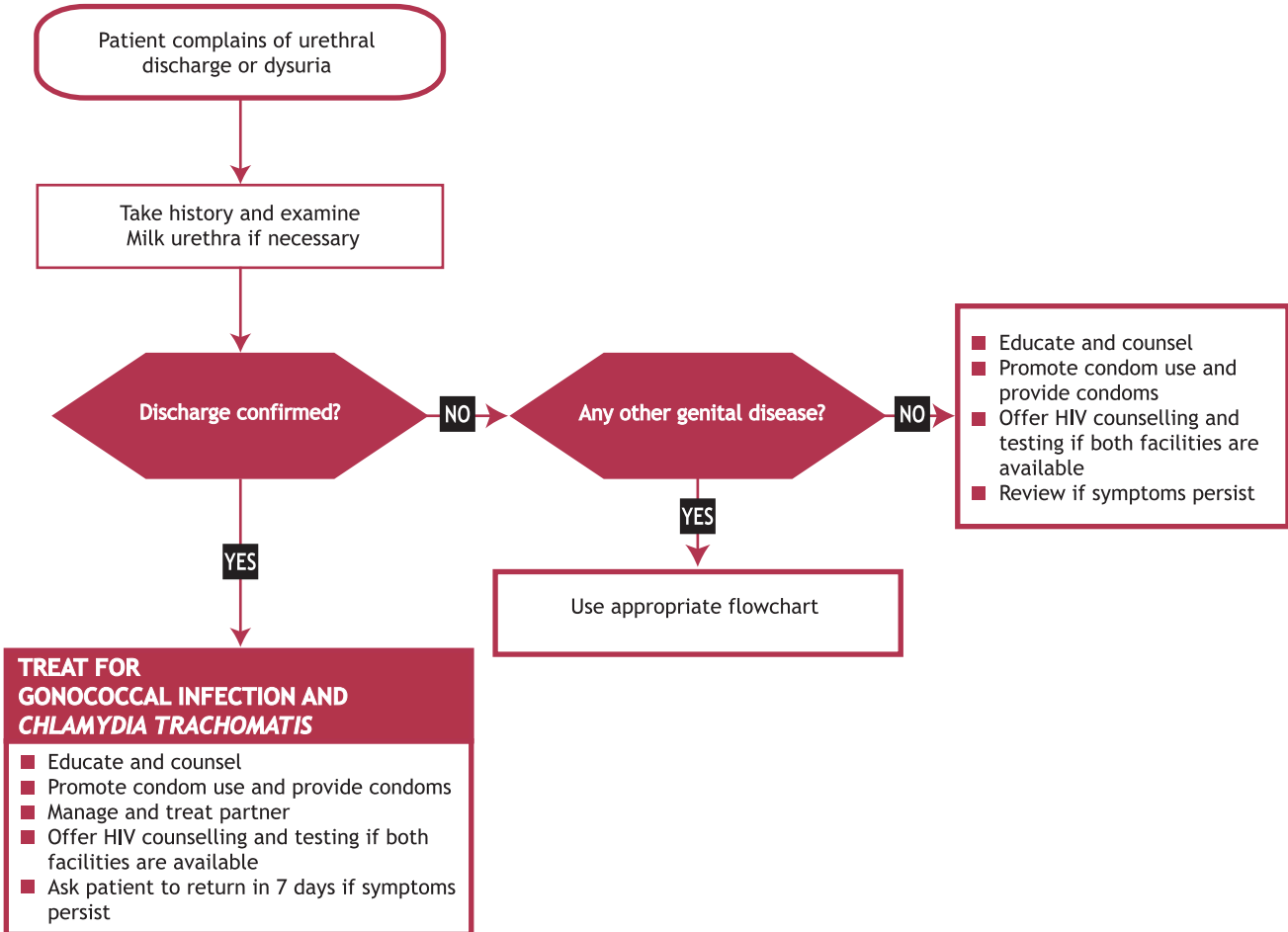
| Treatment options for Gonorrhoea | Treatment options for Chlamydia |
|----------------------------------|--|
| Ciprofloxacin | Doxycycline |
| Ceftriaxone | Azithromycin |
| Cefixime | |
| Spectinomycin | |
| | Alternatives |
| | Amoxicillin |
| | Erythromycin (if Tetracycline contraindicated) |
| | Ofloxacin |
| | Tetracycline |

Note

- WHO recommends that, where possible, single-dose therapy be used.



FIGURE 1. URETHRAL DISCHARGE





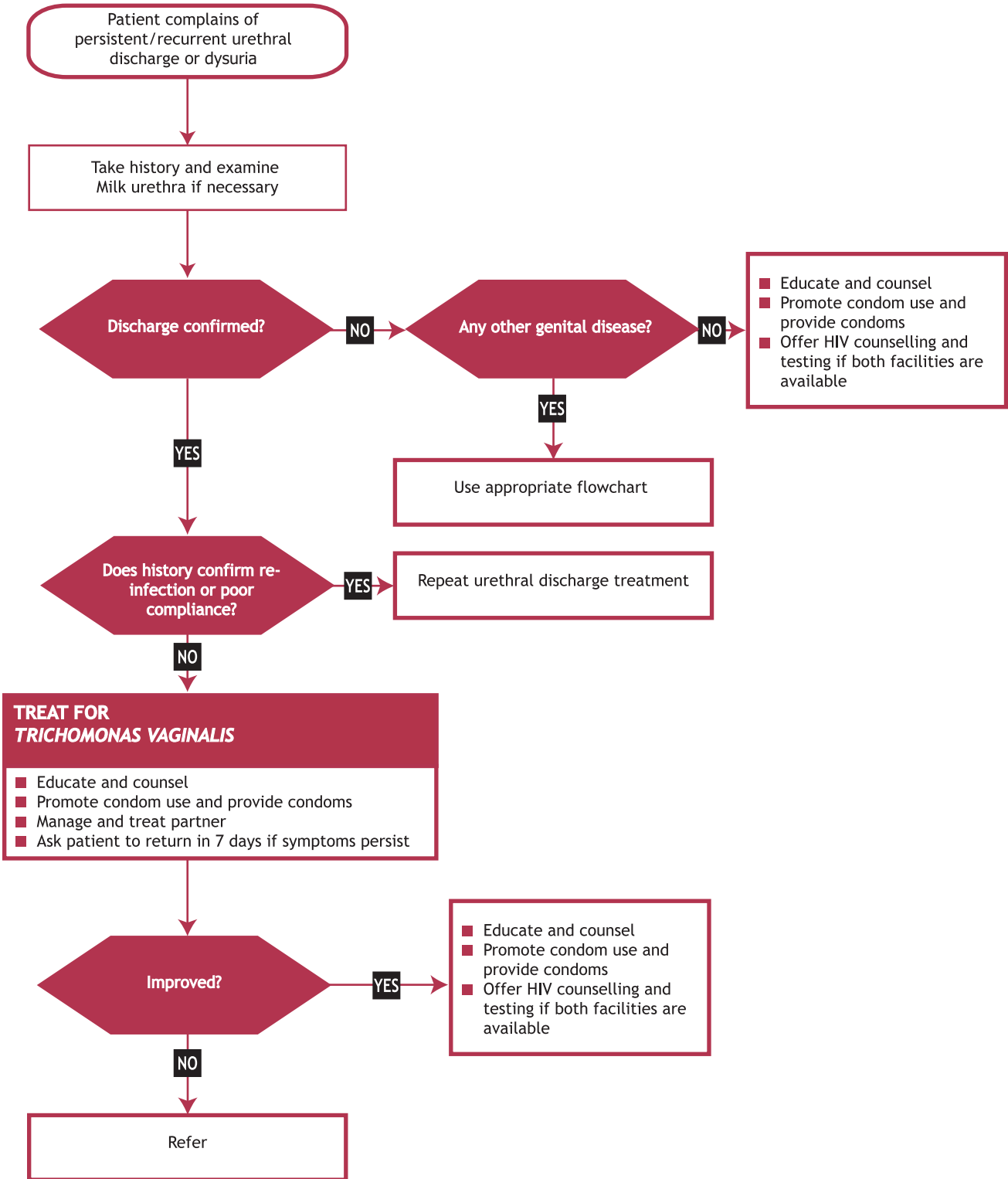
PERSISTENT OR RECURRENT URETHRAL DISCHARGE

Persistent or recurrent symptoms of urethritis may result from drug resistance, poor compliance or reinfection. In some cases there may be infection with *Trichomonas vaginalis* (*T. vaginalis*).

New evidence suggests a high prevalence of *T. vaginalis* in men with urethral discharge in some geographical areas. Where symptoms persist or recur after adequate treatment for gonorrhoea and chlamydia in the index patient and partner(s), the patient should be treated for *T. vaginalis* if the local epidemiological pattern so indicates. If the symptoms still persist at follow-up the patient must be referred. For details, see section 3.9.



FIGURE 2. PERSISTENT/RECURRENT URETHRAL DISCHARGE IN MEN



N.B. This flowchart assumes effective therapy for Gonorrhoea and Chlamydia to have been received and taken by the patient prior to this consultation.



2.2. GENITAL ULCERS

The relative prevalence of causative organisms for GUD varies considerably in different parts of the world and may change dramatically over time. Clinical differential diagnosis of genital ulcers is inaccurate, particularly in settings where several etiologies are common. Clinical manifestations and patterns of GUD may be further altered in the presence of HIV infection.

After examination to confirm the presence of genital ulceration, treatment appropriate to local etiologies and antimicrobial sensitivity patterns should be given. In areas where both syphilis and chancroid are prevalent, for example, patients with genital ulcers should be treated for both conditions at the time of their initial presentation, to ensure adequate therapy in case of loss to follow-up. In areas where either granuloma inguinale or lymphogranuloma venereum (LGV) is prevalent, treatment for either or both conditions should be included for the same reason.

Recent reports from parts of Africa, Asia and Latin America indicate that GUD is more frequently a result of HSV2 infections. This has implications for the efficacy of the syndromic management of GUD if specific antiviral treatment of HSV2 is not considered. In areas of high HIV/ AIDS prevalence, the clinical presentation of these HSV2 ulcers is different from the classical descriptions.

The GUD flowchart presented in this section proposes specific HSV2 treatment, where indicated.

Laboratory-assisted differential diagnosis is also rarely helpful at the initial visit, as mixed infections are common. In areas of high syphilis prevalence, a reactive serological test may only be a reflection of a previous infection and give a misleading picture of the patient's present condition, and a negative test does not necessarily exclude an ulcer of primary syphilis as seroreactivity may take 2–3 weeks to show.



GENITAL ULCERS AND HIV INFECTION

There have been a number of anecdotal reports in the literature suggesting that the natural history of syphilis may be altered as a result of concomitant HIV infection. Some reports have indicated atypical presentations of both primary and secondary syphilis lesions. Some have noted an increase in treatment failure rates among patients with early syphilis who are treated with single-dose therapies of penicillin.

In chancroid, atypical lesions have been reported in HIV-infected individuals. The lesions tend to be more extensive, or multiple lesions may form that are sometimes accompanied by systemic manifestations such as fever and chills. Reports of rapidly aggressive lesions have been noted by some clinicians. This emphasizes the need for early treatment, especially in HIV-infected individuals.

There is evidence to suggest that HIV infection may increase rates of treatment failure in chancroid, especially when single-dose therapies are given. More research is needed to confirm these observations.

In immunosuppressed individuals, herpes simplex lesions may present as persistent multiple ulcers that require medical attention, as opposed to the self-limiting vesicles and ulcers which occur in immunocompetent individuals. Thus, antiviral treatment is particularly important in such instances, to be given therapeutically or prophylactically to offer comfort to the patient. Adequate education needs to be given to the patient as well, to explain the nature and purpose of treatment and in order to avoid false expectations of cure.

Recommended syndromic treatment

- therapy for syphilis (for details see section 3.4)
PLUS EITHER
- therapy for chancroid where it is prevalent (for details see section 3.5)
OR
- therapy for granuloma inguinale where it is prevalent (for details see section 3.6)
OR
- therapy for LGV where it is prevalent (for details see section 3.3)
OR
- therapy for HSV2 infection where indicated (for details, see section 3.7)

**AT A GLANCE****Genital Ulcer Disease***For details, see sections 3.3 – 3.7*

| Drug options for syphilis | Drug options for chancroid | Drug options for granuloma inguinale | Drug options for LGV | Drug options for genital herpes |
|-------------------------------------|----------------------------|--------------------------------------|----------------------|---------------------------------|
| Benzathine | Ciprofloxacin | Azithromycin | Doxycycline | Acyclovir |
| benzylpenicillin | Erythromycin | Doxycycline | Erythromycin | Valaciclovir |
| | Azithromycin | | | Famciclovir |
| Alternatives | Alternatives | Alternatives | Alternatives | |
| Procaine | Ceftriaxone | Erythromycin | Tetracycline | |
| benzylpenicillin | | Tetracycline | | |
| | | Trimethoprim/ sulfamethoxazole | | |
| Penicillin allergy and non-pregnant | | | | |
| Doxycycline | | | | |
| Tetracycline | | | | |

13

Note

- The decision to treat for chancroid, granuloma inguinale or LGV depends on the local epidemiology of the infections.
- Specific treatment for herpes genitalis is recommended as it offers clinical benefits to most symptomatic patients. Health education and counselling regarding the recurrent nature of genital herpes lesions, the natural history, sexual transmission, probable perinatal transmission of the infection and available methods to reduce transmission, are an integral part of genital herpes management (see section 3.7).

**Genital Ulcer Disease Management**

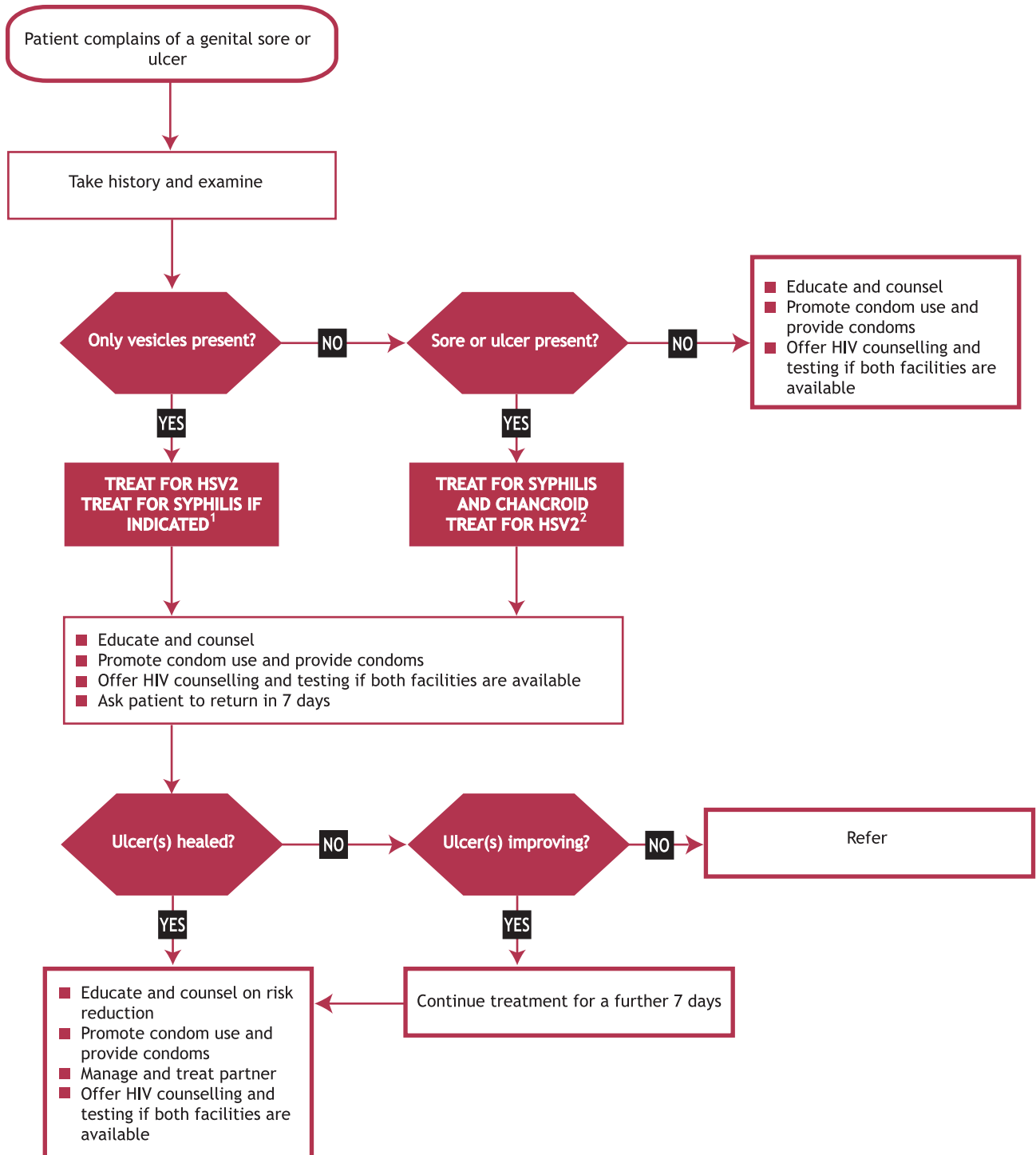
- Treat for syphilis, and, depending upon local epidemiology, either chancroid, granuloma inguinale or lymphogranuloma venereum
- Aspirate any fluctuant glands (surgical incision should be avoided)
- Educate and counsel on risk reduction
- Offer syphilis serologic testing and HIV serologic testing where appropriate facilities and counselling are available
- Review if lesion not fully healed in 7 days
- Promote condom use and provide condoms

Herpes Simplex Management

- Advise on basic care of the lesion (keep clean and dry)
- Provide or prescribe specific antiviral herpes treatment according to local policy
- Educate and counsel on compliance, risk reduction and natural history of HSV2 infection
- Offer syphilis and HIV serologic testing where appropriate facilities and counselling are available
- Promote condom use and provide condoms
- Advise to return in 7 days if lesion is not fully healed, and sooner if there is clinical deterioration; if so, treat for other causes of GUD as per guidelines



FIGURE 3. GENITAL ULCERS



1 Indications for syphilis treatment:

- RPR positive; and
- Patient has not been treated for syphilis recently.

2 Treat for HSV2 where prevalence is 30% or higher, or adapt to local conditions.



INGUINAL BUBO

Inguinal and femoral buboes are localised enlargements of the lymph nodes in the groin area, which are painful and may be fluctuant. They are frequently associated with LGV and chancroid. In many cases of chancroid an associated genital ulcer is visible. Non-sexually transmitted local and systemic infections (e.g. infections of the lower limb or tuberculous lymphadenopathy) can also cause swelling of inguinal lymph nodes.

16

Recommended syndromic treatment

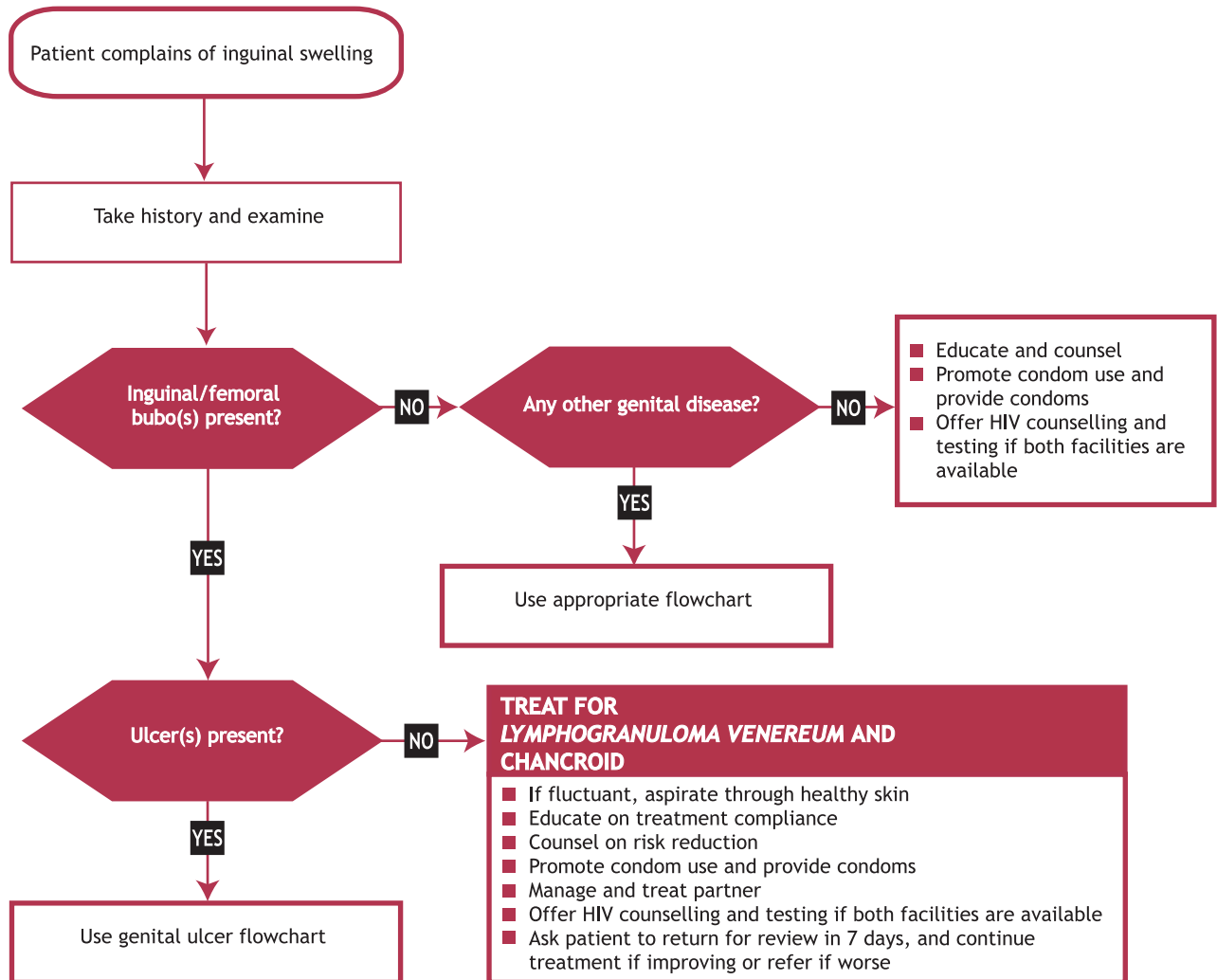
- ciprofloxacin, 500 mg orally, twice daily for 3 days
- **AND**
- doxycycline, 100 mg orally, twice daily for 14 days
- **OR**
- erythromycin, 500 mg orally, four times daily for 14 days

Note

- Some cases may require longer treatment than the 14 days recommended above. 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.



FIGURE 4. INGUINAL BUBO





2.3. SCROTAL SWELLING

Inflammation of the epididymis (epididymitis) usually manifests itself by acute onset of unilateral testicular pain and swelling, often with tenderness of the epididymis and vas deferens, and occasionally with erythema and oedema of the overlying skin. In men under 35 years this is more frequently caused by sexually transmitted organisms than in those over 35 years. When the epididymitis is accompanied by urethral discharge, it should be presumed to be of sexually transmitted origin, commonly gonococcal and/or chlamydial in nature. The adjacent testis is often also inflamed (orchitis), giving rise to epididymo-orchitis.

In older men, where there may have been no risk of a sexually transmitted infection, other general infections may be responsible, for example, *Escherichia coli*, *Klebsiella* spp. or *Pseudomonas aeruginosa*. A tuberculous orchitis, generally accompanied by an epididymitis, is always secondary to lesions elsewhere, especially in the lungs or bones. In brucellosis, usually caused by *Brucella melitensis* or *Brucella abortus*, an orchitis is usually clinically more evident than an epididymitis.

In pre-pubertal children the usual etiology is coliform, pseudomonas infection or mumps virus. Mumps epididymo-orchitis is usually noted within a week of parotid enlargement.

It is important to consider other non-infectious causes of scrotal swelling, such as trauma, testicular torsion and tumour. Testicular torsion, which should be suspected when onset of scrotal pain is sudden, is a surgical emergency that needs urgent referral.

If not effectively treated, STI-related epididymitis may lead to infertility.

Recommended syndromic treatment

■ therapy for uncomplicated gonorrhoea (for details, see section 3.1)

PLUS

■ therapy for chlamydia (for details, see section 3.2)

**AT A GLANCE****Scrotal swelling**

For details, see sections 3.1 and 3.2

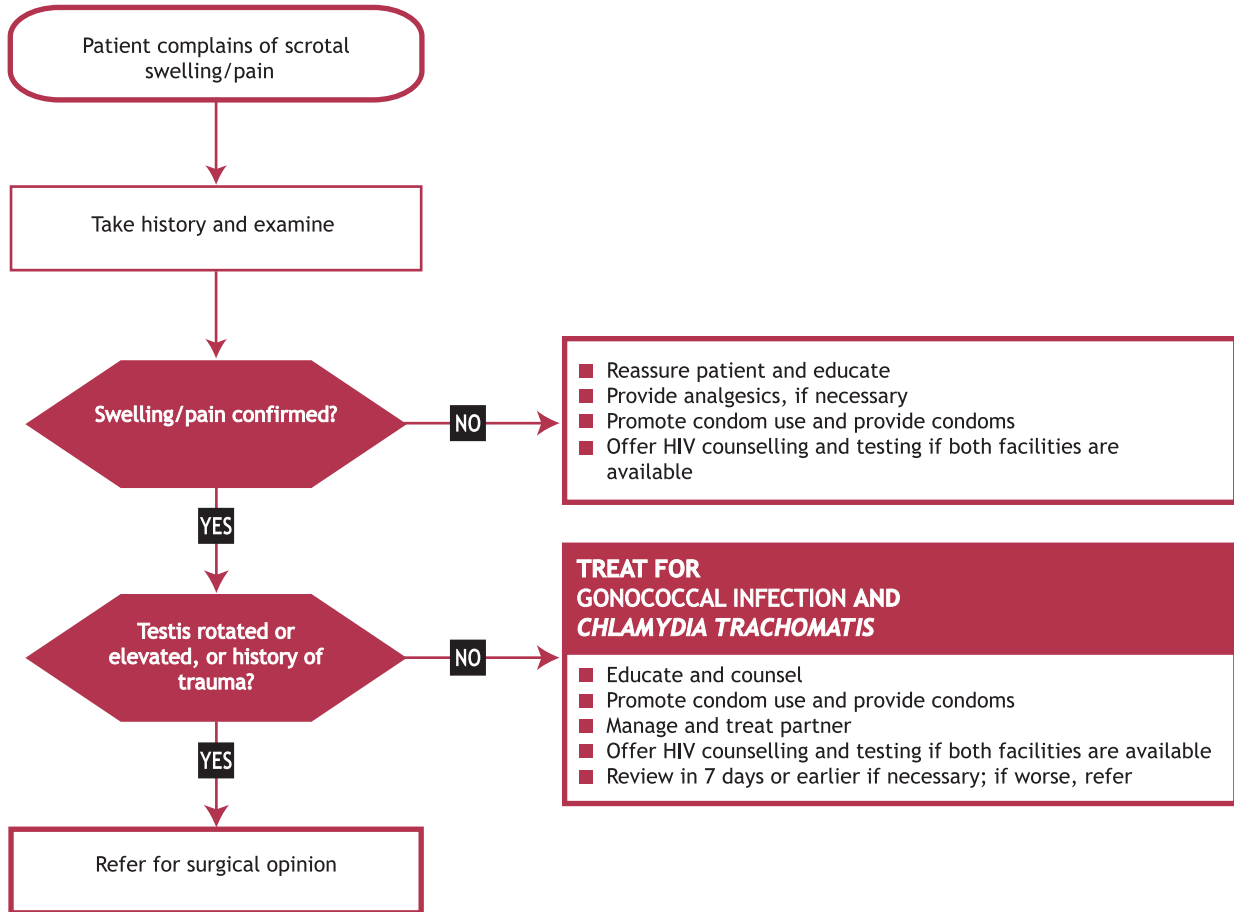
| Drug options for Gonorrhoea | Drug options for Chlamydia |
|-----------------------------|---|
| Ciprofloxacin | Doxycycline |
| Ceftriaxone | Azithromycin |
| Spectinomycin | |
| Cefixime | |
| Alternatives | |
| | Amoxicillin |
| | Ofloxacin |
| | Erythromycin (if Tetracycline is contraindicated) |
| | Tetracycline |

Adjuncts to therapy

Bed rest and scrotal support until local inflammation and fever subside.



FIGURE 5. SCROTAL SWELLING





2.4. VAGINAL DISCHARGE

A spontaneous complaint of abnormal vaginal discharge (in terms of quantity, colour or odour) is most commonly a result of a vaginal infection. It may in rare cases be caused by mucopurulent STI-related cervicitis. *T. vaginalis*, *C. albicans* and bacterial vaginosis (BV) are the commonest causes of vaginal infection. *N. gonorrhoeae* and *C. trachomatis* cause cervical infection. The clinical detection of cervical infection is difficult because a large proportion of women with gonococcal or chlamydial cervical infection is asymptomatic. The symptom of abnormal vaginal discharge is highly indicative of vaginal infection, but poorly predictive for cervical infection. Thus, all women presenting with vaginal discharge should receive treatment for trichomoniasis and BV.

Among women presenting with discharge, one can attempt to identify those with an increased likelihood of being infected with *N. gonorrhoeae* and/or *C. trachomatis*. To identify women at greater risk, therefore, of cervical infection, an assessment of a woman's risk status may be useful, especially when risk factors are adapted to the local situation. Given that microscopy requires special training, is time consuming and adds relatively little given the amount of time and resources it requires, it is generally not recommended at the primary health care level. However, in settings where Gram stain can be carried out in an efficient manner, such as a referral clinic, identification of Gram-negative intracellular diplococci and/or *T. vaginalis* can be attempted.

Knowledge of the local prevalence of gonococcal and/or chlamydia in women presenting with vaginal discharge is important when making the decision to treat for cervical infection. The higher the prevalence, the stronger the justification for treatment. Women with a positive risk assessment have a higher likelihood of cervical infection than those who are risk negative. Women with vaginal discharge and a positive risk assessment should, therefore, be offered treatment for gonococcal and chlamydia cervicitis.

Where resources permit, the use of laboratory tests to screen women with vaginal discharge should be considered. Such screening could be applied to all women with discharge or selectively to those with discharge and a positive risk assessment.



In some countries, syndromic management flowcharts have been used as a screening tool to detect cervical infection among women not presenting with a genital complaint (e.g. in family planning settings). While this may assist in detecting some women with cervical infections, it is likely that there will be substantial over-diagnosis.

CERVICAL INFECTION

Recommended syndromic treatment

- therapy for uncomplicated gonorrhoea (for details, see section 3.1)

PLUS

- therapy for chlamydia (for details, see section 3.2)

AT A GLANCE

Cervical infection

For details, see sections 3.1 and 3.2

| Drug options for Gonorrhoea | Drug options for Chlamydia |
|-----------------------------|---|
| Ciprofloxacin | Doxycycline |
| Ceftriaxone | Azithromycin |
| Cefixime | |
| Spectinomycin | |
| | Alternatives |
| | Amoxicillin |
| | Ofloxacin |
| | Erythromycin (if Tetracycline is contraindicated) |
| | Tetracycline |

Note

- Tetracyclines are contraindicated in pregnancy.



VAGINAL INFECTION

Recommended syndromic treatment

- therapy for *T. vaginalis* (for details, see section 3.9)

PLUS

- therapy for BV (for details, see section 3.10)

AND, WHERE INDICATED,

- therapy for *C. albicans* (for details, see section 3.11)

AT A GLANCE

Vaginal infection

For details, see sections 3.9–3.11

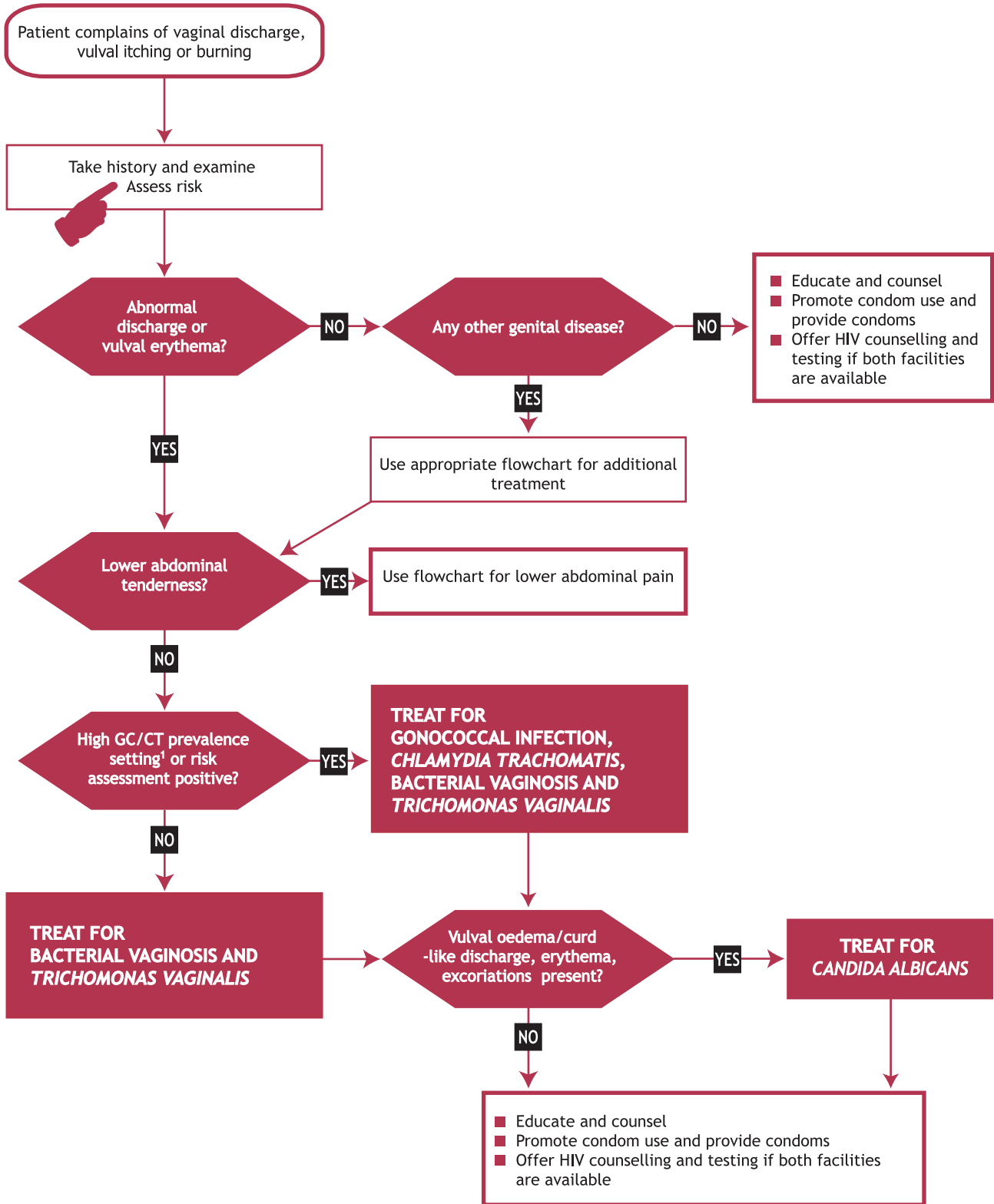
| Drug options for BV | Drug options for <i>T. vaginalis</i> | Drug options for candida |
|---------------------------|--------------------------------------|--------------------------|
| Metronidazole | Metronidazole | Miconazole |
| | Tinidazole | Clotrimazole |
| | | Fluconazole |
| Alternatives | Alternatives | |
| Clindamycin | | |
| Metronidazole gel | | |
| Clindamycin vaginal cream | Nystatin | |

Note

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



FIGURE 6. VAGINAL DISCHARGE

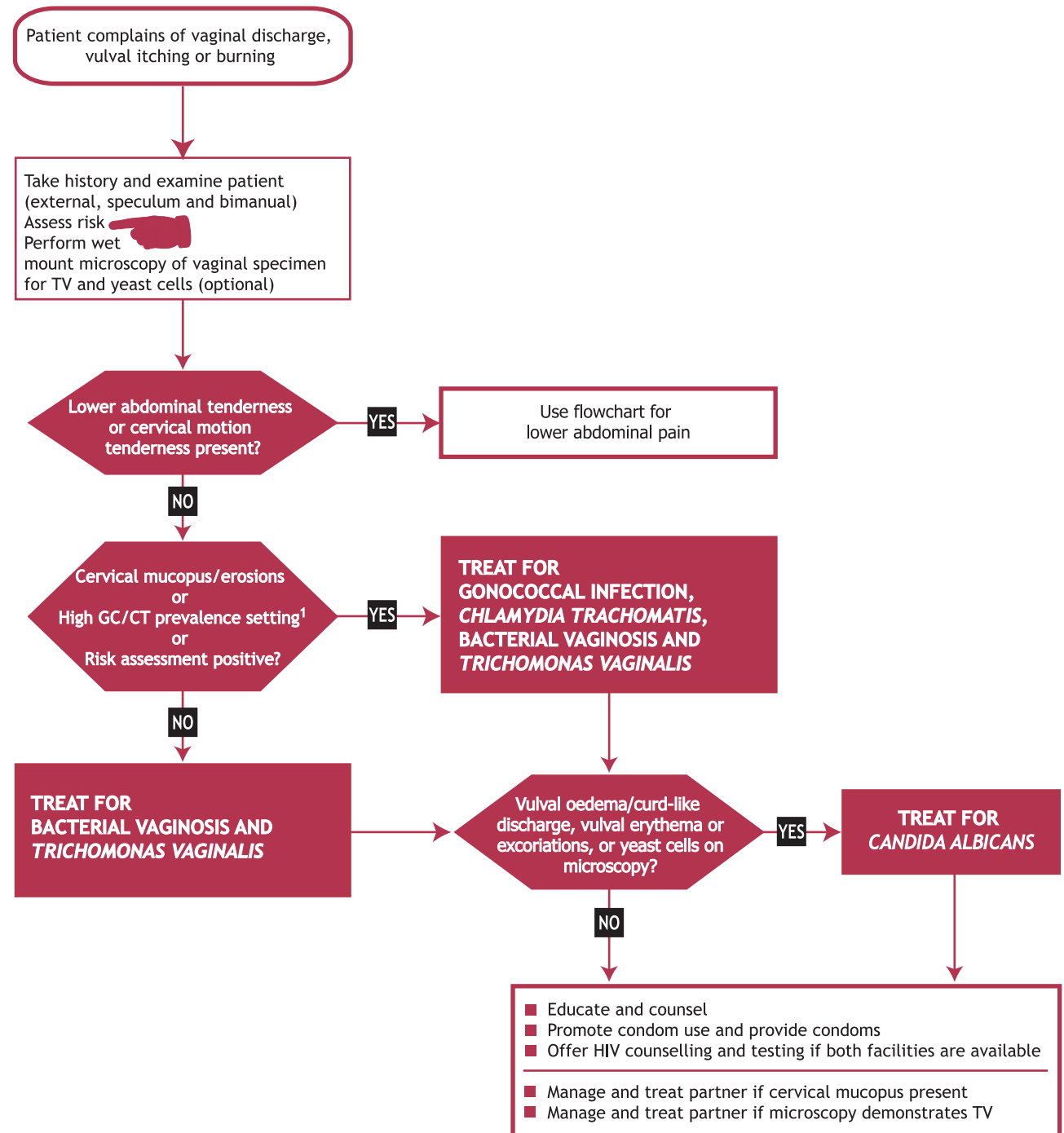


Risk factors need adaptation to local social, behavioural and epidemiological situation.

¹ The determination of high prevalence levels needs to be made locally.



**FIGURE 7. VAGINAL DISCHARGE:
BIMANUAL & SPECULUM, WITH OR WITHOUT MICROSCOPE**

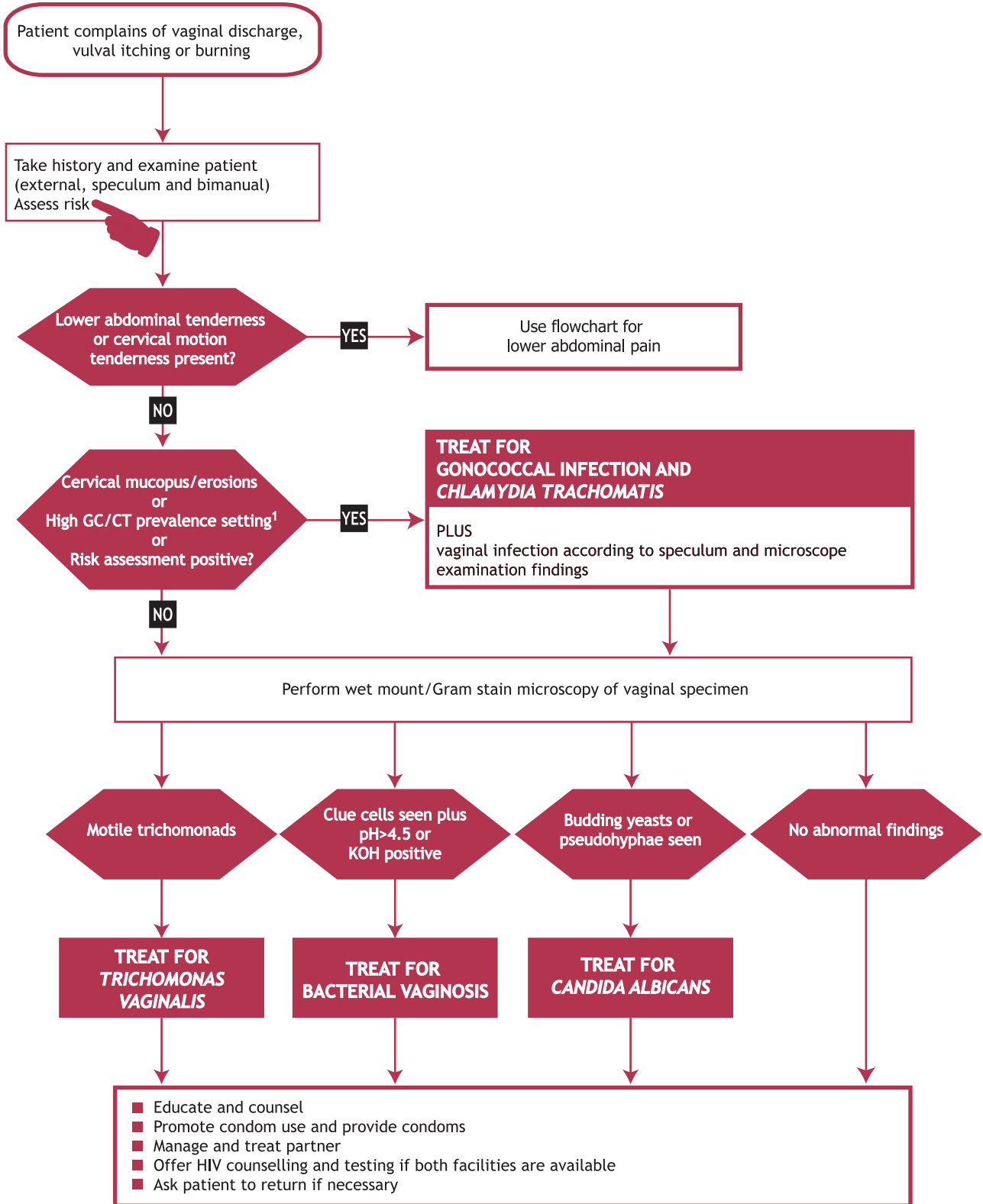


Risk factors need adaptation to local social, behavioural and epidemiological situation.

¹ The determination of high prevalence levels needs to be made locally.



FIGURE 8. VAGINAL DISCHARGE: BIMANUAL, SPECULUM & MICROSCOPE



Risk factors need adaptation to local social, behavioural and epidemiological situation.

¹ The determination of high prevalence levels needs to be made locally.



2.5. LOWER ABDOMINAL PAIN

All sexually active women presenting with lower abdominal pain should be carefully evaluated for the presence of salpingitis and/or endometritis – elements of pelvic inflammatory disease (PID). In addition, routine bimanual and abdominal examination should be carried out on all women with a presumptive STI since some women with PID or endometritis will not complain of lower abdominal pain. Women with endometritis may present with complaints of vaginal discharge and/or bleeding and/or uterine tenderness on pelvic examination. Symptoms suggestive of PID include abdominal pain, dyspareunia, vaginal discharge, menometrorrhagia, dysuria, fever, and sometimes nausea and vomiting.

PID is difficult to diagnose because clinical manifestations are varied. PID becomes highly probable when one or more of the above symptoms are seen in a woman with adnexal tenderness, evidence of lower genital tract infection, and cervical motion tenderness. Enlargement or induration of one or both fallopian tubes, a tender pelvic mass, and direct or rebound tenderness may also be present. The patient's temperature may be elevated but is normal in many cases. In general, clinicians should err on the side of over-diagnosing and treating suspected cases.

Hospitalization of patients with acute PID should be seriously considered when:

- the diagnosis is uncertain;
- surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded;
- a pelvic abscess is suspected;
- severe illness precludes management on an outpatient basis;
- the patient is pregnant;
- the patient is unable to follow or tolerate an outpatient regimen; or
- the patient has failed to respond to outpatient therapy.

Many experts recommend that all patients with PID should be admitted to hospital for treatment.

Etiological agents include *N. gonorrhoeae*, *C. trachomatis*, anaerobic bacteria (*Bacteroides* spp. and Gram-positive cocci). Facultative Gram-negative rods and *Mycoplasma hominis* have also been implicated. As it is impossible to differentiate between these clinically, and a precise microbiological diagnosis is difficult, the



treatment regimen must be effective against this broad range of pathogens. The regimen recommended below are based on this principle.

OUTPATIENT THERAPY

Recommended syndromic treatment

- single-dose therapy for uncomplicated gonorrhoea (see section 3.1. Single-dose ceftriaxone has been shown to be effective; other single-dose regimen have not been formally evaluated as treatments for PID)

PLUS

- doxycycline, 100 mg orally, twice daily, or tetracycline, 500 mg orally, 4 times daily for 14 days

PLUS

- metronidazole, 400–500 mg orally, twice daily for 14 days

Note

- Patients taking metronidazole should be cautioned to avoid alcohol.
- Tetracyclines are contraindicated in pregnancy.

Adjuncts to therapy: removal of intrauterine device (IUD)

If PID should occur with an IUD in place, treat the PID using appropriate antibiotics. There is no evidence that removal of the IUD provides any additional benefit.^{2,3,4} Thus, if the individual should wish to continue its use, it need not be removed. If she does not want to keep the IUD, removal of the IUD is recommended after antimicrobial therapy has been commenced. When the IUD is removed, contraceptive counselling is necessary.

Follow-up

Outpatients with PID should be followed up after 72 hours and admitted if their condition has not improved.

² Soderberg G. and Lindgren S. Influence of an intrauterine device on the course of an acute salpingitis. *Contraception*, 1981. 24(2):137-43.

³ Teisala K. Removal of an intrauterine device and the treatment of acute pelvic inflammatory disease. *Ann Med*, 1989. 21(1):63-5.

⁴ Larsson B. and Wennergren M. Investigation of a copper-intrauterine device (Cu-IUD) for possible effect on frequency and healing of pelvic inflammatory disease. *Contraception*, 1977. 15(2):143-9.

**INPATIENT THERAPY****Recommended syndromic treatment options for PID**

1. Ceftriaxone, 250 mg by intramuscular injection, once daily

PLUS

■ doxycycline, 100 mg orally or by intravenous injection, twice daily, or tetracycline, 500 mg orally 4 times daily

PLUS

■ metronidazole, 400–500 mg orally or by intravenous injection, twice daily, or chloramphenicol, 500 mg orally or by intravenous injection, 4 times daily

2. Clindamycin, 900 mg by intravenous injection, every 8 hours

PLUS

■ gentamicin, 1.5 mg/kg by intravenous injection every 8 hours

3. Ciprofloxacin, 500 mg orally, twice daily, or spectinomycin 1 g by intramuscular injection, 4 times daily

PLUS

■ doxycycline, 100 mg orally or by intravenous injection, twice daily, or tetracycline, 500 mg orally, 4 times daily

PLUS

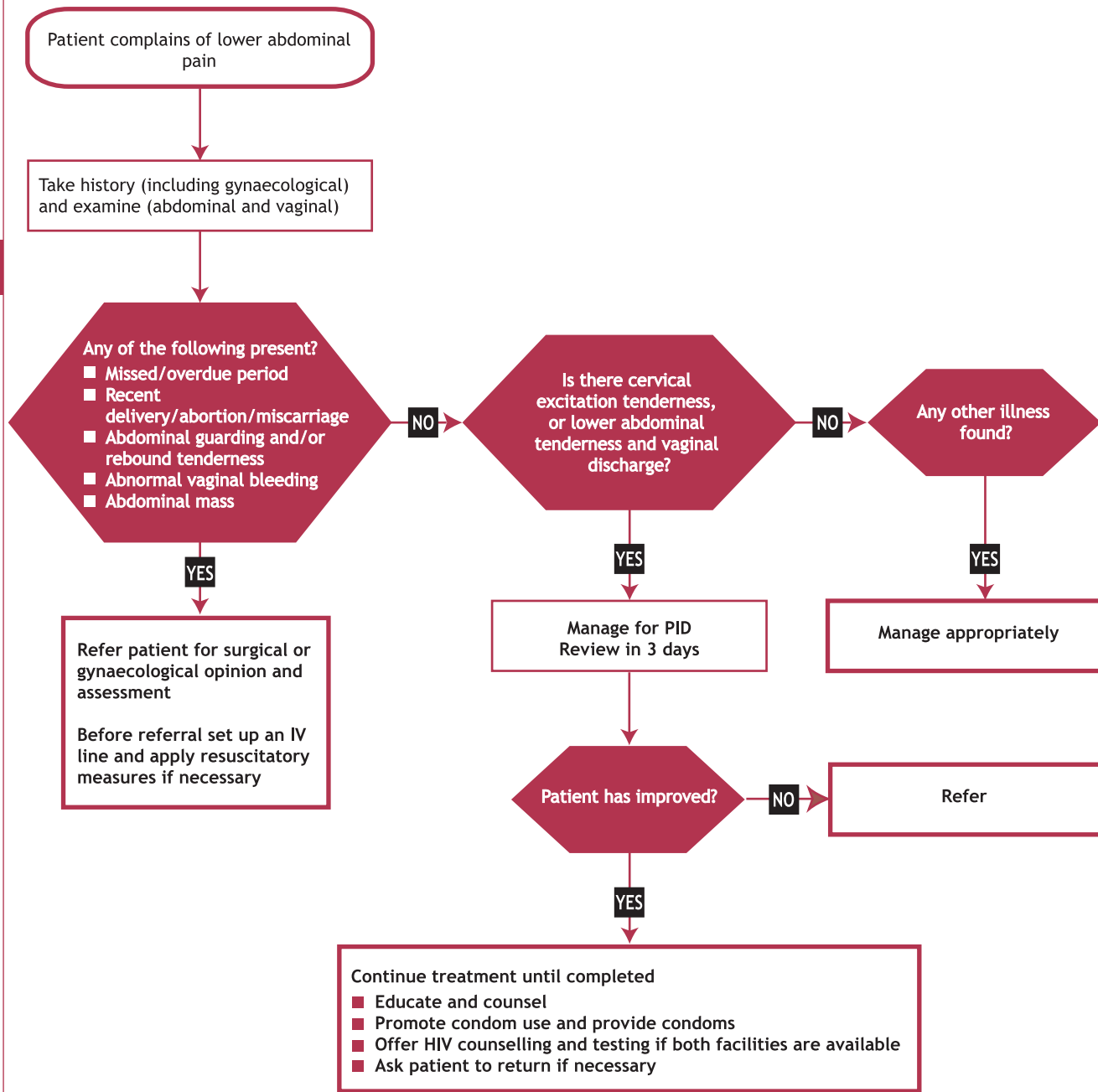
■ metronidazole, 400–500 mg orally or by intravenous injection, twice daily, or chloramphenicol, 500 mg orally or by intravenous injection, 4 times daily

Note

- For all three regimen, therapy should be continued until at least two days after the patient has improved and should then be followed by either doxycycline, 100 mg orally, twice daily for 14 days, or tetracycline, 500 mg orally, 4 times daily, for 14 days.
- Patients taking metronidazole should be cautioned to avoid alcohol.
- Tetracyclines are contraindicated in pregnancy.



FIGURE 9. LOWER ABDOMINAL PAIN





2.6. NEONATAL CONJUNCTIVITIS

Neonatal conjunctivitis (ophthalmia neonatorum) can lead to blindness when caused by *N. gonorrhoeae* and treatment is delayed. The most important sexually transmitted pathogens which cause ophthalmia neonatorum are *N. gonorrhoeae* and *C. trachomatis*. In developing countries, *N. gonorrhoeae* accounts for 20–75% and *C. trachomatis* for 15–35% of cases brought to medical attention. Other common causes are *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus* spp. and *Pseudomonas* spp. Newborn babies are generally presented because of redness and swelling of the eyelids or “sticky eyes”, or because of discharge from the eye(s).

As the clinical manifestations and possible complications of gonococcal and chlamydial infections are similar, in settings where it is impossible to differentiate between the two infections, treatment should be provided to cover both. This would include single-dose therapy for gonorrhoea and multiple dose therapy for chlamydia.

AT A GLANCE

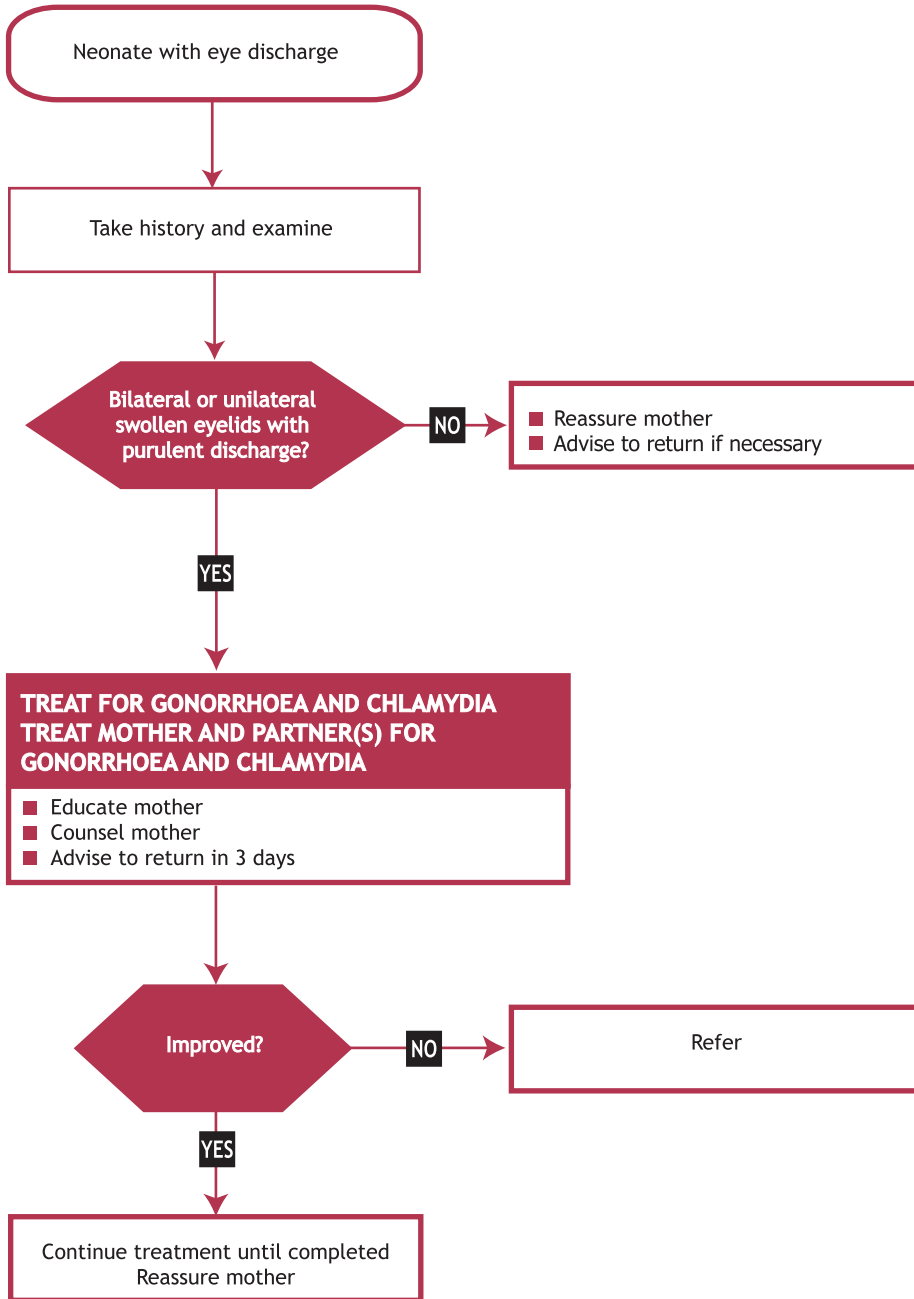
Neonatal conjunctivitis

For details, see sections 3.1 and 3.2

| Drug options for Gonorrhoea | Drug options for Chlamydia |
|-----------------------------|----------------------------|
| Ceftriaxone | Erythromycin |
| Alternatives | |
| Kanamycin | |
| Spectinomycin | |



FIGURE 10. NEONATAL CONJUNCTIVITIS





3. TREATMENT OF SPECIFIC INFECTIONS

3.1. GONOCOCCAL INFECTIONS

A large proportion of gonococcal isolates worldwide are now resistant to penicillins, tetracyclines, and other older antimicrobial agents. Therefore, these drugs can no longer be recommended for the treatment of gonorrhoea.

It is important to monitor local *in vitro* susceptibility, as well as the clinical efficacy of recommended regimen.

In general it is recommended that concurrent anti-chlamydia therapy be given to all patients with gonorrhoea, as described in section 3.2, because dual infection is common. This does not apply to patients in whom a specific diagnosis of *C. trachomatis* has been excluded by a laboratory test.

UNCOMPLICATED ANOGENITAL INFECTION

Recommended regimen

- ciprofloxacin, 500 mg orally, as a single dose

OR

- ceftriaxone, 125 mg by intramuscular injection, as a single dose

OR

- cefixime, 400 mg orally, as a single dose

OR

- spectinomycin, 2 g by intramuscular injection, as a single dose

Note

- Ciprofloxacin is contraindicated in pregnancy, and is not recommended for use in children and adolescents.
- There are variations in the anti-gonococcal activity of individual quinolones, and it is important to use only the most active.



DISSEMINATED GONOCOCCAL INFECTION

Recommended regimen

- ceftriaxone, 1 g by intramuscular or intravenous injection, once daily for 7 days (alternative third-generation cephalosporins may be required where ceftriaxone is not available, but more frequent administrations will be needed)

OR

- spectinomycin, 2 g by intramuscular injection, twice daily for 7 days. There are some data to suggest that therapy for 3 days is adequate

Note

- For gonococcal meningitis and endocarditis the same dosages apply but for endocarditis the duration of therapy will need to be increased to 4 weeks.

GONOCOCCAL OPHTHALMIA

This is a serious condition that requires systemic therapy as well as local irrigation with saline or other appropriate solutions. Irrigation is particularly important when the recommended therapeutic regimen are not available. Careful hand washing by personnel caring for infected patients is essential.

A. Adult gonococcal conjunctivitis

Recommended regimen

- ceftriaxone, 125 mg by intramuscular injection, as a single dose

OR

- spectinomycin, 2 g by intramuscular injection, as a single dose

OR

- ciprofloxacin, 500 mg orally, as a single dose

Note

- This regimen is likely to be effective although there are no published data on its use in gonococcal ophthalmia.

Alternative regimen where the recommended agents are not available

- kanamycin, 2 g by intramuscular injection, as a single dose

**Follow-up**

Careful monitoring of clinical progress is important.

B. Neonatal gonococcal conjunctivitis**Recommended regimen**

- ceftriaxone, 50 mg/kg by intramuscular injection, as a single dose, to a maximum of 125 mg

Alternative regimen where ceftriaxone is not available

- kanamycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg

OR

- spectinomycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg

Note

- Single-dose ceftriaxone and kanamycin are of proven efficacy. The addition of tetracycline eye ointment to these regimen is of no documented benefit.

Follow-up

Patients should be reviewed after 48 hours.

Prevention of ophthalmia neonatorum

Gonococcal ophthalmia neonatorum is preventable with timely eye prophylaxis. The infant's eyes should be carefully cleaned immediately after birth. The application of 1% silver nitrate solution or 1% tetracycline ointment to the eyes of all infants at the time of delivery is strongly recommended as a prophylactic measure. However, ocular prophylaxis provides poor protection against *C. trachomatis* conjunctivitis. Infants born to mothers with gonococcal infection should receive additional treatment.

Recommended regimen for infants born to mothers with gonococcal infection

- ceftriaxone 50 mg/kg by intramuscular injection, as a single dose, to a maximum of 125 mg



Alternative regimen where ceftriaxone is not available

- kanamycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg

OR

- spectinomycin, 25 mg/kg by intramuscular injection, as a single dose, to a maximum of 75 mg

3.2. CHLAMYDIA TRACHOMATIS INFECTIONS (OTHER THAN LYMPHOGRANULOMA VENEREUM)

36

TREATMENT OF SPECIFIC INFECTIONS

UNCOMPLICATED ANOGENITAL INFECTION

Recommended regimen

- doxycycline, 100 mg orally, twice daily for 7 days

OR

- azithromycin, 1 g orally, in a single dose

Alternative regimen

- amoxicillin, 500 mg orally, 3 times a day for 7 days

OR

- erythromycin, 500 mg orally, 4 times a day for 7 days

OR

- ofloxacin, 300 mg orally, twice a day for 7 days

OR

- tetracycline, 500 mg orally, 4 times a day for 7 days

Note

- Doxycycline and other tetracyclines are contraindicated during pregnancy and lactation.

- Current evidence indicates that 1 g single-dose therapy of azithromycin is efficacious for chlamydial infection.

- There is evidence that extending the duration of treatment beyond 7 days does not improve the cure rate in uncomplicated chlamydial infection.

- Erythromycin should not be taken on an empty stomach.



Follow-up

Compliance with the 7-day regimen is critical. Resistance of *C. trachomatis* to recommended treatment regimen has not been observed.

CHLAMYDIAL INFECTION DURING PREGNANCY

Recommended regimen

- erythromycin, 500 mg orally, 4 times a day for 7 days

OR

- amoxicillin, 500 mg orally, three times a day for 7 days

Note

- Doxycycline (and other tetracyclines) and ofloxacin are contraindicated in pregnant women.
- Preliminary data suggest that azithromycin is safe to use in pregnant women.^{5,6} However, the number of women in the trials so far is too small to assess safety for use in pregnancy as rare adverse outcomes are unlikely to be detected.
- Erythromycin estolate is contraindicated during pregnancy because of drug-related hepato-toxicity. Hence, only erythromycin base or erythromycin ethylsuccinate should be used.

NEONATAL CHLAMYDIAL CONJUNCTIVITIS

All newborn infants with conjunctivitis should be treated for both *N. gonorrhoeae* and *C. trachomatis*, because of the possibility of mixed infection.

Recommended regimen

- erythromycin syrup, 50 mg/kg per day orally, in 4 divided doses for 14 days

Alternative regimen

- trimethoprim 40 mg with sulfamethoxazole 200 mg orally, twice daily for 14 days

⁵ Adair CD et al. Chlamydia in pregnancy: a randomized trial of azithromycin and erythromycin. *Obstet Gynecol*, 1998, 91:165-168.

⁶ Wehbeh HA et al. Single dose azithromycin for chlamydia in pregnant women. *J Reprod Med*, 1998, 43:509-514.



Note

- There is no evidence that additional therapy with a topical agent provides further benefit. If inclusion conjunctivitis recurs after therapy has been completed, erythromycin treatment should be reinstated for 2 weeks.

INFANTILE PNEUMONIA

Recommended regimen

- erythromycin syrup, 50 mg/kg per day (given orally in four doses) for 14 days

Note

- The optimal duration of therapy has not been definitively established, but treatment should not be less than 14 days.

3.3. LYMPHOGRANULOMA VENEREUM

There are limited published data on the treatment of LGV. Treatment recommendations are based on expert opinion and a comparative study published in the WHO Bulletin in 1963.⁷

Recommended regimen

- doxycycline, 100 mg orally, twice daily for 14 days
- OR**
- erythromycin, 500 mg orally, 4 times daily for 14 days

Alternative regimen

- tetracycline, 500 mg orally, 4 times daily for 14 days

Note

- Tetracyclines are contraindicated in pregnancy.
- Fluctuant lymph nodes should be aspirated through healthy skin. Incision and drainage or excision of nodes may delay healing. Some patients with advanced disease may require treatment for longer than 14 days, and sequelae such as strictures and/or fistulae may require surgery.

⁷ Greaves AB. The frequency of lymphogranuloma venereum in persons with perirectal abscesses, fistulae-in-ano, or both. *Bulletin of the World Health Organization*, 1963, 29:797-801.



3.4. SYPHILIS

CLINICAL PRESENTATION SUMMARY

Syphilis is a systemic disease from the outset and is caused by the spirochaete, *Treponema pallidum* (*T. pallidum*). The infection can be classified as congenital (transmitted from mother to child *in utero*) or acquired (through sex or blood transfusion).

Acquired syphilis is divided into early and late syphilis. Early syphilis comprises the primary, secondary and early latent stages. Late syphilis refers to late latent syphilis, gummatous, neurological and cardiovascular syphilis.

Primary syphilis is characterised by an ulcer or chancre at the site of infection or inoculation. Secondary syphilis manifestations include a skin rash, condylomata lata, mucocutaneous lesions and generalised lymphadenopathy.

As its name implies, latent syphilis has no clinical manifestations. Early latent syphilis is infection of less than two years duration. An infection of more than two years duration without clinical evidence of treponemal infection is referred to as late latent syphilis. WHO has based this division on the infectiousness of syphilis and its response to therapy. Early stages are more infectious but respond better to treatment.

In the early phase of primary syphilis the cardiolipin/non-treponemal tests, such as the Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests may be negative and should, therefore, not be interpreted as absence of syphilis infection.

Therapeutic considerations

A treponemicidal level of antimicrobials needs to be achieved in the serum and cerebrospinal fluid (CSF) to provide effective treatment for syphilis. A penicillin level of greater than 0.018 mg per litre is considered sufficient, and needs to be maintained for at least 7–10 days in early syphilis, and for a longer duration in late syphilis. Long-acting benzathine benzylpenicillin, at a dose of 2.4 million



units, provides a treponemicidal penicillinaemia for up to three weeks and is recommended for late syphilis treatment.

Parenteral, rather than oral, penicillin treatment is preferred as it provides guaranteed bioavailability and supervised treatment. More data are required before either ceftriaxone or oral azithromycin can be generally recommended. Azithromycin has the advantage of being effective against *C. trachomatis*, *H. ducreyi* and the gonococcus.

Management of patients with cardiovascular syphilis should include consultation with a cardiologist. All patients with cardiovascular syphilis and neurosyphilis should be monitored for many years. The follow-up should include clinical, serological, CSF and, based on the clinician's assessment of the individual patient's condition, radiological examinations.

Follow-up of patients treated for syphilis

The follow-up of patients treated for early syphilis should be based on available medical services and resources. The clinical condition of the patients should be assessed and attempts made to detect reinfection during the first year after therapy. Patients with early syphilis who have been treated with appropriate doses and preparations of benzathine benzylpenicillin should be evaluated clinically and serologically, using a non-treponemal test, after three months to assess the results of therapy. A second evaluation should be performed after six months and, if indicated by the results at this point, again after 12 months to reassess the condition of the patient and detect possible reinfection.

At all stages of the disease, repeat treatment should be considered when:

- clinical signs or symptoms of active syphilis persist or recur;
- there is confirmed increase in the titre of a non-treponemal test.

Examination of the CSF should be undertaken before repeat treatment, unless reinfection and a diagnosis of early syphilis can be established. Patients should be re-treated with the schedules recommended for syphilis of more than two years' duration. In general, only one re-treatment course is indicated because adequately treated patients often maintain stable, low titres of non-treponemal tests.



SYPHILIS AND HIV INFECTION

All patients with syphilis should be encouraged to undergo testing for HIV infection because of the high frequency of dual infection and its implications for clinical assessment and management. Neurosyphilis should be considered in the differential diagnosis of neurological disease in HIV-infected individuals. In cases of congenital syphilis, the mother should be encouraged to undergo testing for HIV; if her test is positive, the infant should be referred for follow-up.

Recommended therapy for early syphilis in HIV-infected patients is no different from that in patients not infected with HIV. However, some authorities advise examination of the CSF and/or more intensive treatment with a regimen appropriate for all patients with the dual infections of *T. pallidum* and HIV, regardless of the clinical stage of syphilis. In all cases, careful follow-up is necessary to ensure adequacy of treatment.

SYPHILIS IN PREGNANCY

Pregnant women should be regarded as a separate group, requiring close surveillance, in particular to detect possible reinfection after treatment has been given. It is also important to treat their sexual partner(s). Pregnant patients at all stages of pregnancy, who are not allergic to penicillin, should be treated with penicillin according to the dosage schedules recommended for the treatment of non-pregnant patients at a similar stage of the disease.

The effectiveness of erythromycin in all stages of syphilis and its ability to prevent the stigmata of congenital syphilis are both highly questionable, and many failures have been reported. Its efficacy in neurosyphilis is probably low. Although data are lacking, consideration should probably be given to using an extended course of a third-generation cephalosporin in pregnant women whose penicillin allergy is not manifested by anaphylaxis.

Penicillin desensitisation of pregnant women with syphilis requires that the procedure be performed in a hospital setting. This is not feasible at most primary health care settings and cannot be recommended as a routine procedure.



Follow-up

Following treatment, quantitated non-treponemal serological tests should be performed at monthly intervals until delivery, and re-treatment should be undertaken if there is serological evidence of reinfection or relapse.

CONGENITAL SYPHILIS

Congenital syphilis is divided into early (first two years of life) and late (becomes apparent later in life).

Prevention of congenital syphilis is feasible. Programmes should implement effective screening strategies for syphilis in pregnant women. Screening for syphilis should be conducted at the first prenatal visit. Some programmes have found it beneficial to repeat the tests at 28 weeks of pregnancy and at delivery in populations with a high incidence of congenital syphilis.

Congenital syphilis may occur if the expectant mother has syphilis, but the risk is minimal if she has been given penicillin during pregnancy. All infants of seropositive mothers should be examined at birth and at monthly intervals for three months until it is confirmed that serological tests are, and remain, negative. Any antibody carried over from mother to baby usually disappears within three months of birth. Where available, IgM-specific serology may aid diagnosis.

All infants born to seropositive mothers should be treated with a single intramuscular dose of benzathine benzylpenicillin, 50 000 IU/kg whether or not the mothers were treated during pregnancy (with or without penicillin). Hospitalization is recommended for all symptomatic babies born to mothers who were seropositive. Symptomatic infants and asymptomatic infants with abnormal CSF (up to two years of age) should be treated as for early congenital syphilis.

Early congenital syphilis generally responds well, both clinically and serologically, to adequate doses of penicillin. Recovery may be slow in seriously ill children with extensive skin, mucous membrane, bone or visceral involvement. Those in poor nutritional condition may succumb to concurrent infections, such as pneumonia.



TREATMENT REGIMEN FOR SYPHILIS

EARLY SYPHILIS

(primary, secondary, or latent syphilis of not more than two years' duration)

Recommended regimen

- benzathine benzylpenicillin,⁸ 2.4 million IU by intramuscular injection, at a single session. Because of the volume involved, this dose is usually given as two injections at separate sites

Alternative regimen

- procaine benzylpenicillin,⁹ 1.2 million IU by intramuscular injection, daily for 10 consecutive days

Alternative regimen for penicillin-allergic non-pregnant patients

- doxycycline, 100 mg orally, twice daily for 14 days

OR

- tetracycline, 500 mg orally, 4 times daily for 14 days

Alternative regimen for penicillin-allergic pregnant patients

- erythromycin, 500 mg orally, 4 times daily for 14 days

LATE LATENT SYPHILIS

(infection of more than two years' duration without evidence of treponemal infection)

Recommended regimen

- benzathine benzylpenicillin, 2.4 million IU by intramuscular injection, once weekly for 3 consecutive weeks

⁸ Benzathine benzylpenicillin synonyms: benzathine penicillin G; benzylpenicillin benzathine; benzathine penicillin.

⁹ Procaine benzylpenicillin synonyms: procaine penicillin G.



Alternative regimen

- procaine benzylpenicillin, 1.2 million IU by intramuscular injection, once daily for 20 consecutive days

Alternative regimen for penicillin-allergic non-pregnant patients

- doxycycline, 100 mg orally, twice daily for 30 days

OR

- tetracycline, 500 mg orally, 4 times daily for 30 days

Alternative regimen for penicillin-allergic pregnant patients

- erythromycin, 500 mg orally, 4 times daily for 30 days

NEUROSYPHILIS

Recommended regimen

- aqueous benzylpenicillin,¹⁰ 12–24 million IU by intravenous injection, administered daily in doses of 2–4 million IU, every 4 hours for 14 days

Alternative regimen

- procaine benzylpenicillin, 1.2 million IU by intramuscular injection, once daily, and probenecid, 500 mg orally, 4 times daily, both for 10–14 days

This regimen should be used only for patients whose outpatient compliance can be assured.

Note

- Some authorities recommend adding benzathine benzylpenicillin, 2.4 million IU by intramuscular injection, in 3 consecutive doses once weekly, after completing these regimen, but there are no data to support this approach. Benzathine benzylpenicillin, 2.4 million IU by intramuscular injection does not give adequate therapeutic levels in the CSF.

¹⁰ Aqueous benzylpenicillin synonyms: benzylpenicillin potassium; benzylpenicillin sodium; crystalline penicillin, penicillin G potassium; penicillin G sodium.

**Alternative regimen for penicillin-allergic non-pregnant patients**

- doxycycline, 200 mg orally, twice daily for 30 days

OR

- tetracycline, 500 mg orally, 4 times daily for 30 days

Note

- The above alternatives to penicillin for the treatment of neurosyphilis have not been evaluated in systematic studies. Although their efficacy is not yet well documented, third-generation cephalosporins may be useful in the treatment of neurosyphilis.
- The central nervous system may be involved during any stage of syphilis. Clinical evidence of neurological involvement (e.g. optic or auditory symptoms, or cranial nerve palsies) warrants examination of the CSF. However, examination of the CSF is also highly desirable in all patients with syphilis of more than two years' duration, or of uncertain duration, in order to evaluate the possible presence of asymptomatic neurosyphilis. Some experts recommend consulting a neurologist when caring for a patient with neurosyphilis. Careful follow-up is essential.

CONGENITAL SYPHILIS**A. Early congenital syphilis (up to 2 years of age)****AND****Infants with abnormal CSF****Recommended regimen**

- aqueous benzylpenicillin 100 000–150 000 IU/kg/day administered as 50 000 IU/kg/dose IV every 12 hours, during the first 7 days of life and every 8 hours thereafter for a total of 10 days

OR

- procaine benzylpenicillin, 50 000 IU/kg by intramuscular injection, as a single daily dose for 10 days

Note

- Some experts treat all infants with congenital syphilis as if the CSF findings were abnormal. Antimicrobials other than penicillin (e.g. erythromycin) are not



recommended for congenital syphilis except in cases of allergy to penicillin. Tetracyclines should not be used in young children.

B. Congenital syphilis of 2 or more years

Recommended regimen

- aqueous benzylpenicillin, 200 000–300 000 IU/kg/day by intravenous or intramuscular injection, administered as 50 000 IU/kg/dose every 4–6 hours for 10–14 days

Alternative regimen for penicillin-allergic patients, after the first month of life

- erythromycin, 7.5–12.5 mg/kg orally, 4 times daily for 30 days

3.5. CHANCROID

The causative organism is a Gram-negative facultative anaerobic bacillus, *H. ducreyi*. The infection is common in several parts of the world including Africa, the Caribbean and south-east Asia. Owing to widespread antimicrobial resistance in all geographical areas, tetracyclines and penicillins are not recommended for treatment of chancroid. To enhance compliance, single-dose treatments with effective antibiotics are preferred.

Management of lesions

No special treatment is required. Ulcerative lesions should be kept clean. Fluctuant lymph nodes should be aspirated as required through the surrounding healthy skin. Incision and drainage or excision of nodes may delay healing and is not recommended.

Follow-up

All patients should be followed up until there is clear evidence of improvement or cure. In patients infected with HIV, treatment may appear to be less effective, but this may be a result of coinfection with genital herpes or syphilis. Since chancroid and HIV infection are closely associated, and therapeutic failure is likely to be seen with increasing frequency, patients should be followed up weekly until there is clear evidence of improvement.

**Recommended regimen**

- ciprofloxacin, 500 mg orally, twice daily for 3 days

OR

- erythromycin base, 500 mg orally, 4 times daily for 7 days

OR

- azithromycin, 1 g orally, as a single dose

Alternative regimen

- ceftriaxone, 250 mg by intramuscular injection, as a single dose

3.6. GRANULOMA INGUINALE (DONOVANOSIS)

Donovanosis is caused by the intracellular Gram-negative bacterium *Klebsiella granulomatis*, (previously known as *Calymmatobacterium granulomatis*). The disease presents clinically as painless, progressive, ulcerative lesions without regional lymphadenopathy. The lesions are highly vascular and can easily bleed on contact.

Treatment should be continued until all lesions have completely epithelialized.

Recommended regimen

- azithromycin, 1 g orally on first day, then 500 mg orally, once a day

OR

- doxycycline, 100 mg orally, twice daily

Alternative regimen

- erythromycin, 500 mg orally, 4 times daily

OR

- tetracycline, 500 mg orally, 4 times daily

OR

- trimethoprim 80 mg/sulfamethoxazole 400 mg, 2 tablets orally, twice daily for a minimum of 14 days

Note

- The addition of a parenteral aminoglycoside such as gentamicin should be carefully considered for treating HIV-infected patients.



Follow-up

Patients should be followed up clinically until signs and symptoms have resolved.

3.7. GENITAL HERPES INFECTIONS

The primary cause of genital herpes is the herpes simplex virus type 2 (HSV2) infection. It is highly prevalent in human populations in many parts of the world, and is the most common cause of GUD worldwide. The major public health importance of HSV2 relates to its potential role in facilitating HIV transmission.

There is no known cure for genital herpes, but the course of symptoms can be modified if systemic therapy with acyclovir, or its analogues, is started as soon as possible following the onset of symptoms. Treatment can be expected to reduce the formation of new lesions, the duration of pain, the time required for healing, and viral shedding. However, it does not appear to influence the natural history of recurrent disease. Topical therapy with acyclovir produces only minimal shortening of the duration of symptomatic episodes and is not recommended.

Recurrent infections

Most patients with a first episode of genital herpes infection will have recurrent episodes of genital lesions. Episodic or suppressive antiviral therapy will shorten the duration of genital lesions. Many patients benefit from antiviral therapy, therefore options for such treatment should be discussed with all patients. Many patients who have recurrent disease benefit from episodic therapy if treatment is started during the prodrome or within one day after onset of lesions. If episodic treatment of recurrences is chosen, the patient should be provided with antiviral therapy, or a prescription for the medication, so that treatment can be initiated at the first sign of prodrome or genital lesions.

HERPES IN PREGNANCY

During the first clinical episode of genital herpes, treat with oral acyclovir.

Vaginal delivery in women who develop primary genital herpes shortly before delivery puts babies at risk for neonatal herpes. Babies born to women with recurrent disease are at very low risk. Genital cultures late in pregnancy are poor predictors of shedding during delivery. Careful history taking and physical



examination serve as a guide to the need for caesarean section in mothers with genital herpes lesions.

HERPES AND HIV COINFECTION

In people whose immunity is deficient, persistent and/or severe mucocutaneous ulcerations may occur, often involving large areas of perianal, scrotal or penile skin. The lesions may be painful and atypical, making a clinical diagnosis difficult. The natural history of herpes sores may become altered. Most lesions of herpes in HIV-infected persons will respond to acyclovir, but the dose may have to be increased and treatment given for longer than the standard recommended period. Subsequently, patients may benefit from chronic suppressive therapy. In some cases the patients may develop thymidine-kinase deficient mutants for which standard antiviral therapy becomes ineffective.

SUPPRESSIVE THERAPY

Daily suppressive therapy reduces the frequency of genital herpes recurrences by more than 75% among patients who have frequent recurrences (six or more recurrences per year). Safety and efficacy have been documented among patients receiving daily therapy with acyclovir for as long as six years, and with valaciclovir and famciclovir for one year. Suppressive therapy has not been associated with the emergence of clinically significant acyclovir resistance among immunocompetent patients.

Suppressive treatment with acyclovir reduces, but does not eliminate, asymptomatic viral shedding. Therefore, the extent to which suppressive therapy may prevent HSV transmission is unknown.

TREATMENT OPTIONS FOR GENITAL HERPES

Recommended regimen for first clinical episode

- acyclovir, 200 mg orally, 5 times daily for 7 days
- OR
- acyclovir, 400 mg orally, 3 times daily for 7 days
- OR
- valaciclovir, 1 g orally, twice daily for 7 days



OR

- famciclovir, 250 mg orally, 3 times daily for 7 days

Recommended regimen for recurrent infection

- acyclovir, 200 mg orally, 5 times daily for 5 days

OR

- acyclovir, 400 mg orally, 3 times daily for 5 days

OR

- acyclovir, 800 mg orally, twice daily for 5 days

OR

- valaciclovir, 500 mg orally, twice daily for 5 days

OR

- valaciclovir, 1000 mg orally, once daily for 5 days

OR

- famciclovir, 125 mg orally, twice daily for 5 days

Recommended regimen for suppressive therapy

- acyclovir, 400 mg orally, twice daily, continuously

OR

- valaciclovir, 500 mg orally, once daily

OR

- valaciclovir, 1000 mg orally, once daily

OR

- famciclovir, 250 mg orally, twice daily

Note

- Some experts recommend discontinuing acyclovir after one year of continuous use so that the recurrence rate can be reassessed. The lowest continuous dose that will suppress recurrences in an individual can only be determined empirically.

Recommended regimen for severe disease

- acyclovir, 5–10 mg/kg IV, every 8 hours for 5–7 days or until clinical resolution is attained

**Recommended regimen in severe herpes simplex lesions with coinfection with HIV**

- acyclovir, 400 mg orally, 3–5 times daily until clinical resolution is attained

Recommended regimen for neonates

- acyclovir, 10 mg/kg intravenously, 3 times a day for 10–21 days

3.8. VENEREAL (GENITAL) WARTS

The human papilloma virus (HPV) is the causative agent for this common STI. Genital warts are painless and do not lead to serious complications, except where they cause obstruction, especially in pregnant women. The removal of the lesion does not mean that the infection has been cured. No treatment is completely satisfactory. In most clinical situations podophyllin, podophyllotoxin or trichloroacetic acid (TCA) is used to treat external genital and perianal warts. Cryotherapy with liquid nitrogen, solid carbon dioxide or cryoprobe is preferred by many physicians when available. Cryotherapy is non-toxic, does not require anaesthesia and, if carried out properly, does not result in scarring.

Sexual partner(s) should be examined for evidence of warts. Patients with anogenital warts should be made aware that they are contagious to sexual partners. The use of condoms is recommended to help reduce transmission.

Specific types of HPV may give rise to invasive carcinoma of the cervix. It is recommended practice to examine the cervix in all female STI patients, and to perform regular cervical smears in this population for Papanicolaou examination. However, a high percentage of smears in adolescents may appear, incorrectly, to be abnormal.

The available treatments for visible anogenital warts are either: patient-applied (podophyllotoxin or imiquimod), removing the need for frequent clinic visits; or provider-administered. Podophyllotoxin 0.5% solution may be applied with a cotton swab. The gel can be applied with a finger.



Recommended regimen for venereal warts

A. Chemical

Self-applied by patient

- podophyllotoxin 0.5% solution or gel, twice daily for 3 days, followed by 4 days of no treatment, the cycle repeated up to 4 times (total volume of podophyllotoxin should not exceed 0.5 ml per day)

OR

- imiquimod 5% cream applied with a finger at bedtime, left on overnight, 3 times a week for as long as 16 weeks. The treatment area should be washed with soap and water 6–10 hours after application. Hands must be washed with soap and water immediately after application.

Note

- The safety of both podophyllotoxin and imiquimod during pregnancy has not been established.

Provider-administered

- podophyllin 10–25% in compound tincture of benzoin, applied carefully to the warts, avoiding normal tissue. External genital and perianal warts should be washed thoroughly 1–4 hours after the application of podophyllin. Podophyllin applied to warts on vaginal or anal epithelial surfaces should be allowed to dry before the speculum or anoscope is removed. Treatment should be repeated at weekly intervals
- where available, podophyllotoxin 0.5%, one of the active constituents of podophyllin resin, is recommended. Its efficacy is equal to that of podophyllin, but it is less toxic and appears to cause less erosion
- some experts advise against the use of podophyllin for anal warts. Large amounts of podophyllin should not be used because it is toxic and easily absorbed. Its use during pregnancy and lactation is contraindicated

OR

- TCA 80–90%, applied carefully to the warts, avoiding normal tissue, followed by powdering of the treated area with talc or sodium bicarbonate (baking soda) to remove unreacted acid. Repeat application at weekly intervals .

**B. Physical**

- cryotherapy with liquid nitrogen, solid carbon dioxide, or a cryoprobe. Repeat applications every 1–2 weeks

OR

- electrocauterization

OR

- surgical removal

VAGINAL WARTS**Recommended regimen**

- cryotherapy with liquid nitrogen

OR

- podophyllin 10–25%. Allow to dry before removing speculum

OR

- TCA 80–90%

CERVICAL WARTS

Treatment of cervical warts should not be started until the results from a cervical smear test are known. Most experts advise against the use of podophyllin or TCA for cervical warts.

Recommendations for treatment of cervical warts

- management should include consultation with an expert
- pap smear
- No TCA or podophyllin

MEATAL AND URETHRAL WARTS

Accessible meatal warts may be treated with podophyllin 10–25%, in compound tincture of benzoin, or podophyllotoxin 0.5%, where available. Great care should be taken to ensure that the treated area is dry before contact with normal, opposing epithelial surfaces is allowed. Low success rates with podophyllin are reported.

Urethroscopy is necessary to diagnose intra-urethral warts, but they should be suspected in men with recurrent meatal warts. Some experts prefer electrocauterization



removal. Intra-urethral instillation of a 5% cream of fluorouracil or thiotepa may be effective, but neither has been adequately evaluated. Podophyllin should not be used.

Recommended treatments

■ cryotherapy

OR

■ podophyllin 10–25%

3.9. TRICHOMONAS VAGINALIS INFECTIONS

The flagellated protozoan, *T. vaginalis*, is almost exclusively sexually transmitted in adults. The infection may be asymptomatic. Symptomatic trichomoniasis presents with an offensive vaginal discharge and vulval itching in women, and urethritis in men.

Management of sexual partners

Sexual partner(s) should be notified and treated, and patients should be advised against sexual intercourse until both the index patient and the partner(s) are treated. Trichomoniasis is frequently asymptomatic in men but is increasingly recognized as a cause of symptomatic non-gonococcal, non-chlamydial urethritis.

TRICHOMONIASIS IN PREGNANCY

T. vaginalis infection has been shown to be associated with adverse pregnancy outcomes, particularly premature rupture of membranes, pre-term delivery and low birth weight. This association is particularly important in symptomatic women. Further studies are needed to demonstrate the impact of treating trichomoniasis on the prevention of adverse pregnancy outcomes.

Although metronidazole is not recommended for use in the first trimester of pregnancy, treatment may be given where early treatment has the best chance of preventing adverse pregnancy outcomes. In this instance a lower dose should be used (2 g single oral dose rather than a long course). Studies and meta-analyses have not demonstrated a consistent association between metronidazole use during pregnancy and teratogenic or mutagenic effects in newborns.



Follow-up

Patients should be asked to return after seven days if symptoms persist. Reinfection should be carefully excluded. Patients not cured following initial treatment often respond favourably to repeat treatment with the seven-day regimen. Resistance to the 5-nitroimidazoles has been reported, and may be one cause of treatment failure.

Patients not cured with the repeated course of metronidazole may be treated with a regimen consisting of metronidazole 2 g orally, daily, together with 500 mg applied intravaginally each night for 3–7 days. Vaginal preparations of metronidazole are available in many parts of the world, but are only recommended for the treatment of refractory infections, not for the primary therapy of trichomoniasis. An alternative regimen consists of 400 mg or 500 mg metronidazole¹¹ orally, twice daily for seven days.

Recommended regimen for vaginal infections

- metronidazole, 2 g orally, in a single dose

OR

- tinidazole, 2 g orally, in a single dose

Note

- The reported cure rate in women ranges from 82% to 88% but may be increased to 95% if sexual partners are treated simultaneously.

Alternative regimen

- metronidazole, 400 mg or 500 mg orally, twice daily for 7 days

OR

- tinidazole, 500 mg orally, twice daily for 5 days

Note

- Other 5-nitroimidazoles are also effective, both in single and in multiple dose regimen.

¹¹ Metronidazole is available in either 200 mg or 250 mg capsules.



- Patients taking metronidazole or other imidazoles should be cautioned not to consume alcohol while they are taking the drug, and up to 24 hours after taking the last dose.
- Metronidazole is generally not recommended for use in the first trimester of pregnancy (see text above).
- Asymptomatic women with trichomoniasis should be treated with the same regimen as symptomatic women.

Recommended regimen for urethral infections

- metronidazole, 400 mg or 500 mg orally, twice daily for 7 days

OR

- tinidazole, 500 mg orally, twice daily for 5 days

Recommended regimen for neonatal infections

- metronidazole, 5 mg/kg orally, 3 times daily for 5 days

Note

- Infants with symptomatic trichomoniasis or with urogenital colonization persisting past the fourth month of life should be treated with metronidazole.

3.10. BACTERIAL VAGINOSIS

Bacterial vaginosis (BV) is a clinical syndrome resulting from replacement of the normal hydrogen peroxide-producing *Lactobacillus* sp. in the vagina by high concentrations of anaerobic bacteria, such as *Gardnerella vaginalis* and *Mycoplasma hominis*. The cause of the microbial alteration is not fully understood.

Whereas trichomoniasis is an STI, BV is an endogenous reproductive tract infection. Treatment of sexual partners 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.

Additional studies are needed to confirm the relationship between altered vaginal microflora and the acquisition of HIV.



BV IN PREGNANCY

There is evidence that BV is associated with an increased incidence of adverse pregnancy outcomes (e.g. premature rupture of membranes, preterm delivery and low birth weight). Symptomatic pregnant women should be treated, and those with a history of previous pre-term delivery should be screened to detect asymptomatic infections. Pregnant women with recurrence of symptoms should be re-treated. Screening of asymptomatic pregnant women without a prior history of preterm delivery is not recommended.

Metronidazole is not recommended for use in the first trimester of pregnancy, but it may be used during the second and third trimesters. If treatment has to be given during the first trimester, then in order to reduce the risks of any adverse effects, lower doses are recommended.

BV AND SURGICAL PROCEDURES

Women with BV scheduled to undergo reproductive tract surgery or a therapeutic abortion should receive treatment with metronidazole.

Recommended regimen for BV

- metronidazole, 400 mg or 500 mg orally, twice daily for 7 days

Note

- Patients taking metronidazole should be cautioned not to consume alcohol while they are taking the drug and up to 24 hours after taking the last dose.

Alternative regimen

- metronidazole, 2 g orally, as a single dose

OR

- clindamycin 2% vaginal cream, 5 g intravaginally, at bedtime for 7 days

OR

- metronidazole 0.75% gel, 5 g intravaginally, twice daily for 5 days

OR

- clindamycin, 300 mg orally, twice daily for 7 days



Follow-up

Patients should be advised to return if symptoms persist as re-treatment may be needed.

Recommended regimen for pregnant women

- metronidazole, 200 or 250 mg orally, 3 times daily for 7 days, after first trimester
- metronidazole 2 g orally, as a single dose, if treatment is imperative during the first trimester of pregnancy (see text above)

Alternative regimen

- metronidazole, 2 g orally, as a single dose
- OR
- clindamycin, 300 mg orally, twice daily for 7 days
- OR
- metronidazole 0.75% gel, 5 g intravaginally, twice daily for 7 days

3.11. CANDIDIASIS

VULVO-VAGINAL CANDIDIASIS

In the majority of cases, vulvo-vaginal candidiasis is caused by *Candida albicans* (*C. albicans*). Up to 20% of women with the infection may be asymptomatic. If symptoms occur, they usually consist of vulval itching, soreness and a non-offensive vaginal discharge, which may be curdy. Clinical examination may reveal vulval erythema (redness) or excoriations from scratching and vulval oedema.

Vulvo-vaginal candidiasis is usually not acquired through sexual intercourse. Although treatment of sexual partners is not recommended, it may be considered for women who have recurrent infection. A minority of male partners may have balanitis, which is characterised by erythema of the glans penis or inflammation of the glans penis and foreskin (balanoposthitis).

Therapy generally involves topical application of any of a wide variety of imidazoles (e.g. miconazole, clotrimazole, econazole, butoconazole, terconazole) or nystatin. Although they are generally more expensive, imidazoles require shorter courses of treatment and appear to be more effective than nystatin.



VULVO-VAGINAL CANDIDIASIS IN PREGNANCY

Although there are now some effective single-dose oral treatments, they are not known to be safe or effective. Therefore, only topical azoles should be used to treat pregnant women. Of those treatments that have been investigated for use during pregnancy, the most effective are miconazole, clotrimazole, butoconazole and terconazole.

VULVO-VAGINAL CANDIDIASIS AND HIV INFECTION

Candidiasis at several sites, including the vulva and vagina, is an important correlate of HIV infection. It is often quite severe and frequently relapses. Prolonged treatment is generally required and chronic suppressive therapy is frequently employed.

RECURRENCES

It is recommended that predisposing factors such as antibiotic use, the use of antiseptic/antibiotic vaginal preparations or vaginal douching be reduced or eliminated. Simultaneous treatment of a rectal focus with oral nystatin or fluconazole is not useful in preventing recurrences. Other underlying factors for recurrent vulvo-vaginal candidiasis include uncontrolled diabetes mellitus, immunosuppression, and corticosteroid use.

BALANOPOSTHITIS

Balanoposthitis refers to an inflammation involving the glans penis and the foreskin. When caused by *C. albicans* it is characteristically found in men with underlying immunosuppressive disease or uncontrolled diabetes mellitus.

Recommended regimen for vulvo-vaginal candidiasis

- miconazole or clotrimazole, 200 mg intravaginally, daily for 3 days
- OR
- clotrimazole, 500 mg intravaginally, as a single dose
- OR
- fluconazole, 150 mg orally, as a single dose

**Alternative regimen**

- nystatin, 100 000 IU intravaginally, daily for 14 days

Recommended topical application regimen for balanoposthitis

- clotrimazole 1% cream, twice daily for 7 days

OR

- miconazole 2% cream, twice daily for 7 days

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Alternative regimen

- nystatin cream, twice daily for 7 days

3.12. SCABIES

The causative mite, *Sarcoptes scabiei*, is transmitted by protracted direct bodily contact. In adults this is often through sexual contact. However, there are situations in which scabies is transmitted through close body contact not related to sexual activity. This can occur when people live or spend time at very close quarters, such as in schools, overcrowded housing and in institutions such as nursing homes and psychiatric hospitals. In order to prevent social stigmatization, the labelling of scabies as an STI should be avoided when the likely cause is body contact. In addition, the management recommendations are different for patients presenting with sexually acquired scabies. For outbreaks of scabies related to non-sexual bodily contact, treatment of all people involved is critical.

The mites can burrow into the skin of a contact person within one hour. Proteases (enzymes) in mite faecal matter generate a hypersensitivity reaction which leads to the characteristic symptom of pruritus (itch), usually 2–6 weeks after infestation.

Special considerations

Pruritus sometimes persists for several weeks after adequate therapy. A single repeat treatment after one week may be appropriate if there is no clinical improvement. Additional weekly treatments are warranted only if live mites can be demonstrated. If reinfection can be excluded and compliance assured, topical anti-inflammatory therapy may be considered, as an allergic reaction may be the



reason for the clinical manifestation. Clothing or bed linen that has possibly been contaminated by the patient in the two days prior to the start of treatment should be washed and dried well, or dry-cleaned.

Treatment of scabies in adults, adolescents and older children

Recommended regimen

- lindane 1% lotion or cream, applied thinly to all areas of the body from the neck down and washed off thoroughly after 8 hours

OR

- permethrin cream 5%

OR

- benzyl benzoate 25% lotion, applied to the entire body from the neck down, nightly for 2 nights; patients may bathe before reapplying the drug and should bathe 24 hours after the final application

OR

- crotamiton 10% lotion, applied to the entire body from the neck down nightly for 2 nights and washed off thoroughly 24 hours after the second application; an extension to 5 nights is necessary in some geographical areas (crotamiton has the advantage of an antipruritic action)

OR

- sulphur 6% in petrolatum, applied to the entire body from the neck down nightly for 3 nights; patients may bathe before reapplying the product and should bathe 24 hours after the final application

Note

- Lindane is not recommended for pregnant or lactating women.
- Resistance to lindane has been reported in some areas.

Treatment of scabies in infants, children under 10 years of age, pregnant or lactating women

Recommended regimen

- crotamiton 10%, as above

OR

- sulphur 6%, as above

OR



- permethrin 5% cream, applied in the same way as the sulphur regimen described above

Contacts

Sexual contacts and close household contacts should be treated as above.

3.13. PUBIC LICE

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TREATMENT OF SPECIFIC INFECTIONS

The louse, *Phthirus pubis*, is the cause of pubic lice. The infestation is usually transmitted by sexual contact. Patients usually seek medical care because of pruritus.

Recommended regimen

- lindane 1% lotion or cream, rubbed gently but thoroughly into the infested area and adjacent hairy areas and washed off after 8 hours; as an alternative, lindane 1% shampoo, applied for 4 minutes and then thoroughly washed off

OR

- pyrethrins plus piperonyl butoxide, applied to the infested and adjacent hairy areas and washed off after 10 minutes; retreatment is indicated after 7 days if lice are found or eggs are observed at the hair-skin junction. Clothing or bed linen that may have been contaminated by the patient in the two days prior to the start of treatment should be washed and dried well, or dry-cleaned.

OR

- permethrin 1%, as above

Note

- Lindane is not recommended for pregnant or lactating women.

Special considerations

Infestation of the eyelashes should be treated by the application of an occlusive ophthalmic ointment to the eyelid margins daily for 10 days to smother lice and nits. The ointment should not be applied to the eyes.



4. KEY CONSIDERATIONS UNDERLYING TREATMENTS

4.1. THE CHOICE OF ANTIMICROBIAL REGIMEN

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KEY CONSIDERATIONS UNDERLYING TREATMENTS

EFFICACY

Efficacy is the most important criterion when choosing from available regimen. STI therapy regimen should, ideally, cure at least 95% of those infected with a bacterial STI. Regimen yielding lower cure rates should be used only with great caution since in a population of unstable susceptibility patterns, they may select for resistant strains and rapidly limit their own usefulness. Such caution should be applied to regimen yielding cure rates of between 85% and 95%. Regimen with still lower cure rates are unacceptable.

In order to reduce the risk of development and transmission of resistant strains of sexually transmitted pathogens to the wider population, special programmes for effective case management should be designed for groups at high risk, such as sex workers and their clients. *Treatment regimen for these groups should be nearly 100% effective*, and efforts should be made to promote health-seeking behaviour in these populations, preferably through the use of a participatory approach with peer educators and peer health care providers.

Efficacy data cannot be transferred reliably from one population (or in some situations, from one sub-population) to another. Thus, ideally, assessments should be based on well-designed studies conducted in the populations where the treatment will be applied. As a consequence of changes in the local epidemiology of resistant *N. gonorrhoeae* and *H. ducreyi*, therapeutic efficacy against these infections changes over time. Periodic surveillance of clinical efficacy, and/or *in vitro* sensitivity is recommended. If resistance levels and cure rates are not known in an area, the regimen used should be those which can reasonably be expected to



produce acceptable cure rates under the most adverse ecological conditions. Few comparative clinical trials are large enough to define small differences in efficacy between highly effective antimicrobial regimen.

Note

- In order to ensure efficacy, practitioners are cautioned not to use less than the recommended dosages.

SAFETY

Toxicity is a second major concern in STI treatments because of the frequency with which patients become reinfected and their consequent exposure to repeated courses of antimicrobials. In addition, treatment of resistant STI agents often requires achievement of relatively high serum levels of antimicrobials, in some cases for periods of seven days or more. Combination regimen further increase the risk of adverse drug reactions. Pregnancy, which is relatively common in sexually active groups with a high incidence of STIs, represents a special situation in which additional considerations of fetal safety become important. The safety of the fluoroquinolones in pregnant women and adolescents is uncertain and limits their use in these groups. In some areas, doxycycline is not used because of the danger of photosensitization. Tetracyclines are contraindicated in pregnancy and children under eight years.

The prominence of third-generation cephalosporins in the recommended regimen results from their combination of high efficacy, even against relatively resistant organisms, and low toxicity.

COST

Cost is a major limiting factor in all locations. Kanamycin is chosen in preference to spectinomycin, for example, in the treatment of gonorrhoea in some parts of the developing world, because of its lower cost. In calculating the total cost of various regimen, however, it is important to consider the costs associated with less effective therapies: repeat treatment, further transmission of infection, complications, and selection for increased microbial resistance. Choosing the most appropriate regimen may be facilitated by the use of a formal decision analysis. Sensitivity analyses can sometimes compensate for uncertainties in primary data.



COMPLIANCE AND ACCEPTABILITY

Patient compliance with STI treatment regimen is a problem which seriously limits the effectiveness of multidose regimen such as those involving erythromycin and tetracyclines. Single-dose or very-short-course regimen should therefore be given preference. Appropriate counselling and health education have been shown to increase compliance and should be a part of clinical management.

Extra effort is required to achieve compliance among adolescent patients as they are often less tolerant of side-effects. They may also not want others to know that they are taking medication. Health workers must ensure that instructions are fully understood – especially if several regimen are involved – including the implications of failure to complete treatment.

In some societies, oral regimen are strongly preferred to injections, whereas among other groups, injections may be seen as the only acceptable form of treatment. In view of the emergence and spread of HIV infection, preference should be given to oral regimen in order to reduce the risks associated with needle-stick injuries. Patient education on the efficacy of oral preparations must be included in STI management.

AVAILABILITY

The geographical distribution and availability of drugs vary considerably. The regional availability of some excellent drugs could be improved by their inclusion on national essential drugs lists.

COEXISTENT INFECTIONS

When several STIs are prevalent in a population, coinfection may be a common occurrence. Unfortunately, the ability to treat common coinfections with single drugs has been reduced by the development of resistance to the tetracyclines in *N. gonorrhoeae*. In most cases, dual therapy is now required for simultaneous gonococcal and chlamydial infections. Coincident chancroid and syphilis require a multi-drug regimen. The severity of disease caused by several sexually transmitted pathogens (e.g. herpes simplex virus, *H. ducreyi*, *T. pallidum*) may be increased in HIV infection and AIDS, and treatment must be intensified and prolonged.



RISK OF REDUCING DRUG EFFICACY FOR OTHER INDICATIONS

More effective but expensive drugs should not be reserved for referral centres. The use of less effective regimen at the primary care level quickly discourages patients from seeking the most readily and rapidly available care and fosters the transmission of infection and the risk of antimicrobial resistance developing to selected antibiotics.

Simultaneous treatment with several agents has been used to prevent the emergence of resistance in individuals during therapy for tuberculosis. The efficacy of this technique in preventing the emergence of resistance in STI populations is unknown. Unfortunately resistance to a number of antimicrobials is sometimes acquired simultaneously by *N. gonorrhoeae*. The use of multiple drugs to treat polymicrobial processes (e.g. PID) or presumed simultaneous infection (e.g. tetracycline for chlamydial coinfection in cases of gonorrhoea), is widely practised and recommended.

4.2. COMMENTS ON INDIVIDUAL DRUGS

CEPHALOSPORINS

Several third-generation cephalosporins have been shown to be effective in the treatment of gonorrhoea. Cefixime has the advantage of being an oral preparation. It is also likely to be effective against chancroid, but has not yet been evaluated in this condition. The efficacy of ceftriaxone in the treatment of gonorrhoea and chancroid has been well documented. There is a strong positive correlation between the minimum inhibiting concentrations of penicillins and cephalosporins.

In addition to treating uncomplicated anogenital gonorrhoea, single-dose ceftriaxone is effective in gonococcal ophthalmia neonatorum, conjunctivitis and pharyngeal infection. Because of its cost it is tempting to use doses of ceftriaxone below 125 mg. However, this is likely to accelerate the development of resistance and such regimen are not recommended.



MACROLIDES

Azithromycin is an azalide antibiotic, which is structurally related to the macrolide erythromycin. It is slightly less potent than erythromycin against some Gram-positive organisms but demonstrates a superior activity against a wide variety of Gram-negative organisms, including *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Haemophilus influenza* and *Haemophilus ducreyi*.

It is characterized by a broader spectrum of activity and lower incidence of adverse events and drug interactions. It has a low plasma concentration, but a high and prolonged cellular and tissue concentration resulting in extensive tissue distribution and intracellular accumulation. This makes it an ideal antimicrobial for the management of infections in deep tissues. On account of its long tissue half-life a single daily oral dosage of 1 g is recommended in the treatment of genital chlamydia infection.

Although oral azithromycin taken as a 2 g dose is effective against *N. gonorrhoeae*, WHO does not currently recommend it for routine treatment of this infection because of the drug's increased gastrointestinal intolerance at this dose level. Furthermore, studies in Brazil and three Caribbean countries (Trinidad, Guyana and St Vincent) and the USA have reported the emergence of isolates of *N. gonorrhoeae* with reduced sensitivity to azithromycin.^{12,13,14}

Azithromycin has also been shown to be effective against other STIs such as chancroid, donovanosis and early syphilis, but more data are needed before a general recommendation for its use in these infections can be made.

Preliminary data indicate that azithromycin is safe for pregnant women, although the number of women in the trials of the drug to date have been small and the duration of follow-up rather short. The drug is currently classified in "Pregnancy category B".¹⁵ Randomized studies comparing the use of a single-dose azithromycin

¹² Centre for Disease Control and Prevention. Fluoroquinolone resistance in *Neisseria gonorrhoeae*, Hawaii, 1999, and decreased susceptibility to azithromycin in *N. gonorrhoeae*, Missouri, 1999, *JAMA* 2000 Oct 18; 284(15):1917-9

¹³ Young H, Moyes A, Mcmillan A. Azithromycin and erythromycin resistant *Neisseria gonorrhoeae* following treatment with azithromycin. *Int J STD AIDS*, 1997, 8:299-302.

¹⁴ Dillon R, Li H, Sealy J, Ruben M. The Caribbean GASP Network, Prabhakar P. Antimicrobial susceptibility of *Neisseria gonorrhoeae* isolates from three Caribbean Countries: Trinidad, Guyana and St. Vincent. *Sex Transm Dis*, 2001, 28(9): 508-14

¹⁵ Pregnancy category B - found safe in animal studies no data in humans.



regimen with erythromycin for the treatment of chlamydia in pregnant women found that not only did azithromycin substantially improve the cure rates, it also reduced the occurrence of side-effects associated with use of standard courses of erythromycin.¹⁶ In one study, significantly fewer gastrointestinal side-effects were noted in the azithromycin group than in the erythromycin group (11.9% versus 58.1%, $P < 0.01$), while both azithromycin and erythromycin had similar treatment efficacy (88.1% versus 93.0%, $P > 0.05$). As there are no data on the presence of azithromycin in breast milk the drug should be administered to nursing mothers only when there are no suitable alternatives. Available data on the safety of azithromycin suggest that it can be provided even at the primary health care level on condition that health care workers are appropriately educated to advise patients to be aware of the drug's potential mild adverse effects.

SULPHONAMIDES

Sulphonamides were the first effective systemic antibacterial drugs used in humans. They are primarily bacteriostatic and act by interfering with bacterial synthesis of folic acid. They are metabolized in the liver and excreted by the kidneys. Generally they are administered orally, making them preferable to other antibacterials. However, with rise in bacterial resistance to these drugs, their role and importance has decreased and they have been largely replaced by other antibacterials that are more effective and less toxic.

The addition of trimethoprim to sulphonamides gives a combination drug¹⁷ that is more effective owing to the synergetic action of the two components; the combination also helps to decrease bacterial resistance by inhibiting simultaneously two sequential steps of bacterial metabolism. However, this combination has reached the limit of its usefulness in the management of STIs such as chlamydia and gonorrhoea. Although there are some countries that still use this combination for the treatment of gonococcal infections, it is not an ideal antimicrobial agent for this infection.

Sulphonamides are not recommended in the last trimester of pregnancy as they may induce jaundice in the neonate; they are also not recommended for the treatment of

¹⁶ Wehbeh HA et al. Single-dose azithromycin for Chlamydia in pregnant women. *J Reprod Med*, 1998, 43(6):509-14.

¹⁷ The most commonly known combination of this type is trimethoprim/sulphamethoxazole (formerly known as co-trimoxazole).



infections in neonates and nursing mothers because the hepatic enzymes system in neonates is immature.

QUINOLONES

Earlier agents such as rosoxacin are no longer recommended. However, some of the new fluoroquinolones show considerable promise as oral agents for the treatment of gonorrhoea. Their use is contraindicated in pregnancy and they are not recommended for use in children and adolescents, although ciprofloxacin has been licensed in Denmark for the single-dose prophylaxis of meningococcal disease in children.

The *in vitro* activity of individual fluoroquinolones against *N. gonorrhoeae* varies considerably. There is some evidence of increased minimal inhibitory concentrations in strains isolated after treatment with less active agents. Ciprofloxacin is considered to be the agent with the greatest activity against *N. gonorrhoeae*.

Quinolone-resistant *N. gonorrhoeae* (QRNG) has become common in parts of Asia and the Pacific. In 1996 the proportions of quinolone-resistant gonococci reported in these areas ranged from less than 1% in New Zealand to 15% in the Republic of Korea, 24% in Hong Kong Special Administrative Region of China, 53% in Cambodia and 66% in the Philippines.

In the USA, QRNG is becoming increasingly common in western regions. Quinolones are no longer recommended for the treatment of gonorrhoea in the State of Hawaii, and are to be used cautiously in California.¹⁸

Resistance of *N. Gonorrhoeae* to quinolones will continue to spread across the globe. It is imperative that surveillance for antimicrobial resistance be strengthened in order to guide treatment recommendations.

Experience in the treatment of chlamydial infection with fluoroquinolones is limited. Of the currently studied agents, ofloxacin has the greatest potential when given as 300 mg twice daily for seven days. This is effective against both gonorrhoea and

¹⁸ Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. *MMWR*, 2002, 51(RR-6):1-80



chlamydial infection, but the usefulness of the regimen is limited by the duration of therapy, which may affect compliance, and by the drug's high cost.

TETRACYCLINES

A number of tetracyclines of equal efficacy are available. These can be substituted for doxycycline and tetracycline hydrochloride as appropriate.

4.3. ANTIMICROBIAL RESISTANCE IN *N. GONORRHOEAE*

There are two main types of antimicrobial resistance in *N. gonorrhoeae*:

- chromosomal resistance involves penicillins and a wide range of other therapeutic agents such as tetracyclines, spectinomycin, erythromycin, quinolones, thiamphenicol, and cephalosporins;
- plasmid-mediated resistance affects penicillins and tetracyclines.

Chromosomally resistant *N. gonorrhoeae*, penicillinase-producing gonococci, and plasmid-mediated, tetracycline-resistant strains are all increasing and have had a major impact on the efficacy of traditional regimen for treating gonorrhoea.

Chromosomal resistance in *N. gonorrhoeae* has been observed since the introduction of sulphonamides in the 1930s. Its significance today is that chromosomal-resistant strains are often resistant to a number of antimicrobial agents that have been used to treat gonorrhoea. There is also cross-resistance between penicillin and the second- and third-generation cephalosporins. Although not yet of any significance in relation to the clinical use of ceftriaxone, this trend is disturbing. The high-level spectinomycin resistance reported sporadically in gonococci is also chromosomally mediated.

The effectiveness and usefulness of current surveillance of gonococcal resistance are limited, and a simple instrument for assessing and monitoring gonococcal antimicrobial resistance needs to be developed. Lack of standardization of sensitivity testing methodology continues to be a problem. Standard methods should be used and should include a set of reference strains. Disc-diffusion sensitivity testing remains poorly standardized, one problem being the limited availability of antimicrobial discs of the correct content.



4.4. ANTIMICROBIAL RESISTANCE IN *H. DUCREYI*

The surveillance of antimicrobial susceptibility in *H. ducreyi* is complicated by the technical difficulties of performing sensitivity testing. Very few centres provide data.

H. ducreyi has developed resistance to a number of different antimicrobials, but with the exception of two strains isolated in Singapore in the early 1980s, resistance to erythromycin has not been reported, therefore, erythromycin remains the recommended treatment. Ceftriaxone and ciprofloxacin are suitable alternatives, since *in vitro* resistance has not been reported to either drug, although frequent treatment failures were observed with ceftriaxone among both HIV-positive and HIV-negative patients in a study conducted in Nairobi, Kenya, in 1991. Single-dose azithromycin therapy appears to be another promising alternative, but further data are required.

Plasmid-mediated resistance has been found against ampicillin, sulphonamides, tetracycline, chloramphenicol and streptomycin. All *H. ducreyi* strains now contain beta-lactamase coding plasmids, several of which have been described. Neither penicillin nor ampicillin is now effective against chancroid. Tetracycline resistance is also widespread. As with *N. gonorrhoeae*, *H. ducreyi* can also carry a large plasmid capable of mobilizing smaller, non-conjugative resistance plasmids. Trimethoprim and tetracycline resistance can occur in the absence of plasmids.

Resistance to sulphonamides is now widespread, and strains with reduced sensitivity to trimethoprim are becoming increasingly prevalent in south-east Asia, in parts of Africa and in north America. Where strains remain sensitive to trimethoprim, treatment with this agent alone or combined with a sulphonamide remains effective.

Plasmid-controlled aminoglycoside-inactivating enzymes have reduced the usefulness of these antimicrobials in treating chancroid in south-east Asia. At present this is not the case in Africa or elsewhere.



5. PRACTICAL CONSIDERATIONS IN STI CASE MANAGEMENT

5.1. THE PUBLIC HEALTH PACKAGE FOR STI PREVENTION AND CONTROL

Effective prevention and control of STIs can be achieved using a combination of responses constituting the “public health package”. The essential components of this package are shown below.

The public health package for STI prevention and control: essential components

- promotion of safer sexual behaviour
- condom programming – encompassing a full range of activities from condom promotion to the planning and management of supplies and distribution
- promotion of health care-seeking behaviour
- integration of STI prevention and care into primary health care, reproductive health care facilities, private clinics and others
- specific services for populations at risk – such as female and male sex workers, adolescents, long-distance truck drivers, military personnel and prisoners
- comprehensive case management of STI
- prevention and care of congenital syphilis and neonatal conjunctivitis
- early detection of symptomatic and asymptomatic infections.

5.2. COMPREHENSIVE CASE MANAGEMENT OF STIs

One of the essential components of the public health package is comprehensive case management of STIs, which comprises identification of the syndrome, antimicrobial treatment for the syndrome, education of the patient, condom supply, counselling, and notification and management of sexual partners.



IDENTIFICATION OF THE SYNDROME

The feasibility of providing STI case management must be assured within any health care setting, whether within the public or private sector. An essential component will be privacy for consultation. Depending on the source of care, there may also be need to provide facilities such as an examination table or couch with adequate lighting, gloves, syringes, specula, sterilization equipment and laboratory supplies.

For individuals seeking evaluation for an STI, appropriate care consists of the following components:

- history taking, including behavioural, demographic and medical risk assessment
- physical examination, particularly of the genital area, an activity which, in some settings, needs to be treated with greater sensitivity and understanding
- establishment of a syndromic or laboratory based diagnosis
- curative or palliative therapy, using the most effective antimicrobial for the pathogen, at the first port of call of the patient
- patient education and counselling (where counselling services are available), including information on:
 - compliance
 - nature of infection
 - importance of partner notification and partner treatment
 - risk reduction and prevention of further STI transmission
 - HIV risk perception and assessment
- clinical follow up when appropriate and feasible.

There are four major components of STI control:

- education of individuals at risk on modes of disease transmission and means of reducing the risk of transmission
- detection of infection in asymptomatic subjects and in subjects who are symptomatic but unlikely to seek diagnostic and therapeutic services
- effective management of infected individuals seeking care
- treatment and education of the sexual partners of infected individuals.

The prevention of STIs is based primarily on changing the sexual behaviours that put people at risk and on promoting the use of condoms.



ANTIMICROBIAL TREATMENT FOR THE SYNDROME

Whichever means is used for diagnosis – flowcharts or laboratory tests – the availability and use of effective antimicrobials is an absolute requirement. The drugs must be available at the first point of contact with a patient with an STI. Effective treatment must also be available and used in the private sector.

EDUCATION OF THE PATIENT

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Patients should be informed, among other things, about the nature of the infection and the importance of taking the full course of medication.

A consultation for an STI is a unique opportunity to provide education on the prevention of HIV and STIs to people who, by definition, are at risk for these infections. Adolescents are an especially important target group for primary prevention because much of their active sexual and reproductive life lies ahead. Furthermore, adolescents may be less inclined to appreciate the risks of acquiring an STI.

Clinics and practitioners who treat patients with STIs should make resources available for the promotion of safer sexual behaviour. Behavioural assessment is an integral part of the STI history and patients should be educated in methods of lowering their risk of acquiring STIs and HIV, including abstinence, careful selection of partners and use of condoms.

Condoms should be available in any health care facility providing STI services. Instruction in their proper use should also be provided. Although condoms do not provide absolute protection from any infection, if properly used they greatly reduce the risk of infection. The question of pregnancy prevention should also be addressed and dual protection emphasized. Adolescents should be instructed on where to access advice on contraception and future supplies of condoms.

CONDOM SUPPLY

The promotion of condom use requires health authorities to ensure that there is an adequate supply of good-quality, affordable condoms at health facilities and at other distribution points in the community. Social marketing of condoms is another way of increasing access to condoms.



COUNSELLING

A consultation for an STI provides an opportunity for the health worker to discuss and explore with the patient, on a one-to-one basis, his or her risk factors for HIV/STIs and other issues related to prevention and treatment. Frequently this consists of the provision of information about STIs and their prevention, condom use and partner notification. This is education for prevention and is an essential part of an STI consultation.

However, merely providing information is usually not sufficient to enable patients accurately to assess their own risk of infection, deal with the challenges of informing their partner(s), prevent future infections, or deal with the complications of STIs. Some issues which arise during an STI consultation may provoke emotional reactions in the patient. Therefore, counselling is needed in addition to education.

Counselling is defined here as an interactive confidential process in which a care provider helps a patient to reflect on issues associated with STIs and to explore possible lines of action. There is often a need for skills building and practising different behaviours. This may require multiple visits. Counselling is more time-consuming than the traditional means of information provision and also requires from health care workers more empathy and understanding of the social and economic situation of a patient, as well as the ability to overcome their own attitudes and avoid making judgements.

Issues that should be addressed in a counselling session include:

- informing the partner(s) or spouse about the STI diagnosis (options: either the patient or the health care provider informs the partner(s) or spouse)
- assessing the patient's risk for HIV and deciding whether or not to undergo testing for HIV
- learning about, and coming to terms with, worrisome complications of STIs, such as infertility and congenital syphilis
- dealing with an incurable STI, such as herpes genitalis, which may be transmitted to the partner(s) or spouse
- preventing future infections, including strategies to discuss and introduce condom use with partner(s) or spouse
- confidentiality, disclosure and the risk of violence or stigmatizing reactions from spouse, partner(s), family or friends



- enabling patients to take control of their own life and their responsibilities for disease prevention.

Before offering counselling to STI patients, the care provider needs to:

- identify the needs of the client, who may feel anxiety about a particular aspect of the STI, or may have a particular need for confidential risk assessment and planning for risk reduction
- have the counselling skills, the privacy, and the time (usually 15–20 minutes), including the availability for follow-up discussions, as appropriate.

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These resources are usually not available at a busy STI clinic or general outpatient clinic. It is, therefore, suggested that when a counselling need is identified, the patient should be referred to a nearby counselling service, if this is available. If it is not, then a health or social worker may be designated to provide the counselling. This person should be trained and should be accorded the necessary space and time to provide the counselling. While not all adolescents will need to be referred for counselling, they have a well-recognized need to be able to talk to someone they can trust and who is well-informed. Having links to local support groups involved with young people can reinforce the clinical advice given at the clinic and encourage patients to return to the clinic in the future if required.

In many developing countries, where health resources are scarce, counselling services are not always generally available. However, it is recognized that some of the qualities needed in counselling – compassion, sensitivity and communication skills – are qualities that many health workers already possess and apply on a daily basis in their interactions with patients. Even in the absence of formal training in counselling, health workers should be encouraged to engage their patients in a dialogue about STIs to explore risk assessment and personal behavioural options, and to identify those requiring further emotional support if such support is available.

NOTIFICATION AND MANAGEMENT OF SEXUAL PARTNERS

Contacting the sex partners of clients with an STI, persuading them to present themselves at a site offering STI services, and treating them – promptly and effectively – are essential elements of any STI control programme. These actions, however, should be carried out with sensitivity and consideration of social and cultural factors to avoid ethical and practical problems such as rejection and violence, particularly against women.



The sexual partners of STI patients are likely to be infected and should be offered treatment. Further transmission of STIs and reinfection can be prevented by referral of sexual partners for diagnosis and treatment. Female partners of male STI patients may well be asymptomatic; thus, partner notification and management offers an opportunity to identify and treat people who otherwise would not receive treatment. Partner notification should be considered whenever an STI is diagnosed, irrespective of where care is provided.

Notification can be by patient referral or by provider referral. In patient referral, an infected patient is encouraged to notify partner(s) of their possible infection without the direct involvement of health care providers while in provider referral, health care providers or other health care workers notify a patient's partner(s).

Partner notification should be conducted in such a way that all information remains confidential. The process should be voluntary and non-coercive. The aim is to ensure that the sexual partners of STI patients, including those without symptoms, are referred for evaluation.

Management of sexual partners is based on knowledge of the index patient's diagnosis (syndromic or specific). The following three strategies can be adopted for the treatment of partners:

- offer immediate epidemiological treatment (treatment based solely on the diagnosis of the index patient) without any laboratory investigation
- offer immediate epidemiological treatment, but obtain specimens for subsequent laboratory confirmation
- delay treatment until the results of definitive laboratory tests are available.

The strategy selected will depend on:

- the risk of infection
- the seriousness of the disease
- the availability of effective diagnostic tests
- the likelihood of a person returning for follow-up
- the available infrastructure for follow-up of patients
- the availability of effective treatment
- the likelihood of spread if epidemiological treatment is not given.



Note

- WHO recommends that epidemiological treatment (with the same treatment regimen used for the index patient) should be given to all sexual partners.

5.3 ACCESS TO SERVICES

The provision of accessible, acceptable and effective services is important for the control of STIs. In most developing and industrialized countries, patients will have a choice of services from which to seek STI care. Possible sources are found within the public sector, the private sector and the informal sector. In ensuring universal access to appropriate STI programmes, it should be recognized that patients seek care from a mixture of these sources. In many countries most STI care is obtained outside the public sector. A balanced and comprehensive programme may require the strengthening of all health care providers that are able to provide STI services.

It is often argued that high-quality STI care should be delivered by specialist clinical staff in categorical STI clinics. However, inaccessibility, unacceptability and the many human and economic resources required make this an impractical method of service provision for the general public.

It is recommended that routine STI services be integrated into primary health care. Clinics specializing in STI treatment (sometimes called categorical clinics) may be particularly useful in providing primary care in urban settings for specific groups such as sex workers and their clients, migrant workers, truckers, and any other group with poor access to health care. Because they have a concentration of STI expertise, these clinics can also offer referral services for primary care services, hospital outpatient departments, private practitioners, etc. In a few selected cases the specialized clinics should also be strengthened as reference centres to train health care providers in STI treatment, epidemiological information (e.g. the prevalence of etiological agents within the syndromes and antimicrobial susceptibility), and operational research (e.g. studies on the feasibility and validity of algorithmic approaches).

Adolescents often lack information about existing services, such as where they are, what times they operate, how much they cost, etc. Even if they know about these services they are often reluctant to seek help for diagnosis and treatment. They are



often embarrassed and worried about social stigmatization. They also fear negative reactions from health workers and lack of confidentiality. There are initiatives under way in many countries to make health services more adolescent-friendly and more responsive to their particular needs.



6. CHILDREN,¹⁹ ADOLESCENTS AND SEXUALLY TRANSMITTED INFECTIONS

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PRACTICAL CONSIDERATIONS IN STI CASE MANAGEMENT

During the past decade, the sexual abuse and assault of children and adolescents have come to be recognized as serious social problems requiring the attention of policy-makers, educators, and the variety of professionals who deliver social and health services. As researchers begin to document the serious effects of sexual abuse on the mental and physical health of this group, the management of the victims is emerging as an important aspect of child and adolescent health care in both the industrialized and the developing worlds.

A standardized approach to the management of STIs in children and adolescents who are thought to have been sexually abused is important because the infection may be asymptomatic. An STI which remains undiagnosed and untreated may result in an unanticipated complication at a later stage and may be transmitted to others.

Health care providers have not always been aware of the link between sexual abuse and STI in children. Previously, children thought to have been sexually abused were not routinely screened for STI. Children diagnosed with an STI were also not investigated for the source of infection, but were assumed to have acquired the infection by non-sexual means, such as through the use of a contaminated towel or through contact with an infected person in overcrowded sleeping quarters.

The identification of a sexually transmissible agent in a child beyond the neonatal period, in the vast majority of cases, is suggestive of sexual abuse. However, exceptions do exist: for example, rectal or genital infection with *C. trachomatis* in young children may be caused by perinatally acquired infection, which may persist for up to three years. In addition, BV and genital mycoplasma have been identified

¹⁹ WHO defines children as persons between the ages of 0 and 9 years.



in both abused and non-abused children. Genital warts, although suggestive of assault, are not specific for abuse without other evidence. When the only evidence of abuse is the isolation of an organism or the detection of antibodies to a sexually transmissible agent, findings should be carefully confirmed and considered.

In children and adolescents, cases of sexual abuse of both sexes are probably far more widespread than is commonly recognized. Most cases involve relatives, friends and other adults in close and legitimate contact with the child or adolescent. The perpetrator may be difficult to identify. Health workers who suspect abuse must consider the options available for specialized counselling, social support and redress.

It must be stressed that the psychological and social support services should be included for complete management of these patients.

6.1. EVALUATION FOR SEXUALLY TRANSMITTED INFECTIONS

Examination of children and adolescents for sexual assault or abuse should be arranged so as to minimize further trauma. The decision to evaluate the individual for STIs must be taken on a case-by-case basis.

Health care workers dealing with children and adolescents must show respect and maintain confidentiality. They should be trained to elicit a good medical and sexual history and know how to overcome the patient's fear of pelvic examination.

Situations involving a high risk of STIs and a strong indication for testing include:

- alleged offender known to have an STI or to be at high risk for STIs
- symptoms and signs of an STI on physical examination.

Special care must be taken in collecting the required specimens in order to avoid undue psychological and physical trauma to the patient. The clinical manifestations of some STIs may be different in children and adolescents compared to those of adults. Some infections are asymptomatic or unrecognised. A paediatric speculum is rarely, if ever, needed in examination of pre-pubescent sexual assault victims. Indeed, in these situations, skill, sensitivity and experience are more important than any specially developed technology. Practitioners undertaking examinations



and specimen collection should be specially trained in child and adolescent abuse/assault evaluation.

The scheduling of examinations should be based on the history of assault or abuse. If initial exposure is recent, a follow-up visit, approximately one week after the last sexual exposure will be needed to repeat the physical examination and to collect additional specimens, in order to allow sufficient time for infections to incubate.

Similarly, to allow sufficient time for antibodies to develop, an additional follow-up visit at approximately 12 weeks after the last sexual exposure is also necessary to collect sera. A single examination may be sufficient if the child or adolescent has been abused over an extended period of time and/or the last alleged episode of abuse has occurred some time before the patient presents for medical evaluation. The following recommendation for scheduling examinations is a general guide.

INITIAL EXAMINATION

An initial examination and any follow-up examination should include:

- Cultures for *N. gonorrhoeae* and *C. trachomatis* from specimens collected from the pharynx and anus in both sexes, the vagina in girls, and the urethra in boys. Cervical specimens should not be collected from pre-pubertal girls. In boys, a meatal specimen of urethral discharge is an adequate substitute for an intraurethral swab specimen when a discharge is present. Only standard culture systems for the isolation of *N. gonorrhoeae* should be used.
- Wet-mount microscopic examination of a vaginal swab specimen for *T. vaginalis* infection. The presence of clue cells suggests BV in a child with vaginal discharge. The significance of clue cells or other indicators of BV as an indicator of sexual exposure in the presence or absence of vaginal discharge is unclear.
- Tissue culture for herpes simplex virus (where available) and dark-field microscopy or direct fluorescent antibody testing for *T. pallidum* from a specimen collected from vesicles or ulcers in children of all ages and in adolescents.
- Collection of a serum sample to be preserved for subsequent analysis if follow-up serological tests are positive. If the last sexual exposure occurred more than 12 weeks before the initial examination, serum should be tested immediately for antibodies to sexually transmitted agents. Agents for which suitable tests are available include *T. pallidum*, HIV and hepatitis B virus. The choice of agents for serological tests should be made on a case-by-case basis.



EXAMINATION AT 12 WEEKS FOLLOWING ASSAULT

An examination at approximately 12 weeks following the last sexual exposure is recommended to allow time for antibodies to infectious agents to develop. Serological tests for the following agents should be considered: *T. pallidum*, HIV and hepatitis B virus.

The prevalence of infections with the above agents varies greatly among communities. It will be important to know whether risk factors are present in the abuser/assailant. Results of hepatitis B virus tests must be interpreted carefully, since hepatitis B virus may be transmitted by non-sexual modes as well as sexually. Again, the choice of tests must be made on a case-by-case basis.

PRESUMPTIVE TREATMENT

There are few data upon which to establish the risk of a child acquiring an STI as a result of sexual abuse. The risk is believed to be low in most circumstances, though documentation to support this position is inadequate.

Presumptive treatment for children who have been sexually assaulted or abused is not widely recommended since girls appear to be at lower risk of ascending infection than adolescent or adult women and regular follow-up can usually be assured. However, some children or their parents/guardians may be very concerned about the possibility of contracting an STI, even if the risk is perceived to be low by the health care practitioner. Addressing patient concerns may be an appropriate indication for presumptive treatment in some settings.

SUSCEPTIBILITY AND CLINICAL PRESENTATION OF STI IN CHILDREN AND ADOLESCENTS

There are differences in the epidemiology of STIs in adolescents and adults, and though clinical presentations are similar, adolescents are regarded as being more biologically susceptible to infection and at increased risk of morbidity. Some of these differences have been obscured through the common practice of reporting adolescents (10–19 years) in the same category as youth (15–24 years) and through general inattention to young females who are married and pregnant.

In the majority of cases, the presentation of STIs is similar to that seen in adults. At the time of puberty and adolescence, the female genital tract undergoes changes



in response to increasing levels of ovarian hormones. Along with anatomical and physiological changes, the vaginal epithelium begins to secrete mucus. The mucus secretion causes the adolescent girl to develop a white vaginal discharge, which is physiological. Generally, therefore, vaginal discharge is a poor predictor of the presence of either gonococcal or chlamydial infection.

Susceptibility

In pre-pubescent girls the columnar epithelium extends from the endo-cervical canal to the porto-vaginalis of the cervix. This cervical ectropion, normally present in 60–80% of sexually active adolescents, is associated with an increased risk of *C. trachomatis* infection. Moreover, *N. gonorrhoeae*, which infects the columnar epithelium, readily colonises this exposed surface. Exposure to oncogenic pathogens, such as the human papilloma virus, enhances the risk of dyskaryosis and carcinoma at an early age. Additionally, because cervical mucus production and humoral immunity are absent until ovulation begins, the risk of complications is higher in the immature adolescent exposed to infection as opposed to the physically mature woman. Ascending infection and subsequent PID are consequently more frequent in the sexually active pre-pubescent adolescents and those in early puberty.

CERVICAL INFECTIONS

Approximately 85% of gonococcal infection in females will be asymptomatic. However, there may be vulval itching, minor discharge, urethritis or proctitis. In pre-pubescent girls, a purulent vulvo-vaginitis may occur.

Similarly, *C. trachomatis* infection is asymptomatic in the majority of cases. Symptoms which may occur in the adolescent are inter-menstrual bleeding, post-coital bleeding and an increase in vaginal secretions.

GENITAL ULCER DISEASE

Presentation of syphilis is the same in adolescents and adults. The stages of primary chancre, secondary syphilis manifestations, latent syphilis and serological responses are the same in both groups.



ANOGENITAL WARTS

Warts present as condylomatous, papular or flat lesions, much the same as in adults.

VAGINAL INFECTION

T. vaginalis, candidiasis and BV are the three common pathological causes of an abnormal vaginal discharge. *T. vaginalis* is sexually transmitted and causes an offensive malodorous discharge with vulval soreness and irritation. It may also present no symptoms at all.

C. albicans is uncommon in adolescents prior to puberty. If present, the adolescent may have a discharge, vulval itching, dyspareunia, a peri-anal soreness or a fissuring at the introitus. Attacks of candida vulvitis may be cyclical in nature and correspond to menstruation.

BV does not produce a vulvitis and the adolescent will not complain of itching or soreness.





ANNEX 1

LIST OF PARTICIPANTS

MEETING OF THE ADVISORY GROUP ON SEXUALLY TRANSMITTED DISEASE TREATMENT GENEVA, 11-14 MAY 1999

- **Dr Hilda Abreu**, Departamento de Enfermedades de Transmision Sexual, Ministerio de Salud Pública, Uruguay
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ANNEX 2

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