17

Sexually Transmitted Infections and Reproductive Tract Infections

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INTRODUCTION

Importance of the problem

Sexually transmitted infections (STIs) are defined as infections that spread primarily through person-to-person sexual contact. However, several of these infections, in particular HIV, syphilis and hepatitis B, can also be transmitted via mother-to-child-transmission during pregnancy and childbirth, blood products or tissue transfer. There are more than 30 different sexually transmissible bacteria, viruses and parasites[1]. STIs should be distinguished from reproductive tract infections (RTIs). RTIs are defined as infections of the genital organs and include endogenous infections such as bacterial vaginosis and vulvovaginitis candidiasis. These two infections are mostly not sexually transmitted and they can occur in women who have never had a sexual relationship. RTIs also include exogenous infections, such as septic abortion due to unsafe procedures and post-partum infections. Thus the term STIs and RTIs only partly overlap. The concept of STI refers to the way of transmission, and the concept RTI to the site where the infection develops.

The following chapter includes selected curable STIs and RTIs based on a synthesis of what is generally discussed in textbooks of gynecology and obstetrics and World Health Organization (WHO) publications on STIs as well as treatment guidelines. Treatment advice is based on WHO treatment guidelines[2,3] and Cochrane reviews[4,5], and is restricted to drugs listed in the Interagency List of Essential Medicines for Reproductive Health[6].

The STIs discussed in this chapter include bacterial vaginosis, trichomoniasis, candidiasis, chlamydia, gonorrhea, pelvic inflammatory disease (PID), syphilis, genital herpes, chancroids, lymphogranuloma venereum, granuloma venereum, condylomata acuminata and septic abortion. This chapter will not include human papilloma virus (HPV) and cervical cancer (Chapter 26), or HIV (Chapter 18). Other STIs such as hepatitis B which do not cause infections of the sexual organs, or post-partum infections which are discussed in textbooks of obstetrics, are not included in this chapter.

Epidemiology

STIs are a major public health problem in all regions of the world. WHO estimated in 2005 that about 448 million curable infections occur every year worldwide in adult men and women[7]. The burden of STIs falls primarily on low- and middle-income countries with 110 million in Africa, 71 million in South and South-East Asia and 109 million in the Western Pacific regions. In addition many people are infected with non-curable STIs, mainly viral diseases such as HIV/AIDS, hepatitis B or genital herpes. About 536 million people aged 15–49 years were estimated to be living with herpes simplex virus type 2 worldwide in 2003[8] (Tables 1 and 2).

Table 1 Common curable STIs (2005 WHO estimation)

	Million cases per year
Gonorrhea (*Neisseria gonorrhoeae*)	88
Chlamydia infection (*Chlamydia trachomatis*)	101
Syphilis infection (*Treponema pallidum*)	11
Trichomoniasis (*Trichomonas vaginalis*)	204
Chancroid (*Haemophilus ducreyi*)	6

Table 2 Common viral infections of interest in gynecology and obstetrics

HIV/AIDS (human immunodeficiency virus)	2.6 million new infections in 2009
Genital herpes (herpes simplex virus type 2)	23.6 million new infections in 2003
Genital warts (HPV predominantly types 6 and 11)	
HPV types 16 and 18	Prevalence of 12% in women aged >15 years; 530,000 cases of cervical cancer every year

HPV, human papillomavirus

Untreated STIs, excluding HIV, are estimated to account for 17% of the economic loss due to disease. Most importantly, for both men and women, STIs are associated with an increased risk of both acquisition and transmission of HIV. The risk of HIV transmission is about two to five times higher in people with an STI, highest in people with an ulcerative STI[9,10] (level 1 evidence). Recent evidence suggests that genital herpes (herpes simplex 2) may be responsible for fuelling a large part of HIV infection[11] (level 1 evidence).

STIs are more frequent in young women than men and more frequent in low-income countries where diagnostics and treatment are limited. Reasons discussed for the high prevalence of STIs in low-income countries are demographic factors (more young people), urbanization, migrant labor, prostitution, concurrent partnerships, lack of access to quality care for STIs, and for prevention efforts, including screening programs[12].

Another important factor is that a number of STIs are asymptomatic which hampers control efforts. For example, up to 70% of women and a significant proportion of men with gonococcal and/or chlamydial infections may experience no symptoms at all (see also section on 'Management of asymptomatic STIs/RTIs: screening').

Common complications of sexually transmitted infections

Besides the higher risk of HIV infection, STIs cause many serious complications. Particularly, untreated chlamydial infection is estimated to be the cause of at least a third of female infertility. Also, women who have had PID are six to ten times more likely to have an ectopic (tubal) pregnancy than those who have not had one.

Moreover, untreated STIs are associated with congenital and perinatal infections in neonates. Particularly, early untreated maternal syphilis infection causes stillbirth and neonatal deaths resulting in an overall perinatal mortality of 40%.

Up to 35% of pregnancies among women with untreated gonococcal infection result in spontaneous abortions and premature deliveries, and up to 10% in perinatal deaths. Up to 50% of children born to mothers with untreated gonorrhea and 30% of children born to mothers with untreated chlamydial infection will develop a serious eye infection or conjunctivitis (ophthalmia neonatorum). This is, however, easily preventable[1].

MANAGEMENT AND TREATMENT OF SYMPTOMATIC SEXUALLY TRANSMITTED INFECTIONS AND REPRODUCTIVE TRACT INFECTIONS

Sexually transmitted infection syndromes and the syndromic approach to patient management

Although many different pathogens cause STIs or RTIs, many have a similar or overlapping clinical appearance, known as signs (what the individual or the healthcare provider sees on examination) and symptoms (what the patient feels, such as pain or itching). Signs and symptoms can help health providers make a diagnosis. For example, profuse, purulent, malodorous vaginal discharge is seen in trichomoniasis. But vaginal discharge is also seen in infections other than STIs, such as bacterial vaginosis and vulvovaginal candidiasis. Often more than one etiological cause/microbe is involved in the infection. Gonorrhea and *Trichomonas* alter the discharge. Thus the signs and symptoms are often not specific enough to make an etiological diagnosis.

The traditional method (and gold standard) for diagnosing a specific STI/RTI is by laboratory tests. But, tests for STIs are mostly not available at first-line health facilities and often not at district hospital level in low-resource settings. Some laboratory investigations for diagnosing STIs are expensive or demand advanced techniques. That is why WHO has recommended a syndromic approach to diagnosis and management of STIs in low- and middle-income countries since the 1990s

and it has been the approach of choice since then in most settings. The approach is based on a group of symptoms and easily recognizable signs associated with a number of well-defined etiologies. There is much evidence, that syndromic management is effective for treating STIs and has an impact on the STI epidemic. Dramatic declines in STI rates have been observed following the introduction of control measures based on the syndromic approach[13].

Common symptoms and signs (syndromes) are:

- Urethral discharge in men
- Genital ulcer
- Inguinal bulbo
- Scrotal swelling
- Vaginal discharge
- Lower abdominal pain in women
- Neonatal conjunctivitis.

The syndromic approach is a scientifically derived approach. The antimicrobial regimens are chosen to cover major pathogens responsible for the syndromes in a specific geographical area. Thus guidelines differ from country to country in accordance with epidemiological pattern of STIs and resistance to antibiotic therapy; this is why there is not one treatment approach for all settings. Typically, flowcharts are promoted to assist health workers to decide on the best treatment (Figures 1 and 2). Training modules prepared by WHO are available in different languages[3] and many countries have adapted them to the locally observed resistance patterns of STIs.

The advantage of using this signs and symptom-based approach is that the management of STIs is not dependent on laboratory investigations, which are not available in many first-line health facilities. Moreover not only specialists but also clinicians and nurses can treat patients effectively. However, syndromic management is not unanimously supported. Syndromic management of STIs has been reviewed as being generally effective in treating urethral discharge and genital ulcer disease STIs in men[14] (level 1 evidence). The main challenges are vaginal discharge and PID in women, as the syndromes and signs are less specific[13].

Another big challenge for the control of STIs is that infections are often asymptomatic. Syndromic management is not suitable for treating asymptomatic infections that require a screening approach. Unfortunately, screening is not available at most primary level or district healthcare settings in lower-resource countries, except syphilis testing

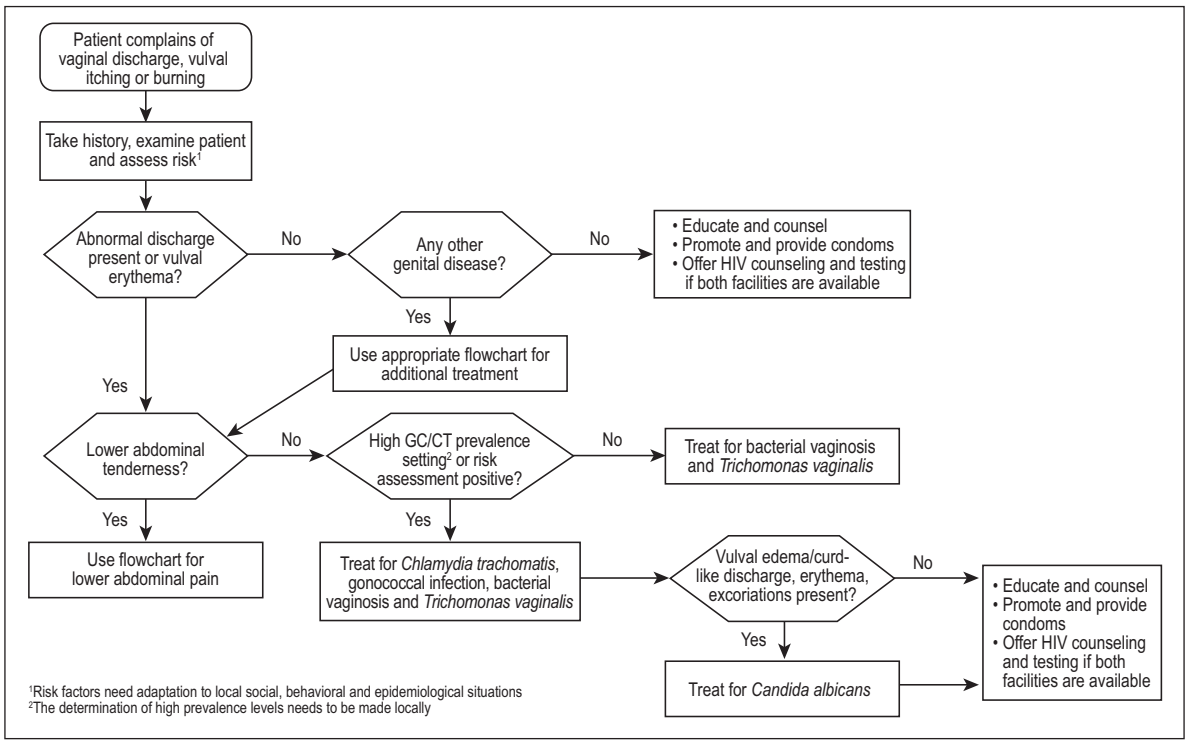

Figure 1 Syndromic approach: vaginal discharge. Source: WHO treatment modules, 2007

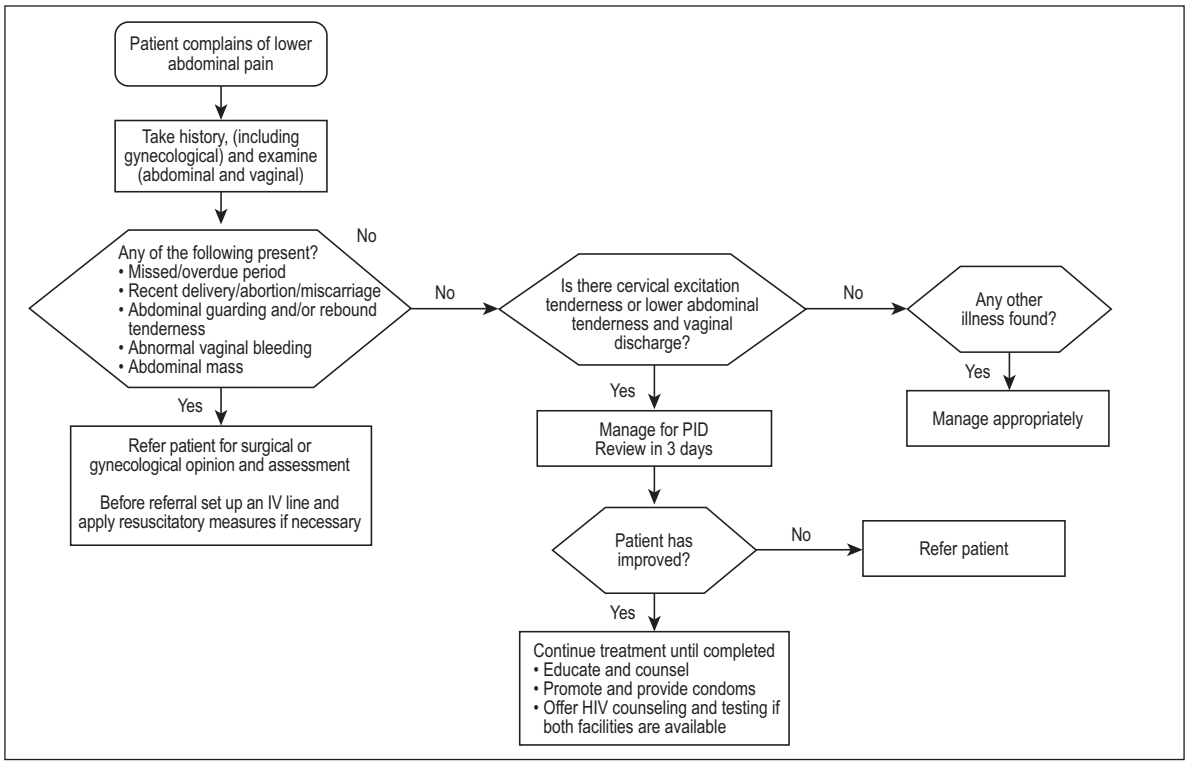

Figure 2 Syndromic management: lower abdominal pain. Source: WHO treatment modules, 2007

during pregnancy which therefore provides an important opportunity not to be missed (see more under Linkages). Furthermore, control efforts need to be put on many pillars, where treatment of symptomatic diseases is one, but prevention of risky sexual relations, partner notification, screening programs during pregnancy and integration of control and prevention with other reproductive health services are others[15].

The syndromic approach has been particularly designed for the primary healthcare level. At the hospital level further investigation such as Gram staining, confirmation test for syphilis and gynecological examination, are possible and should be used to complement syndromic management and in particular to treat patients where treatment according to the syndromic management did not succeed. Third-line therapeutic options, but also more advanced laboratory diagnostic and investigations, are likely to be available at this level.

We strongly advise the reader of this book to adhere to national syndromic management guidelines. The guidelines offer the best treatment for patients at the primary healthcare level and outpatient services. But because they differ slightly in all countries according to the epidemiological pattern of STIs and resistance against antibiotic regimens, we will not include any specific syndromic management treatment advice. We would also like to promote the use of the STI training modules available from the WHO homepage: http://www.who.int/reproductivehealth/publications/rtis/9789241593407index/en/index.html.

The following sections aim to give an overview about clinical presentation, signs and symptoms and possible advanced diagnostics. At a district hospital more advanced laboratory facilities and diagnostic facilities are available and should be used, particularly for patients who were not cured after the first treatment course or patients who have recurrent STIs/RTIs.

Clinical and etiological diagnostic and management of symptomatic sexually transmitted infections and reproductive tract infections

The normal vaginal flora

The normal vaginal flora is composed of several species of bacteria producing lactobacilli which are

maintaining a slightly acid vaginal environment of pH 4.5. This is important as a natural barrier against infections. The type and amount of natural fluids composed of cells, cervical mucus and upper genital tract fluids are determined by hormonal levels. Thus, vaginal excretion or cervical mucus may increase in the middle of the menstrual cycle and can be perceived by women as a vaginal discharge. These cyclic variations do not occur when oral contraceptives are used.

The normal flora can be can analysed by a wet-mount preparation where a vaginal secretion is suspended in 0.5 ml of normal saline and transferred to a slide for microscopy. Microscopy of normal vaginal secretion reveals many superficial epithelial cells, few white blood cells, and few if any clue cells. The same saline preparation can be used to check vaginal secretion in cases of symptomatic STI/RTIs if a microscope is readily available in or near the consultation room (Figure 3).

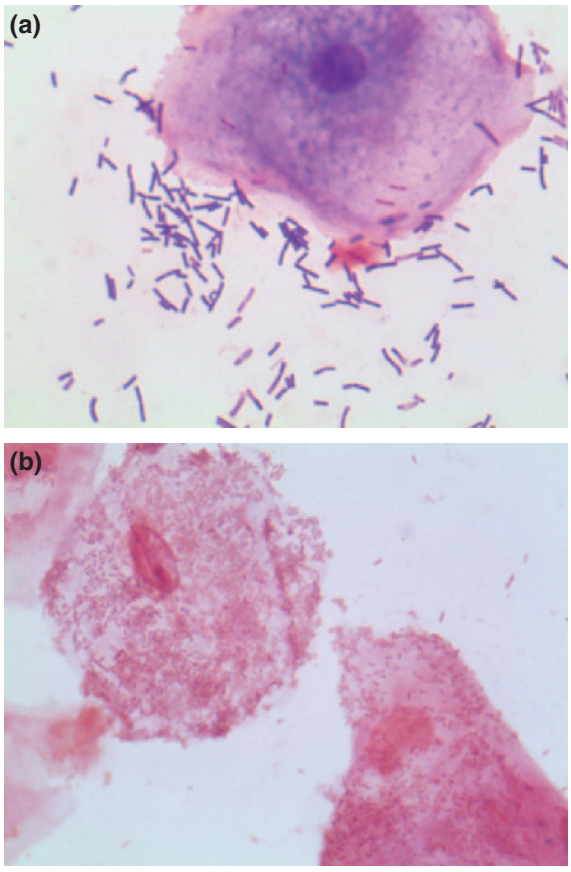

Figure 3 (a) Normal vaginal flora (Gram stain); (b) high Nugent score, bacterial vaginosis (Gram stain). Source: ITM, Antwerp, STI Laboratory

Vaginitis

Bacterial vaginosis Bacterial vaginosis (BV), previously referred to as non-specific vaginitis is an alteration of the normal bacterial flora that results in the loss of lactobacilli and in an overgrowth of predominantly anaerobic bacteria. This makes the concentration of anaerobic bacteria which is normally 1% to be 100–1000 times higher. Thus, BV is a microbial imbalance of the vaginal flora but not an infection with a pathogenic bacterium. It is the most common form of vaginitis. Risk factors are vaginal douche, antibiotic treatment for other conditions and STIs.

Many studies have indicated that women with BV are at increased risk of PID and post-abortal pelvic infection. During pregnancy, BV can cause premature rupture of membranes, preterm labor and delivery.

- *Diagnosis*: pH is higher that 4.5 (usually 4.7–6); vaginal discharge with fishy odor; vaginal secretions are grey and thinly coat the vaginal walls.
- At the health center or district hospital levels, microscopy (wet mount) shows an increased number of clue cells, typically >20% of epithelial cells are clue cells in advanced infection. 'Whiff test': fishy odor if potassium hydroxide (KOH 10%) is added.
- At provincial or referral laboratory, a 'Nugent score' can be performed: a score of 7–10 is consistent with BV (Table 3). The assessment uses Gram stain and determines semiquantitatively

Table 3 Scoring system (0–10) for Gram-stained vaginal smears*

Score†	*Lactobacillus morphotypes*	*Gardnerella and Bacteroides spp. morphotypes*	*Curved Gram-variable rods*
0	4+	0	0
1	3+	1+	1+ or 2+
2	2+	2+	3+ or 4+
3	1+	3+	
4	0	4+	

*Morphotypes are scored as the average number seen per oil immersion field. Note that less weight is given to curved Gram-variable rods. Total score = lactobacilli + *G. vaginalis* and *Bacteroides* spp. + curved rods. †0, no morphotypes present; 1, <1 morphotype present; 2, 1–4 morphotypes present; 3, 5–30 morphotypes present; 4, >30 morphotypes present.

the presence of large Gram-positive *Lactobacillus* morphotypes (Figure 3b).
- *Treatment*: see Table 4.

Note: probiotics (H_2O_2-producing vaginal lactobacilli) have been suggested, but the results are not conclusive[16]. Moreover they are not found as a treatment option in the essential drug lists.

Vulvovaginal candidiasis Vulvovaginal candidiasis (VVC) has traditionally not been considered to be a STI because it occurs in celibate women and because *Candida* is considered part of the normal vaginal flora. The majority of women with sporadic and infrequent infections of VVC have episodes of symptomatic infections in which an etiologic or precipitating factor is not found, but antibiotic use, pregnancy, diabetes or HIV infection might lead to a higher risk of VVC. Nevertheless, studies have confirmed that the transmission of *Candida* organisms by vaginal sexual intercourse and other forms of sexual activity also occurs[17].

Table 4 Overview of common infections and treatment suggestions

Infection	*Treatment*
Vaginitis	
Bacterial vaginosis	Metronidazole 2 g orally (single dose) *or*
Trichomoniasis	Metronidazole 500 mg orally twice a day for 7 days
Candidiasis (yeast)	Miconazole 200 mg vaginal suppository, once a day for 3 days *or*
	Clotrimazole 100 mg vaginal tablets, 2 times a day for 3 days *or*
	Fluconazole 150 mg oral tablet (single dose) *or*
	Nystatin 100,000 units, vaginal tablets once a day for 14 days
Cervicitis	
Gonorrhea	Cefixime 400 mg orally (single dose) *or*
	Ceftriaxone 125 mg, by intramuscular injection *or*
	Spectinomycin 2 g by intramuscular injection
Chlamydia	Azithromycin 1 g orally (single dose) *or*
	Doxycycline 100 mg orally twice a day for 7 days
	(*Pregnant women*: azithromycin 1 g orally (single dose) *or* erythromycin 500 mg 4 times a day for 7 days)
Pelvic inflammatory disease (PID)	Treat for gonorrhea and chlamydia (see above) plus for anaerobic infections with
	Metronidazole 500 mg orally twice a day for 7 days *or*
	Ampicillin 2 g by intravenous or intramuscular injection, then 1 g every 6 h *plus*
	Gentamicin 80 mg by intramuscular injection every 8 h *plus*
	Metronidazole 500 mg or 100 ml by intravenous infusion every 8 h
Genital ulcers	
Syphilis	Benzathine penicillin G 2.4 million units intramuscular injection
Genital herpes	Aciclovir 400 mg orally, 3 times a day for 7 days
Chancroids	Ciprofloxacin 500 mg twice a day for 3 days *or*
	Azithromycin, 1 g orally (single dose) *or*
	Erythromycin 500 mg orally 4 times a day for 7 days (also if patient pregnant) *or*
	Ceftriaxone 250 mg intramuscular injection (single dose)
Lymphogranuloma venereum (LGV)	Doxycycline 100 mg orally twice a day for 14 days *or*
	Erythromycin 500 mg 4 times a day for 14 days
Granuloma venereum (donovanosis)	Azithromycin 1 g orally (single dose) *or*
	Doxycycline 100 mg orally twice a day
Infections following miscarriage, induced abortion or delivery	
Septic abortion, post-partum endometritis	Ampicillin 2 g intravenously or intramuscularly, then 1 g every 6 h *plus*
	Gentamycin 80 mg intramuscularly every 8 h *plus*
	Metronidazole 500 mg orally or intravenously every 8 h

Source: WHO Guidelines, 2005

- *Diagnosis*: vaginal discharge which typically resembles cottage cheese; pruritus, inflammation, vaginal soreness; discharge can vary from watery to thick; pH of the vagina is normal (≤4.5).
- Fungal elements can be confirmed by microscopy (simple saline preparation – wet mount).
- (At the referral laboratory a culture on Sabouraud medium can be performed.)
- *Treatment*: see Table 4.

Trichomonas vaginalis Trichomoniasis is caused by a flagellated parasite, *Trichomonas vaginalis*, which needs an anaerobic environment. The transmission rate is very high. Most people contract the disease after a single exposure to an infected person. Often trichomoniasis is accompanied by BV. The infection may in particular cause premature rupture of membranes and preterm delivery.

- *Diagnosis*: profuse, purulent, malodorous vaginal discharge with bubbles; pH is higher than 5.0.
- *Microscopy* (simple saline – wet-mount preparation) reveals motile (jerky movements) *T. vaginalis* and increased numbers of leukocytes (Figure 4). At the central laboratory, culture and possible DNA amplification (PCR) can also be performed.
- *Treatment*: see Table 4.

Differential diagnosis of vaginitis Where it is not possible to confirm trichomoniasis, candidiasis or BV by microscopic diagnosis, the country-specific syndromic approach guidelines should be followed.

Cervicitis

Gonorrhea Gonorrhea is caused by *Neisseria gonorrhoeae* a Gram-negative diplococcus. While the clinical features of gonococcal urethritis in men are a urethral discharge, often profuse, and dysuria, most women with gonococcal infection are asymptomatic.

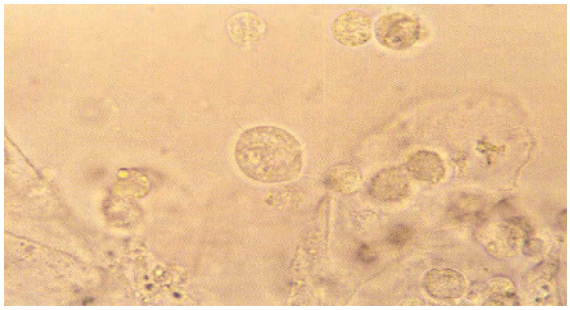

Figure 4 *Trichomnas vaginalis* (wet mount).
Source: ITM, Antwerp, STI Laboratory

- *Diagnosis*: no test is available at first and second levels of care. A reliable and sensitive rapid test is still under development. Gram staining of urethral discharge of men can be done and Gram-negative diplococci are seen inside the leukocytes. Among women, only culture on selective and enriched medium and specific molecular amplification techniques (PCR) can make a definite diagnosis.
- *Treatment*: see Table 4.

Chlamydia Chlamydial infection is cause by *Chlamydia trachomatis*. Symptoms are often unspecific and the infection presents with mild clinical manifestations.

- *Diagnosis – laboratory*: only at the referral or central laboratory with cell culture, antigen detection by direct immunofluorescence or enzyme immunoassay, or molecular amplification. Rapid tests are commercially available but they lack sensitivity; more promising tests are under development.
- *Treatment*: see Table 4. Note: for *C. trachomatis* infection in pregnancy, erythromycin is recommended[5] (level of evidence 1).

Pelvic inflammatory disease

PID is caused by microorganisms colonizing the endocervix and ascending to the endometrium and fallopian tubes. It is a clinical diagnosis implying that the patient has upper genital tract infection and inflammation. The inflammation may be present at any point along a continuum that includes endometritis, salpingitis and peritonitis. PID is normally caused by sexually transmitted microorganisms such as *N. gonorrhoeae* or *C. trachomatis*. A tubo-ovarian abscess is the end-stage of the disease. PID is often accompanied by BV.

- *Diagnosis*: triad of symptoms and signs including pelvic pain, adnexal tenderness and fever. Many patients present with mild symptoms or no symptoms at all. Genitourinary tract infections may indicate PID.
- *Laboratory*: as above.
- *Treatment*: see Table 4. Tubo-ovarian abscess normally responds to antibiotic regimen, but a surgical intervention with drainage might

become necessary. On ultrasound large masses in the ovaries can be seen and free fluid in Douglas' pouch. If in doubt aspiration of this fluid will distinguish pus from blood (see Chapter 12 on ectopic pregnancy). Drainage with a Foley catheter and posterior culdotomy is explained in Chapter 18 (HIV-related gynecological problems). If the symptoms persist a laparotomy with drainage might become necessary.

Differential diagnosis of PID The diagnosis and therapy of PID is particularly difficult because often the PID progresses unnoticed and symptoms are minor particularly in chlamydial infection. Lower abdominal pain can also be caused by many other diseases such as endometriosis, benign and malign ovarian cysts, adnexal torsion or ectopic pregnancy. In addition patients suffering from infertility or marital problems might present with lower abdominal pain, and are often over-treated with antibiotics.

Ophthalmia neonatorum

Ophthalmia neonatorum might present with bi- or unilateral swollen eyelids with purulent discharge caused by *N. gonorrhoeae* or *C. trachomatis* and contracted by newborns during delivery (Figure 5).

- *Treatment*: newborns should be treated with ceftriaxone 125 mg intramuscularly as a single dose. Note: the mother and partner should also be treated for gonorrhea and chlamydia inflection.

Genital ulcer diseases

Genital ulcer diseases are mainly caused by syphilis, genital herpes or chancroid (Figure 6).

Syphilis

- *Diagnosis*: ulcers caused by syphilis are normally bigger, relatively painless and have a smooth, indurated border and a smooth base (Figure 6b). They are not accompanied by lymphadenopathy. These signs of primary syphilis are seen about 2–10 weeks after infection. The secondary stage of syphilis develops 1–3 months after the primary stage. They appear as a macular–papular rash and/or moist papules (condylomata lata). After this secondary stage, the infection enters a latent phase without any signs and symptoms that can last for years. The tertiary stage is characterized by granulomas of the skin, the bones and internal organs. Cardiovascular or neurosyphilis may occur.
- *Laboratory*: positive non-treponemal rapid plasma reagin (RPR) test or venereal disease research laboratory (VDRL) test, the *Treponema*-specific TPHA (*Treponema pallidum* hemagglutination assay) test or the new rapid tests can be used[18].

  WHO first-recommended option for diagnosis of syphilis is RPR confirmed by TPHA (Table 5). However, the time-consuming shaking procedure and difficulties in interpretation has limited the use of the RPR in some resource-poor settings. A new dipstick-type *Treponema*-specific serological test (rapid tests) has been on the market for a few years and provides a good alternative for settings where RPR testing has met difficulties[19,20] and is now recommended as a screening test[18]. This new rapid test is a treponemal test which is very easy to use, can be used with full blood, serum or plasma and can be stored at room temperature. The disadvantage is, as with other treponemal tests, that the test

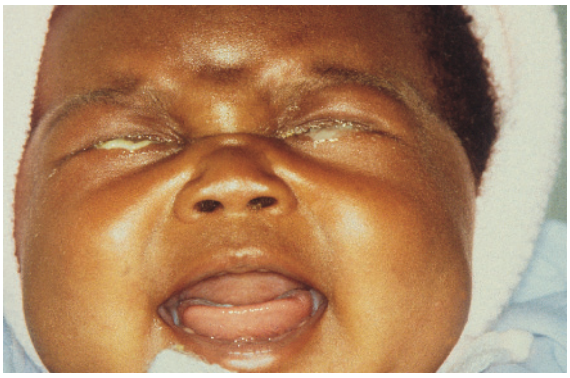

Figure 5 Gonococcal ophthalmia neonatorum. Courtesy Dr Ron Ballard, US Centers for Disease Control and Prevention

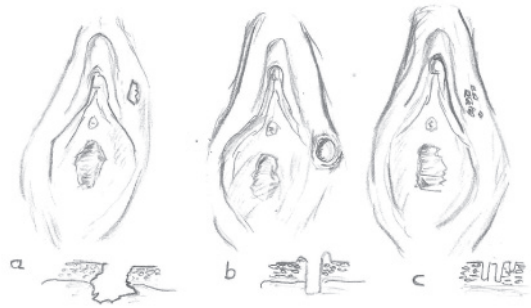

Figure 6 Genital ulcer disease: (a) chancroid; (b) syphilis; and (c) herpes simplex ulcers

cannot distinguish between active and previously treated infection. It should be confirmed by RPR (non-treponemal test). WHO recommends the introduction of the treponemal rapid test only in places where the RPR test has not yet been introduced or poses difficulties because of the demand for a fridge and the use of serum.

- *Screening* for syphilis should be done on-site, and results and treatment should be made available to the woman before she leaves the clinic. Syphilis screening using the RPR is recommended during antenatal care.

Congenital syphilis Syphilis prevalence in pregnant women in sub-Saharan Africa still exceeds 5% in some countries. In women with untreated early syphilis, 25% of pregnancies may end in abortion or in stillbirths and 14% in neonatal deaths[1,15,20]. In addition about one-third of infants of infected mothers are born with congenital syphilis (Figure 7). WHO estimates that 1.5 million cases of congenital syphilis occur every year. Syphilis screening and treatment has shown to reduce stillbirth by 80%[21].

- Congenital syphilis might present with hepatosplenomegaly, lymph node swelling, rhinitis and maculopapular exanthema with moist papules. Late signs of secondary congenital syphilis are teeth deformities, deformities of the skeletal system and deafness.

  Congenital syphilis can be prevented by screening and treatment of the mother during pregnancy. Syphilis screening has been promoted as an essential element of antenatal care for many years and is a very cost-effective public health measure. In recent years, a new, very simple rapid

Table 5 Interpretation of serological tests for syphilis if the new rapid test is used as first choice screening test

Treponemal test (rapid test)	*Non-treponemal test (RPR, VDRL)*	*Likely interpretation*
+	+	Syphilis
–	+	False-positive RPR (no syphilis)
+	–	Primary or latent syphilis, previously treated syphilis
–	–	No syphilis

RPR, rapid plasma regain; VDRL, Venereal Disease Research Laboratory.

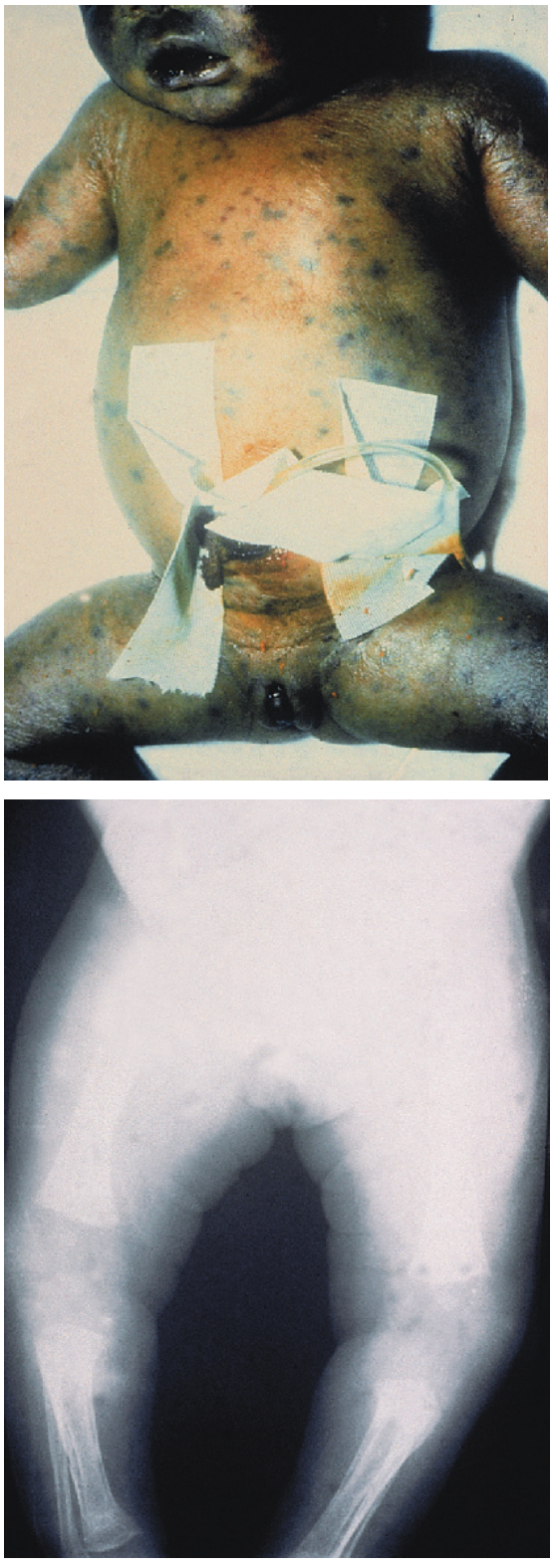

Figure 7 Congenital syphilis. Courtesy Dr Ron Ballard, US Centers for Disease Control and Prevention

point-of-care treponemal test has been made available which presents a cost-effective, easy-to-perform alternative for screening for syphilis in pregnant mothers where RPR is not available[22].

- *Treatment*: children with signs of congenital syphilis and a mother with a positive syphilis test should be treated with aqueous crystalline benzylpenicillin 100,000–150,000 units/kg of body weight intravenously or intramuscularly twice a day for 7 days followed by three times a day for 3 more days or procaine benzylpenicillin 50,000 units/kg of body weight intramuscularly once a day for 10 days. Children born to a syphilis-positive mother should receive 50,000 units/kg of body weight, intramuscularly, in a single dose.

Genital herpes This is the most frequent cause of genital ulcers. The ulcers are often vesicular lesions and look like tiny blisters.

- *Diagnosis*: grouped vesicles mixed with small ulcers, particularly with a history of such lesions.
- *Laboratory*: cell culture, serology, DNA amplification.
- *Treatment*: see Table 4. Note: aciclovir may not be available in many countries or only in clinics specialized for treatment of opportunistic infections of HIV. In this case the patient has to wait for spontaneous remission which normally occurs in a few days. Treatment may include medication with pain killers. Patients should be advised to abstain from sexual intercourse or to use condoms.

Chancroid The ulcers of chancroid (caused by *Haemophilus ducreyi*) have irregular margins, are deep, have undetermined edges, are extremely painful and are accompanied by tender inguinal lymphadenopathy (inguinal bubo) in 70% of cases (Figure 6).

- *Laboratory*: culture on specific media, DNA amplification.
- *Treatment*: see Table 4. Note: other therapeutic regimens based on erythromycin or co-trimoxazole might be efficient.

Lymphogranuloma venereum

- *Diagnosis*: lymphogranuloma venereum is caused by *Chlamydia trachomatis*, serovar L1, L2 and L3 and is more frequent in men than women. The disease presents with a transient, often painless genital or anorectal ulcer which disappears mostly undiagnosed. Two to three weeks later confluent inguinal nodes develop and might show multiple fistulae. These inguinal bubo are often multiple and have fistulae, which helps to distinguish them from a bubo caused by chancroid.
- *Laboratory*: lesion swabs or bubo aspirate can be tested for *C. trachomatis* by cell culture, direct immunofluorescence or molecular amplification. Serovar identification can be performed by various molecular methods. However, diagnosis is mostly done on the basis of clinical appearance.
- *Treatment*: see Table 4.

Granuloma inguinale Granuloma inguinale is a rare STI and is only endemic in a few countries, out of them – South Africa, parts of Asia (India and Papua New Guinea) and parts of South America (Brazil, the Caribbean). The infection is also called donovanosis and is caused by *Klebsiella granulomatis*.

- *Diagnosis*: clinically, the disease commonly presents with a painless, slowly progressing ulcer. The ulcerations bleed easily on contact.
- *Laboratory*: observation of Donovan bodies within histiocytes in Giemsa, Leishman or Wright's stained tissue smear. An alternative is the histological examination for Donovan bodies using Giemsa or silver stain. Amplification methods are not commercially available.
- *Treatment*: see Table 4.

Genital wart and condylomata acuminata Genital warts and condylomata acuminata are caused by HPV subtypes 6 and 11. These two subtypes are so-called low-risk HPV subtypes as they have little or no risk of causing cancerous disease as opposed to subtypes 16 and 18 which cause cervical cancer but not genital warts. Appearance differs from flat papular warts to the typical condylomata acuminata with verrucous and exophytic lesions. Condyloma acuminata may remain unchanged or spontaneously resolve, and the effect of treatment on viral transmission is unclear. However, many women prefer removal, and lesions can be destroyed with sharp or electrosurgical excision. Alternatively self-treatment with 0.5% podophyllotoxin solution or 10–25% podophyllin tincture administered by a health provider is suggested if available[2].

- *Vaccine*: For a few years, two HPV vaccines have been marketed that help protect against two (Cervarix®) or four (Gardasil®) types of HPV. In girls and young women aged 9–26 years, both

vaccines help protect against two types of HPV (16, 18) that cause about 75% of cervical cancer cases, while one of them (Cervarix®) also helps protect against two more types (6, 11) that cause 90% of genital warts cases. The operational issues and effectiveness related to the implementation of this intervention at a wider scale in low-resource countries are being studied. Rwanda is the first country in sub-Saharan Africa to introduce large-scale HPV vaccination[23].

Note: condylomata acuminata are NOT a reason to perform a cesarean section.

Post-abortion infections

Infections following an abortion, also called septic abortion, may follow any kind of abortion whether induced or spontaneous (miscarriages). Still it is more common following illegal abortion and incomplete abortion. Infections following an induced abortion are also called iatrogenic or exogenous infections and the spectrum of bacteria causing the infection differs from common STIs/RTIs. Consequently, the proposed therapy regimen differs slightly from the common regimen primarily targeting chlamydia and gonococci.

Infection will occur first in the uterus but might rapidly spread to the lower abdomen and might present with the symptoms of PID.

- *Diagnosis*: triad of symptoms and signs including pelvic pain, adnexal tenderness and fever, foul-smelling vaginal discharge; history of abortion – speculum examination might show residuals of placenta and/or bleeding.
- *Treatment*: see Table 4. Infections not involving deep tissue can be treated with amoxicillin 500 mg orally three times daily for 5 days PLUS metronidazole 400–500 mg orally three times a day. Severe infection should be treated with intravenous treatment[24]. The therapy should be continued for 2 days after the patient is fever free.

  Note: tetanus status should also be checked and complemented if needed.

The consultation for sexually transmitted infections

A good STI/RTI consultation needs a trained provider with sufficient training, experience and expertise. Elements of a good consultation are:

- Friendly and respectful reception
- Sufficient history taking
- Clinical examination
- Making a diagnosis
- Full treatment course based on the diagnosis
- Providing education and counseling
- Partner notification
- Documentation and registration.

The initial clinical examination does not necessarily include a speculum examination, but if available this should be performed (see also Chapter 1 on how to do that). Speculum examination should be performed in cases of 'recurrent vaginal discharge' to rule out cervical cancer. Also important are clear instructions on how to take the prescribed drugs, when to return to the clinic and a discussion on partner treatment. Patients should be advised to abstain from sexual intercourse until completely cured. Counseling on STIs including HIV and advice for HIV testing are an essential part of a STI consultation.

Male and female patients should be counseled on the consequences of STIs including the risk of spontaneous abortion, infertility and preterm rupture of membranes (if pregnant).

Essentials on diagnosis and treatment using the syndromic approach

The common syndromes distinguished in syndromic management of STIs in women are vaginal discharge, lower abdominal pain and genital ulcer (Table 6).

Flowcharts (see Figures 1 and 2) help the providers to make the diagnosis and treat the patients accordingly. For example, the flowchart on vaginal discharge starts with history taking and examination of signs and symptoms. The provider should verify:

- Whether the patient has abnormal vaginal discharge
- Whether there is any other sign of another STI/RTI such as sores or ulcers
- Whether the patient also has abdominal tenderness
- How the discharge looks – cord-like discharge indicating *Candida albicans* – or other types of discharge indicating BV and trichomoniasis.

The flowcharts always remind about counseling, condom promotion and counseling and testing for HIV if available.

Table 6 Syndromic approach related to STIs/RTIs among women: symptoms, signs and most common causes

Syndrome	*Symptoms*	*Signs*	*Most common causes*
Vaginal discharge	Unusual vaginal discharge; vaginal itching; dysuria (pain of urination); dyspareunia (pain during sexual intercourse)	Abnormal vaginal discharge	*Vaginitis*: • Trichomoniasis • Bacterial vaginosis • Candidiasis *Cervicitis*: • Gonorrhea • Chlamydia
Lower abdominal pain	Lower abdominal pain; dyspareunia	Vaginal discharge; lower abdominal tenderness or palpation; temperature >38°C	Gonorrhea Chlamydia Mixed anaerobes
Genital ulcer	Genital sore	Genital ulcer	Syphilis Chancroid Genital herpes
Neonatal conjunctivitis	Swollen eyelids; discharge; baby cannot open eyes	Edema of the eyelids; purulent discharge	Gonorrhea Chlamydia

Source: Adapted from WHO Training modules, 2007

Vaginal discharge

Syndromic management usually assesses the type of discharge and abdominal tenderness and whether signs for other STIs are present. Treatment advice commonly includes treatment for vaginitis and cervicitis, thus treatment for BV and trichomoniasis and gonococcal or chlamydial infection. Only if the discharge can clearly be attributed to *Candida albicans* (cord-like discharge), is treatment limited to anti-fungal therapy. Also if there are definitely no signs or symptoms indicating cervicitis is present, and neither chlamydial nor gonococcal infection are highly prevalent in the respective setting, treatment advice can be limited to BV and trichomoniasis.

Advanced cervical cancer can cause smelly vaginal discharge. A patient with recurrent 'vaginal discharge' should have a speculum examination and a visual inspection with acetic acid (VIA).

Lower abdominal pain

Flowcharts on lower abdominal pain usually try to exclude whether conditions other than infection are responsible for the pain (see differential diagnosis of PID). Abdominal tenderness during palpation combined with fever and vaginal discharge is a relatively clear indicator of PID. Treatment advice covers gonococcal or chlamydial infection (see Figure 2).

Genital ulcer

Although the clinical picture of syphilis and chancroid differ, treatment advise usually covers both diseases. Syndromic management guidelines for genital ulcer are at the moment under revision to also include treatment for herpes genitalis, which has become the most prevalent cause of genital ulcer disease where successful STI programs have reduced syphilis and chancroid in the population[13].

As explained before, proposed treatment schemes used for the syndromic approach differ slightly in all countries because of different epidemiological and resistance patterns of microbes. Particularly the treatment for gonorrhea has been revised recently because of local resistance to the previously recommended first-line drugs. Clinicians and nurses, particularly at a first-line health facility are advised to use the national syndromic approach treatment guidelines.

Improved treatment of sexually transmitted infections for HIV prevention

Syndromic management and improved STI treatment has been shown in Tanzania to reduce the HIV incidence in the population[25]. Still, the overall effect at a population level on HIV incidence seems to differ between settings and the maturity of the HIV epidemic, meaning to what extent the

epidemic has progressed from infection limited to a sub-group, to most infections occurring in the general, normally low-risk, population. A recent Cochrane review concludes that the published trials do not give clear evidence that improved STI treatment reduces HIV incidence in the population substantially (level of evidence 1)[26].

However, improved STI treatment can substantially improve quality of services provided to the individual, and has a major impact on reducing prevalence of STIs in a population, particularly syphilis infections[13].

Linkages between sexually transmitted infections/HIV and sexual and reproductive health services

Prevention and control of STIs/RTIs include information, counseling and testing, and treatment of symptomatic diseases; thus every contact with the health system should be best used to provide care, be it information and counseling, screening or treatment. Thus STI/RTI prevention and care should very much follow the slogan:

'Counseling at any visits: don't miss the opportunity'.

Addressing STI/HIV in antenatal care is important especially to ensure that syphilis and HIV testing are performed at the first visit (see section on syphilis screening). Linkages between family planning and STI services have been proposed to improve the quality of care and the uptake of services[27,28]. Family planning services should provide information, but also screening and treatment for symptomatic STIs; STI clinics should discuss and provide family planning as part of the consultation or at least refer patients to the respective health provider/clinic if the service cannot be given at the same time.

Also, the consultation for STI/RTI provides an important opportunity for other preventive services, such as screening for cervical cancer using acetic acid (see Chapter 26). Counseling on STI/HIV should also be part of post-abortion care.

Dual protection

Protection against both unwanted pregnancy and STIs is referred to as 'dual protection'[29]. Male or female condoms are the mainstay of dual protection, and can be used alone with the back-up of emergency contraception and/or in combination with a non-barrier contraceptive method, including male or female sterilization. Using condoms as a stand-alone method for dual protection may be compromised because sexually active people are often unwilling to use condoms all the time, for a variety of reasons, which reduces their protective value. Thus, much of the effectiveness of dual protection against unwanted pregnancy will be contingent on another contraceptive method being used.

MANAGEMENT OF ASYMPTOMATIC SEXUALLY TRANSMITTED INFECTIONS/ REPRODUCTIVE TRACT INFECTIONS: SCREENING

Many STIs are asymptomatic. That is why screening programs have a particularly high importance for control of the transmission of STIs. Up to 70% of women and a significant proportion of men with gonococcal and/or chlamydial infections may experience no symptoms at all.

Also, some people do not seek care, even if they experience symptoms because of stigma or lack of access to healthcare. Accurate diagnosis is often a problem in low-resource settings where laboratory tests are limited or not available at all as explained before. Even if the right diagnosis is made, the recommended drugs might not be available, and people might not complete the treatment. Overall, it is said that only a small proportion of people with STIs or RTIs are cured (Figure 8).

Thus, one major problem in treatment of STIs is the fact that only a small proportion of the patients are reached by effective treatment. On the other hand, over-treatment is also a known problem when using syndromic management and patients might get treatment for STIs although their symptoms might be caused by other disorders. Thus, treatment of STIs/RTIs faces both problems, severe under- and but also over-treatment.

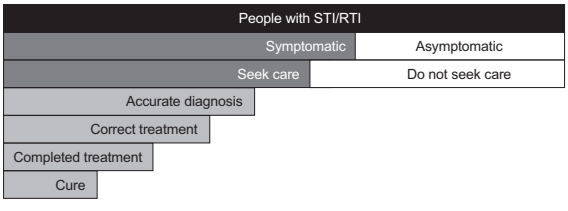

Figure 8 Operational model for STI/RTI control: asymptomatic cases and people who don't seek care. Source: WHO, 2005

Screening would be the best option for infections which are often asymptomatic, such as gonococcal or chlamydial infection; however, no simple, sensitive, specific and affordable test is yet available for these two agents, but research and development are ongoing.

Syphilis screening

Currently affordable and simple screening tests are only available for syphilis. Detection of asymptomatic infection as part of antenatal care is of the utmost importance for prevention and control of syphilis and its consequences – spontaneous abortion and stillbirth. That is why screening and treatment for syphilis at the first antenatal care visit has been recommended as a routine part of antenatal care for many years[20].

The further roll-out and continuous support for prevention of mother-to-child transmission (PMTCT) services provide opportunities to strengthen syphilis screening as the procedures demand very similar knowledge and interventions[19]. Integration of PMTCT and syphilis screening thus provides an important window of opportunity to reduce the burden of STIs.

Screening for other STIs/RTIs, including cervical infections, BV and HIV, should also be offered during antenatal care if testing is available. Unfortunately, affordable and simple tests for cervicitis are not yet available. Asking women during antenatal care about STI symptoms in themselves and their partner and treating symptomatic women using the syndromic approach is what can and should be done is most settings. Also, STI prevention should be promoted during pregnancy as a way of protecting both mother and child, and of safeguarding future fertility.

Periodic presumptive treatment

Mass treatment with antibiotics (azithromycin, ciprofloxacin and metronidazole) in the adult population have been studied in Rakai, Uganda, to prevent new HIV infections. However no difference between the treated population and a comparison group without treatment could be observed. Mass treatment of the entire population is not recommended currently[30].

However, in high-risk groups such as female sex workers, periodic systematic treatment can be used. It is in particular recommended at the initial visit. Whether presumptive treatment should also be given at follow-up visits depends on (1) re-infection rate, (2) feasibility and (3) local resistance patterns. In all cases, counseling and screening and other STI control strategies should be applied.

Partner notification

Partner notification is the set of public health activities that aims at informing the partners of people infected with STI or HIV, and at offering those infected appropriate services and counseling about their risks. The main goal of partner notification is to interrupt the chain of STI transmission as well as preventing re-infection in the patient, but also to prevent secondary infections and complications in the partners. Partner treatment can be considered a 'presumptive treatment' if the partner is asymptomatic.

Partner notification should also include education and counseling of the partners about STI and HIV.

Several ways to encourage partner notification and treatment are used, including the use of notification or referral slips and offering free care. Patient referral is the most common approach as it does not require additional resources. Patients are encouraged to contact their sexual partner themselves. Often they are given a referral slip which has information on diagnosis or a code indicating the diagnosis of the patient who presented with symptoms at the clinic. The other option to ensure partner treatment is that specially trained health staff notify sexual partners and arrange for necessary treatment. This is much more expensive, but also more effective. One can also think of a combination of both methods; or the patient might be given the treatment for their partner.

Note: not all STI/RTI are sexually transmitted. STI care and partner notification should assure that patients are not mislabeled or stigmatized. Given the limitations of the syndromic approach among women, partner notification should be rather encouraged in cases of index male patients with STIs for treating their female partners.

PREVENTION OF SEXUALLY TRANSMITTED INFECTIONS/ REPRODUCTIVE TRACT INFECTIONS

The most effective means to avoid STIs is to abstain from sexual intercourse or to have sexual intercourse

only in long-term, mutually monogamous relationship with an uninfected partner.

Male or female condoms

When used consistently and correctly, these are highly effective in preventing infection.

Female condom

The original version of the female condom, brand names included Reality, Femy and Femidom, was made of polyurethane. A new version, female condom 2, using the cheaper nitrile material, was released and large-scale production of the female condom 2 began in 2007. Results from qualitative studies have shown that women living with HIV in particular can feel more in control when using the female condom compared to the male condom or unprotected sex[31]. The female condom has so far received too little attention at international level[32].

Adult male circumcision

Less effective than abstinence, faithfulness and condom use but promising for the reduction of HIV transmission and probably other STIs is adult male circumcision. Several reviews have indicated that the risk of HIV transmission in men is reduced by 50–60%[33,34] (level of evidence 1). Adult male circumcision does not seem to have an adverse impact on sexual function and can potentially be a highly cost-effective strategy for HIV prevention. There are also some promising results that male circumcision can also prevent other STIs but the evidence is not fully established[35]. Wide-scale implementation of this intervention remains a challenge with a number of operational issues which still need to be addressed. There is no evidence of a direct effect of male circumcision on male to female transmission of HIV or other STIs; that is why circumcision cannot be promoted to reduce infections in women.

Microbicides

Topical microbicides are compounds that can be applied inside the vagina or rectum to protect against STIs including HIV. They can be formulated as gels, creams, films or suppositories. Microbicides may or may not have spermicidal activity (contraceptive effect). At present, an effective microbicide is not yet available on the market. However, results from a recent study using tenofovir (antiretroviral) gel showed an overall reduction of HIV infection by 39% after 30 months among women using the gel. In women who used the drug consistently, infection was reduced by 54%. The study found the gel also reduced the risk of genital herpes by 51%[36].

Prevention of ophthalmia neonatorum

Prevention of ophthalmia neonatorum using eye ointments with erythromycin or tetracycline presents another highly effective prevention strategy. As early as 1881 Credé introduced a prophylaxis with ocular 2% silver nitrate in newborns, later named after him, Credé prophylaxis. Prophylaxis with silver nitrate, 1% erythromycin, 1% tetracycline solution or povidone–iodine has been shown to be effective against the infective agents causing ophthalmia neonatorum, mostly *Chlamydia* and gonococci. Use of prophylaxis has drastically reduced gonococci conjunctivitis in newborns and blindness in Western countries in the 20th century[37]. Currently, prevention of ophthalmia neonatorum with 1% erythromycin or 1% tetracycline solution is part of an essential care package at birth.

The use of eye ointment is effective, cheap and easy to administer. Still, implementation of prevention of ophthalmia neonatorum is limited in many settings despite the wide availability of the 1% erythromycin or 1% tetracycline solution. Reinforcement by clinicians, midwifes and nurses is much needed.

Prevention of septic abortion

Much effort in a health district and district hospital should be put on prevention of unsafe and septic abortion by providing family planning, safe abortion where legal and appropriate post-abortion care. Good clinical practice to empty the uterus after abortion or miscarriage using medical or surgical procedures (manual vacuum aspiration) are important in preventing septic abortion in both spontaneous and induced abortion. More information can be found in the midwifery modules available at the WHO homepage[24] and in Chapter 13 on abortion.

Prevention of iatrogenic or exogenous infection

Finally, prevention of iatrogenic or exogenous infection should include adherence to infection

prevention measures when performing any gynecological procedures as well as proper decontamination and sterilization of equipment. In most countries, national guidelines for infection prevention are available and should be strictly followed.

IMPORTANT LITERATURE AND WEBSITES

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