

Review

Sexually Transmitted Diseases (STDs)—A Synoptic Overview for Urologists

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Abstract

The classical bacteria that cause venereal diseases, e.g. gonorrhea, syphilis, chancroid and inguinal granuloma only account for a small proportion of all known STDs today. Other bacteria and viruses as well as yeasts, protozoa and epizoa must also be regarded as causative organisms of STD. Taken together, all sexually transmitted infections (STI) comprise more than 30 relevant STD pathogens. However, not all pathogens that can be sexually transmitted manifest diseases in the genitals and not all infections of the genitals are exclusively sexually transmitted. Concise information and tables summarising the diagnostic and therapeutic management of STDs in the field of Urology allow a synoptic overview and are in agreement with recent international guidelines of other specialities. Special considerations (i.e. HIV infection, pregnancy, infants, allergy) and recommended regimens may be looked up here.

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1. Definitions and classification

STDs can be categorized as today curable and incurable. The common curable STDs are gonorrhea, chlamydial, mycoplasmal and ureaplasma infections, syphilis, trichomoniasis, chancroid, lymphogranuloma venereum and donovanosis. Even STDs caused by yeast, protozoa and epizoa can be cured. The STDs that are preventable but not curable are the viral STDs and include human immunodeficiency virus (HIV), human papillomavirus (HPV), hepatitis B/C virus (HBV, HCV), cytomegalovirus (CMV) and herpes simplex virus (HSV).

Only those genital infections which are indeed transmitted exclusively sexually will be dealt with below.

Other pathogens that lead to organ manifestations classified under other specialities can merely be mentioned briefly in terms of their sexual transmissibility and co-morbidity. With regard to further details on these pathogens, the reader should refer to guidelines from appropriate specialist societies [11,15,17–22] and internet links [1–9]. Clinical pictures such as urethritis, genital ulcers, prostatitis, and epididymitis that can be caused by various STD pathogens in men will not be treated in this overview.

The following STDs in the field of Urology will be dealt with in a synoptic overview in groups and tables:

- Bacterial STDs
 1. Syphilis
 2. Gonorrhea
 3. Chancroid
 4. Donovanosis/granuloma inguinale
 5. Lymphogranuloma venereum
 6. Chlamydial, mycoplasmal and ureaplasma urethritis

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- Viral STDs
 1. HPV lesions
 2. Genital herpes
 3. Mollusca contagiosa
- STDs caused by protozoa and epizoa
 1. Trichomoniasis
 2. Phthirus pubis crab infestation
 3. Sacroptes scabiei infestation

2. Images of the STDs

Information and images of the STDs are provided by the Dermatology Online Atlas and may be looked up there (http://www.dermis.net/index_d.htm).

3. Bacterial STDs (Table 1)

3.1. Syphilis

Syphilis is one of the oldest and most infectious systemic STDs, particularly in its primary and secondary stages. Unless treated, the infection will progress through a series of stages, during which its symptoms often mimic those of other diseases and make diagnosis difficult. There is a close interrelationship of syphilis and HIV infection, presenting high prevalence rates for both in commercial sex workers, drug addicts, particularly in developing countries.

3.2. Gonorrhoea

An annual incidence of approximately 62 million new cases world-wide of gonorrhoea is estimated, with the greatest number in South and South-East Asia, followed by sub-Saharan Africa. A significant proportion of infected people (up to 80% among women, 10% among men) are asymptomatic. Co-infections with chlamydia and other STDs are very common and must be specifically looked for in diagnostic investigations.

3.3. Chancroid

Poor understanding of the epidemiology and natural history of the disease and the absence of a good lab test make it difficult to undertake prevalence studies and to estimate prevalence and duration of infection. It is estimated that there are approximately 7 million new cases of chancroid annually. The incidence of chancroid varies greatly between countries and regions.

3.4. Donovanosis/granuloma inguinale

Donovanosis is a very rare genital ulcerative STD, primarily found in people who engage in anal sex or oral-anal contact. It is endemic in certain tropical and

developing areas (India, Papua-New Guinea, Central Australia, Southern Africa). Though only moderately contagious it is transmitted most often when the disease is in its early stages.

3.5. Lymphogranuloma venereum

This disease, also known as Durand–Nicolas–Favre disease is relatively rare in developed countries. Lymphogranuloma inguinale is most prevalent in South East Asia, Africa, Central and South America, and the Caribbean. It is characterized by a painful swelling of the lymph nodes, and elephantiasis of the genitals.

3.6. Chlamydial, mycoplasmal and ureaplasma urethritis

Chlamydia trachomatis on one hand, Ureaplasma urealyticum, Mycoplasma hominis and Mycoplasma genitalium probably on the other hand cause non-gonococcal urethritis and account for 30–50% and 10–20% of cases, respectively. 20–30% of men with non-gonococcal urethritis have no organism detected. Asymptomatic infection is common in women, while approximately 70% of men have symptoms like urethral discharge, dysuria, penile irritation and signs of epididymo-orchitis or prostatitis.

3.7. Other bacterial and yeast STDs

Gardnerella vaginalis causes painful bacterial vaginosis. Men may carry the bacterium, but do not seem to be adversely affected by it. Additionally, bacterial vaginosis is not a STD per se, and the change in the balance of bacterial organisms that exist in the vagina is not clearly understood. Other diseases most frequently associated with vaginal discharge are trichomoniasis and candidiasis. Vulvovaginal candidiasis is not usually acquired through sexual intercourse. Treatment of male sex partners is only recommended in rare cases of balanitis or in women who have recurrent infection.

4. Viral STDs (Table 2)

Here sexually transmitted viral infections that typically cause genital tract lesions such as HPV, HSV and MCV infections are focussed on. Other viral STDs, i.e. Acquired Immunodeficiency Syndrome (AIDS), hepatitis, cytomegalic inclusion body disease, Epstein–Barr virus-associated kissing disease may be looked up in the guidelines of other specialities.

4.1. HPV-associated lesions

Condylomata acuminata caused by HPV infection is the most common viral STD world-wide. More than 30

Table 1

Bacterial STDs [1–9,11,18–22]

| STDs | Causes | Symptoms | Diagnosis | Treatment |
|------------|--|---|---|---|
| Syphilis | Treponema pallidum (spirochete bacterium), 90% transmission by sexual contact, transmission by non-sexual contact is rare. Syphilis is classified as acquired or congenital. The incubation period ranges between 10 and 90 days. | <i>Primary stage (lues I):</i> Chancre (not painful) at the location where the bacterium entered the body, usually with regional lymphadenopathy. <i>Secondary stage (lues II):</i> 2–12 weeks later the Treponemas spread throughout the body, causing a rash, small open sores, flu-like fever, swelling of lymph nodes, condylomata lata. <i>Latent and tertiary stages (lues III):</i> Symptoms and infectiousness disappear; one third of untreated persons will progress to the tertiary stage where the bacteria attacking the patients heart, eyes, brain, nervous system, bones and joints. Gummatous syphilis. <i>Final Stage (lues IV):</i> Heart diseases, blindness, insanity, paralysis and death | Microscopic and fluorescence examination of the tissue taken from a chancre or sore may identify the spirochete. <i>Serologic blood tests:</i> Screening by combination of the Venereal Disease Research Laboratories Test (VDRL) or Rapid Plasma Reagin (RPR) and Treponema Pallidum Hemagglutination Test (TPHA); <i>Confirmation</i> by IgG Fluorescence Treponema Antibody Absorption Test (IgG-FTA-Abs) or 19-S-IgM-FTA-Abs. <i>Follow-up testing</i> by VDRL-test or 19-S-IgM-FTA-Abs-test 3, 6, 12 months and annually for another 4 years after treatment. Some HIV infected patients can have atypical serologic test results. | <i>Primary/secondary stages:</i> Benzathine penicillin 1 × 2,4 Mio IU i.m.; or Clemizolpenicillin G 1 Mio IU i.m. for 14 days. No comparative trials have been adequately conducted to guide the selection of the optimal penicillin regimen (i.e. the dose, duration and preparation). <i>Persons allergic to penicillin:</i> doxycycline 2 × 100 mg p.o. for 14 days. Erythromycin 4 × 500 mg for 14 days. <i>Late or unknown stages:</i> Benzathine penicillin, 2.4 Mio IU i.m. on day 1, 8, 15, or Clemizolpenicillin G 1 Mio IU i.m. for 21 days. <i>Persons allergic to penicillin:</i> Doxycycline 2 × 100 mg p.o. for 28 days. Erythromycin 4 × 500 mg p.o. for 28 days. <i>Management of sex partners:</i> Persons who were exposed within the 90 day preceding the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated pre-emptively. |
| Gonorrhoea | Caused by a bacterium (Neisseria gonorrhoeae), which enters the body by mucous membranes of the urethra, cervix, rectum, mouth, throat and eyes. Gonorrhoea is nearly always transmitted by direct sexual contact. Transluminal spread of infection may occur to involve the epididymis and prostate. Haematogenous dissemination is uncommon. | <i>Initial symptoms within two weeks:</i> fever, chills, painful swelling of the genitals and prostate in men. Men report burning during urination, urethral pus and painful bowel movements in rectal infections. In women, infections of the uterus and fallopian tubes are common, resulting in sterility, ectopic pregnancy, and pelvic inflammatory disease. Newborns' eyes might be affected. After the bacteria enter the bloodstream, the disease can affect the joints, heart and brain. Asymptomatic infection of the urethra is rare (<10%). | Microscopic examination of Gram-/methylene blue-stained and specially cultured pus samples will readily confirm the clinical diagnosis by visualization of diplococci in leucocytes. Amplified antigen detection tests or nucleic acid amplification tests offer high sensitivity and provide confirmation of the diagnosis in asymptomatic patients. <i>Follow-up:</i> Patients who have uncomplicated gonorrhoea and who are treated with any of the recommended regimens do not need follow-up testing. Patients who have symptoms that persist after treatment should be evaluated by culture for antimicrobial susceptibility. | World-wide, different strains of gonorrhoea have become resistant to penicillin. Due to the resistances found in different countries and co-infections with other STDs antibiotics such as Ceftriaxone (1 × 0.125 g i.m.), Spectinomycin (1 × 2 g i.m.) or combinations with Tetracycline or Erythromycin should be preferred. Infection acquired in Northern Europe may be treated with Ciprofloxacin (1 × 500 mg p.o.), Ofloxacin (1 × 400 mg p.o.) or Levofloxacin 1 × 250 mg Cefixime (1 × 400 mg p.o.). If chlamydial infection is not ruled out or for population in which chlamydial infection accompanies 10–30% of gonococcal infection dual therapy (Azithromycin 1 g p.o. single dose or Doxycycline 2 × 100 mg for 7 days) is recommended. <i>Management of sex partners:</i> All sex partners of patients who have <i>N. gonorrhoeae</i> infection should be evaluated and treated for <i>N. gonorrhoeae</i> and <i>C. trachomatis</i> infections if their last sexual contact was within 60 days before symptoms or diagnosis of infection in the patient. Patients should be instructed to avoid sexual intercourse until therapy completed. |

Table 1 (Continued)

| STDs | Causes | Symptoms | Diagnosis | Treatment |
|--|--|--|---|--|
| Chancroid | Bacterial disease caused by <i>Haemophilus ducreyi</i> , which is transmitted by direct sexual contact. Uncircumcised men are more likely to contract the disease than circumcised men. | 3–14 days after contact, a tender bump develops where the bacteria entered the body. The bump transforms into one or more shallow sores, which will break open and become the typical painful soft chancre. The lymph nodes in the groin are pus-filled (bubos), and often burst through the skin. | Usually diagnosed by microscopic examination of a smear sample (Gram-stained). This should be confirmed by a culture. The presence of other STDs has to be ruled out. PCR testing is possible. Test for HSV performed on the ulcer exudates usually is negative. | Chancroid has become resistant to penicillin, Tetracycline and Erythromycin in some cases. Preferred treatments now involve Azithromycin (1 × 1 g p.o.), Ceftriaxone (1 × 0.25 g i.m.) or Ciprofloxacin (2 × 500 mg p.o. for 3 days) or Erythromycin 3 × 500 mg for 7 days. Bubos may need to be drained. |
| Donovanosis/ Granuloma inguinale | A chronic, mildly contagious STD caused by an intracellular bacterium (<i>Calymmatobacterium granulomatis</i>) | Red, vulnerable, easily bleeding sores on and around the genitals and anus are typically noticed one week to several months after initial exposure to the bacteria. In men the lesions appear first on the head or shaft of the penis. The sores are not very painful, but can spread throughout the groin and cause abscesses. In extreme cases, their dissemination can give rise to cancer. Lymphadenopathy is unusual. | Generally diagnosed by visual observation of the external symptoms. Gram-stained samples will show the bacteria, which can be cultured under special conditions only. Donovan bodies are found in macrophages on tissue crush preparation or biopsy. Co-infections with other STDs are known. | Azithromycin (1 × 1 g per week, for 3 weeks) or Erythromycin (4 × 500 mg p.o. for 3 weeks) or Doxycycline (2 × 100 mg for 3 weeks) or Trimetho-prim-Sulfamethoxazole (2 × 1 (800/160 mg) die for 3 weeks) or Ciprofloxacin 2 × 750 mg for 3 weeks or until all lesions have completely healed. Sometimes wound resection is necessary. Scars left by the sores are regarded as precancerous. Therefore, annual examinations are recommended. |
| Lymphogranuloma venereum | Caused by <i>Chlamydia trachomatis</i> (serotypes L1–L3), which is spread by direct sexual contact, particularly in homosexuals who engage in anal sex. Proctocolitis and perianal or perirectal fistulas and strictures may result. | First symptoms may be a sore resembling a pimple, blister or soft bump at the point of infection 3–30 days after exposure. 1–2 weeks later, the lymph nodes swell, creating a painful, pus-filled bulge. The disease progresses slowly causing fever, throbbing pain and breaking of the skin, leaving masses of scar tissue. | The chlamydia have to be cultured in special cell cultures (Mc Coy cells) and can be diagnosed by fluorescence antibody tests. Complement fixation titers $\geq 1:64$ are consistent with the diagnosis of Lymphogramuloma venereum. | Doxycycline (2 × 100 mg for 3 weeks) and Erythromycin (4 × 500 mg for 3 weeks) (And Sulfamethoxazole can be used as well.) Buboes may require drainage. |
| Chlamydial, mycoplasmal and ureaplasma urethritis | Non-gonococcal urethritis is caused by <i>Chlamydia trachomatis</i> (serotypes D–K) in 30–50% and <i>Ureaplasma urealyticum</i> and <i>Mycoplasma hominis/genitalium</i> in 10–20%, respectively. All patients who have urethritis should be evaluated for the presence of gonococcal and non-gonococcal infection. Some cases of persistent or recurrent urethritis are due to <i>Trichomonas vaginalis</i> . | 7–21 days after contact signs and symptoms are mainly due to urethritis and complications like anorectal discomfort, reactive arthritis and conjunctivitis (Reiter's syndrome), prostatitis and epididymoorchitis. | The diagnosis of urethritis should be confirmed by demonstrating polymorphonuclear leucocytes in Gram-stained urethral smears or first pass urine specimens. Diagnostic tests include cell cultures (sensitivity range 40–85%), direct antibody assays (sensitivity range 50–90%), Enzyme-immunoassays (sensitivity range 20–85%) and PCR/LCR techniques (sensitivity range 70–95%). First pass urine specimens can be used for PCR/LCR, and urethral swabs will be needed for the other tests. Cooled (4–8 °C) special transport vehicles and cell cultures are mandatory. | Single dose Azithromycin (1 g) or Doxycycline (2 × 100 mg for 7 days); Erythromycin (4 × 500 mg for 7 days); Ofloxacin (2 × 200 mg for 7 days); Levofloxacin 2 × 500 mg for 7 days; Roxithromycin (2 × 150 mg for 7 days); Clarithromycin (2 × 250 mg for 7 days). Abstinence from sexual intercourse for 7 days is recommended. Sex partners (within 60 days) should be evaluated, tested and treated. |

Table 2

Viral STDs [10,12,15–17,22]

| STDs | Causes | Symptoms | Diagnosis | Treatment |
|---------------------|---|--|---|---|
| Genital warts | HPV low-risk genotypes (i.e. HPV 6 or HPV 11) transmitted by intimate sexual contact. Warts develop within 3 weeks to 8 months. Immunodeficiency leads to rapid and extensive growth of HPV lesions, and is associated with higher rates of cancer. | Typically growing without symptoms untreated genital warts can spread and multiply into large clusters. Giant warts (Buschke Löwenstein tumours) are rare. Genital warts may cause a variety of health complications depending on where they are located. Symptoms may range from discomfort and pain, to bleeding and difficulty in urination. | External warts are usually diagnosed visually. Application of acetic acid solution (5%) causes the warts and subclinical flat HPV lesions to whiten, making identification much easier. A magnifying instrument should be used to diagnose subclinical lesions. For demarcation of urethral HPV lesions, fluorescence urethroscopy had been used by analogy with the acetic acid test of the outer genitals [13,14]. Both the acetic acid test and fluorescence urethroscopy are limited in specificity. A tissue biopsy or Pap smear may be taken to determine whether the HPV lesions are cancerous. Routine HPV type analyses have not been recommended up to now. Generally, both sexual partners should be tested for warts. | An update of the guidelines in dermatology, venereology, gynecology and urology [17–19] unanimously recommends treatment options for medically prescribed self-treatment and for exclusively physician-managed treatment. Topically applied drugs such as Podophyllotoxin (0.5% solution or gel) or Imiquimod 5% cream are suitable for therapy at home. Medically applied treatment involves trichloroacetic acid (TCA), cryotherapy, electro-surgery, laser treatment and surgical excisions of the HPV lesions. Irrespective of the therapy used, HPV may persist in the adjacent tissues, resulting in recurrences and the need for further courses of treatment. The development of HPV vaccines may offer new perspectives in therapy. |
| Genital herpes | Herpes simplex viruses (HSV 1 (30%) and HSV 2 (70%)) can cause genital lesions 2–20 days after infection. Most cases of recurrent genital herpes are caused by HSV-2. Herpes virus invades the body via breaks in the skin or moist membranes of the penis, vagina, urethra, anus, vulva or cervix. All practices of intercourse may transmit HSV. HSV may be passed on to the baby during birth as well. | Symptoms can vary. Initially flu-like symptoms, swelling of lymph nodes, chills, fever may be noticed. Fluid-filled blisters are then followed by eruption and ulceration of the skin; both are painful. Clusters on the genitals, buttocks and adjacent areas are typical. Other symptoms may include tenderness, aching pain, itching, burning or tingling. Painful urination and a sensation of abdominal pressure are known. | Sometimes the diagnosis can be made by physical examination alone. Cell culturing (HSV is a labile virus and successful virus culture depends on maintaining the cool (4 °C), rapidly transporting specimens to the laboratory and avoiding freeze-thaw cycles) and type analysis by immunofluorescence tests are standard options for diagnosis. Fluorescence tests can be done without viral amplification in the cell culture, but sensitivity is only fair. PCR and LCR amplification of HSV show much better sensitivity, but the techniques are too expensive for routine use. | Herpes is incurable. Systemic antiviral drugs (Acyclovir 3 × 400 mg or 5 × 200 mg per os, Famciclovir 3 × 250 mg per os, Valacyclovir 2 × 1 g per os) may be used to reduce the discomfort from the sores. Healing might be increased, and pain as well as viral shedding can be reduced. Treatment of first clinical episode (for 7–10 days) or recurrent episodes of genital herpes (for 3–5 days) requires initiation of therapy within the first day of lesion onset. Patients who have frequent recurrences (i.e., ≥6 recurrences per year) may be treated by suppressive therapy: i.e. Valacyclovir (1 × 500 mg p.o./die for 16 weeks) Acyclovir 2 × 400 mg or Famciclovir 2 × 250 mg, for 16 weeks. Suppressive therapy reduces the frequency of genital herpes recurrences by 70–80%. Do not use topical creme. The sex partners of patient who have genital herpes likely benefit from evaluation and counselling. Blisters will regress spontaneously under the control of the immune system. If not, surgical removal by laser, cryotherapy, electro-surgery or chemical treatment is recommended. |
| Mollusca contagiosa | Caused by molluscum contagiosum virus. 2–3 months after infection, a waxy and rounded blister with a dimple on the top develops. Scratching, picking or breaking spreads the virus. | Typical blisters can be flesh-colored, white, pink, yellow or clear. Itching is common, but pain is rare. Clusters of lesions may develop. | The blisters are distinctive, providing typical criteria for visual diagnosis. The diagnosis can be confirmed by light microscopy or electron microscopy of biopsies taken from a blister. | Blisters will regress spontaneously under the control of the immune system. If not, surgical removal by laser, cryotherapy, electro-surgery or chemical treatment is recommended. |

million people will develop genital warts every year. HPV belongs to the same group of viruses that produce common skin warts. However, HPV can also be closely associated with intraepithelial neoplasia and cancer in both genders. Most HPV infections are subclinical or latent—that means that they are not directly visible or that they can only be diagnosed by laboratory testing. Visible signs of the disease include condylomata, Bowen's disease, bowenoid papulosis, Buschke Löwenstein tumors and genital cancer. Though men and women are equally susceptible to infection, women suffer a much higher risk of developing the HPV-associated malignancy.

4.2. Genital herpes

Genital herpes is a chronic, lifelong viral infection, and afflicts up to 80% of adults. There are five different types of herpes viruses. Although they are all spread by direct skin-to-skin contact, only herpes simplex 1 (HSV1) and herpes simplex 2 (HSV2) are considered to be STDs. HSV1 has been found historically on the mouth, and can increasingly be isolated in genital infections. This probably reflects changes in sexual practices. Herpes is incurable today. The associated symptoms may never be manifested or they may come and go periodically throughout a person's lifetime. There are even more people who have no symptoms.

4.3. Mollusca contagiosa

Mollusca contagiosa are self-limiting viral infections of the skin which are spread by sexual contact as well as manual and casual contact. Children are often infected. High prevalence (13%) of mollusca is noticed in HIV-positive adults, probably justifying mollusca to be classified under the STDs. Individual blisters may disappear on their own after several months.

5. STDs caused by protozoa and epizoa

5.1. Trichomoniasis

Trichomoniasis is caused by the parasitic protozoon, *Trichomonas vaginalis*, and is often diagnosed in patients that are infected with other STDs. *Trichomonas* can be transmitted by direct sexual contact or by infected body fluids. Symptoms in men are uncommon, and typically include discharge from the urethra and painful or difficult urination. The protozoon can be found by dark-field microscopy of specimens from the vagina, urethral secretions or in the sediment of urine. Culturing these samples before the microscopic

examination will improve the sensitivity. Generally, treatment should involve both sexual partners. A single dose of Metronidazole (2 g p.o.) should be effective. An alternative regimen is Metronidazole 2 × 500 mg for 7 days [11,22].

5.2. *Phthirus pubis* crab infestation

Phthirus pubis is a tiny insect that infects the pubic hair of its victims and feeds on human blood. They use crab-like claws to grasp the hair of its host and can crawl several centimeters per day. Female lice lay 2–3 eggs daily and affix them to the hairs (nits). During direct sexual contact, the insects can move from one partner to the other. Itching in the pubic area is a telltale sign. Microscopic examination of the lice or the nits can confirm this. Treatment involves application of 1% gamma benzene hexachloride ointment or lotion. The scalp is treated with lindane shampoo. Patients with pediculosis pubis should be evaluated for other STDs.

5.3. *Sarcoptes scabiei* infestation

Sarcoptes scabiei is a whitish-brown, eight-legged mite that burrows into its host to lay its eggs. This burrowing causes a skin irritation or rash. The mites, their feces and eggs cause a progressive sensitivity in the host after about two weeks, producing the characteristic itch. Finding a mite or identifying its bumps and burrows will corroborate any observed diagnosis. There are a variety of topical medications that will clear scabies infestations. These include lindane, petroleum jelly and 5% sulfur mixture.

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