

Sexually transmitted diseases (STDs) – Updating a concise overview for urologists

Peter Schneede¹

¹Department of Urology, Klinikum Memmingen, Memmingen, Germany

Abstract

Worldwide more than 1 million sexually transmitted infections (STIs) are acquired every day.

Given the growing rate of antimicrobial resistance of STIs and otherwise the effective improvements in STD laboratory testing, in STI treatment, and in STI prevention in the last decades urologists need to be periodically updated in this field.

This article straightforwardly continues an Urinary Tract Infection (UTI) Working Group (EAU) STD review, 2003, which has been updated in 2010, and which now has been fully-revised based on the recent national and international STI-guidelines. The 2016 version contents again the successful concept of a concise overview of STIs /STDs being of special interest for urologists, actualizes the recommendations for STI treatment, adds important data on recent antimicrobial resistances, and finally considers new aspects of preventive STI vaccines.

The classical bacteria that cause venereal diseases (e.g. gonorrhea, syphilis, chancroid, and Granuloma inguinale) 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 (i.e. viral hepatitis) and not all infections of the genitals are exclusively sexually transmitted. Some STIs can also be spread through non-sexual means such as via blood or blood products (i.e. HIV). Concise information and tables summarising the diagnostic and therapeutic management of STDs allow a synoptic overview assisting the urologist's clinical work. For more detailed information or questions concerning special considerations (i.e. HIV infection, pregnancy, infants, and allergy) the original guidelines and scientific literature must be looked up directly. Consequently this overview does not address the lists of relevant references, the levels of evidence, or the grades of recommendation. These are included in other chapters of this book or can be found in the recent international guidelines.

Definitions and classification

STDs can be categorized as today curable and incurable. The common curable STDs are gonorrhea, chlamydial and mycoplasmal 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 predominantly viral STDs and include human immunodeficiency virus (HIV), human papillomavirus (HPV), hepatitis B/C virus (HBV, HCV), cytomegalovirus (CMV) and herpes simplex virus (HSV). Symptoms or disease due to the incurable viral infections can be reduced or modified through treatment.

Only those genital infections which are indeed transmitted exclusively sexually will be dealt with below. Other pathogens that lead to nongenital 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 and internet links [1], [2], [3], [4], [5], [6], [7], [8]. Clinical pictures, such as urethritis, vaginal discharge, genital ulcers, prostatitis, and epididymitis which can be caused by various STD pathogens in men will not systematically be treated in this overview.

In general, all urologists should be able to recognize the typical STDs; they should be informed about the recent recommendations on STI management, and of course urologists should know about the communities which are at increased risk for STIs. On the other hand it's necessary for every single urologist to be aware which STDs he can safely handle and what patients are better to be referred to a STD specialist or a STD clinic. STIs have a profound impact on sexual and reproductive health, and STIs can have serious consequences beyond the immediate impact of the infection itself. Especially in case of STI co-infection with HIV or syphilis the clinical presentation of STDs might be different to their typical course and additionally the interpretation of results from laboratory testing might be much more difficult. These patients definitely need professional counseling.

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. Chlamydial and mycoplasmal infection of the urethra
6. Lymphogranuloma venereum

Viral STDs

1. Human papillomavirus-associated genital warts and cancer
2. Mollusca contagiosa
3. Genital herpes

STDs caused by protozoa and epizoa

1. Trichomoniasis
2. Phthirus pubis crab infestation
3. Sacroptes scabiei infestation

Clinical presentation of the STDs

Information and images of the STDs are provided by the Dermatology Online Atlas (www.atlasdermatologico.com.br) or the CDC (www.cdc.gov/std/training/clinicalslides) and may be looked up here.

Bacterial STDs (Table 1)

Syphilis

Syphilis is one of the oldest and most infectious systemic STDs, particularly in its primary and secondary stages. Sexual transmission of *Treponema pallidum* is thought to occur only when mucocutaneous syphilitic lesions are present, typically in the first year of infection. 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. The disease has been divided into stages which are characterized by clinical findings: primary syphilis (i.e., ulcer or chancre at infection site), secondary syphilis (i.e., skin rash, mucocutaneous lesions, Condylomata lata, Lymphadenopathy), tertiary syphilis (i.e., gummatous lesions, cardiovascular lesions, tabes dorsalis, general paresis). Additionally, clinicians also discriminate the early syphilis (<1 year) and the late syphilis (>1 year) due to time of infection. The syphilis infection can be latent that means clinical manifestations are lacking (no risk of sexual transmission) but seroreactivity is positive. In any stage of syphilis a neurosyphilis can result by infection of the central nervous system showing up with early or late neurologic clinical manifestations. 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. All patients who have syphilis should be tested for HIV infection (and other STIs) and retested for HIV after 3 months if the first HIV test result was negative. In many developed countries MSM are at increased risk for syphilis infection and predominantly caused a renaissance of the lues in the last decade.

Gonorrhea (GO)

An annual incidence of approximately 78 million new cases of gonorrhea is estimated world-wide (WHO), 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. The prevalence of gonorrhea infection varies widely among communities and patient populations. Today in the industrial states a large proportion of the GO infected patients are found under men who have sex with men (MSM). And we have to face a tremendous increase of antimicrobial resistances of *Neisseria* species in the last decades which may lead to an approaching era of untreatable gonorrhoea. Prior to therapy *Neisseria gonorrhoeae* cultures should be established. They are required to monitor developing resistance to current treatment regimes. Cultures before start of dual treatment (Ceftriaxone plus Azithromycin) as well as a test of cure after treatment are recommended by some guidelines. Principally, both partners should be treated to reduce the risk for re-infection and transmission of GO.

Chancroid

Poor understanding of the epidemiology and natural history of the disease, the absence of a FDA-cleared PCR test, and the problematic of culturing *Haemophilus ducreyi* 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. The painful genital ulcer has been associated with an increased risk for HIV acquisition and transmission.

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, the Caribbean, central Australia, and southern Africa). Though only moderately contagious it is transmitted most often when the disease is in its early stages. Donovanosis lesions progress and heal slowly. Prolonged therapy until complete healing of all lesions is mandatory to avoid relapse.

Chlamydial and mycoplasmal infection of the urethra

Chlamydia trachomatis on one hand, Mycoplasma genitalium on the other hand typically cause non-gonococcal urethritis and account for 30–50% and 10–20% of cases, respectively. Rarely Ureaplasma urealyticum may be responsible for non-gonococcal, non-chlamydial and non-mycoplasma urethritis [8]. 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. Women may suffer from C. trachomatis associated PID, ectopic pregnancy, and infertility. Mycoplasma genitalium can cause PID, but this occurs less frequently than it does with Chlamydia trachomatis. All patients with non-gonococcal urethritis should be tested for HIV and syphilis.

Lymphogranuloma venereum

This disease, also known as Durand-Nicolas-Favre disease is relatively rare in developed countries, mostly found in men having sex with men (MSM). Lymphogranuloma venereum 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. The infection is invasive, systemic, and might lead to chronic fistulas and strictures when proctocolitis is found. Secondary bacterial infection or co-infection with other STIs may be diagnosed. MSM presenting with proctocolitis should be tested for Chlamydia trachomatis, GO, syphilis and HIV.

Other bacterial and yeast STDs

Gardnerella vaginalis and other anaerobic bacteria cause painful bacterial vaginosis. Men may carry these bacteria, but do not seem to be adversely affected by them. 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. Similar to other diseases (trichomoniasis and candidiasis) the replacement of normal vaginal flora (bacterial vaginosis) most frequently is associated with vaginal discharge.

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.

Table 1: Bacterial STDs [1], [2], [3], [4], [5], [6], [7], [8]

STDs	Causes	Symptoms	Diagnosis	Treatment
				IM=Intramuscularly IV=Intravenously PO=by mouth
				The dosage and the

<p>Syphilis</p>	<p>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.</p>	<p>Primary stage (lues I): Ulcer or Chancre (hard and not painful with raised edges) at any location where the bacterium entered the body, usually with regional lymphadenopathy.</p> <p>Secondary stage (lues II): 2–12 weeks later the Treponemas spread throughout the body, causing a rash, small open sores, flu-like fever, generalized swelling of lymph nodes and systemic organ manifestation showing treponemal dissemination, Condylomata lata</p> <p>Tertiary stages (lues III): 3 to 10 years after infection granulomas and gummas appear; one third of untreated persons will progress to the tertiary stage where the bacteria attacking the patient’s heart, eyes, brain, nervous system, bones and joints. Gummatous</p>	<p>Darkfield microscopic and direct fluorescent antibody (DFA) tests of the tissue taken from a chancre or sore may identify the spirochete for diagnosing early syphilis. NAAT (PCR) of any specimen taken from lesions in primary stage of syphilis is highly specific for Treponema DNA detection, but is not FDA-cleared. Serologic blood tests: Screening always by combination of either a nontreponemal test (i.e., VDRL or RPR) with the confirmation treponemal test (i.e., FTA-ABS or TPPA or EIAs) or by combination of two different treponemal tests (e.g. TPPA/TPHA and the confirmation by FTA-ABS/ IgM-ELISA); Follow-up testing by VDRL-test or 19-S-IgM-FTA-ABS-test after 3, 6, and 12 months, for some indications every year for 3 years. More frequent or longer evaluation</p>	<p>length of treatment depend on the stage and clinical manifestations of the disease. Even the correct selection of the appropriate penicillin preparation is very important! Penicillin G, administered parenterally, is the preferred drug for treatment of all stages of syphilis. Primary/secondary stages: Benzathine penicillin G (1x 2,4 Mio IU IM, 1,2 Mio units left and right gluteal muscle each) Persons allergic to penicillin: Ceftriaxone 2 g IV for 10 days Doxycycline 2 x 100 mg PO for 14 days Late or unknown stages: Benzathine penicillin G 2,4 Mio IU IM (1,2 Mio units on each side of gluteal muscle) on day 1, 8, 15. Persons allergic to penicillin: Ceftriaxone 2 g IV for 14 days Doxycycline 2 x 100 mg PO for 28 days Erythromycin 4x 500 mg PO for 28 days The Jarisch-Herxheimer reaction usually occurring within the first day after treatment for</p>
------------------------	--	---	---	---

		<p>syphilis Final Stage (lues IV): Heart diseases, blindness, insanity, paralysis and death</p>	<p>might be necessary in some patients. Some HIV infected patients can have atypical serologic test results, and generally they need longer and more intensive treatment.</p>	<p>syphilis can be prevented with prednisolone 1 mg/kg PO/IM one hour before first application of antibiotics. Management of sex partners: 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 presumptively.</p>
<p>Gonorrhoea</p>	<p>Caused by a bacterium (<i>Neisseria gonorrhoeae</i>), 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. All patients tested</p>	<p>Initial symptoms within two weeks: 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 (PID). Newborns' eyes might be affected. After the bacteria</p>	<p>Microscopic examination of Gram-/ methylene blue- stained and especially cultured pus samples will readily confirm the clinical diagnosis by visualization of diplococci in leucocytes. Nucleic acid amplification tests (NAAT) and culture are necessary for the detection of gonococcal infection. Culture requires endocervical (women), urethral (men) or rectal and oropharyngeal (both genders) swab specimens to detect <i>Neisseria gonorrhoeae</i>. NAAT for first-catch urine is FDA-cleared. Sensitivity of NAATs for the detection of GO in urogenital and nongenital anatomic</p>	<p>World-wide, different strains of gonorrhoea have become resistant to penicillin and quinolones. Later treatment failures with Cefixime or other oral cephalosporin followed by Ceftriaxone treatment failures and resistance to tetracycline single therapy have been reported. Today consequently, dual treatment with Ceftriaxone and Azithromycin is recommended for GO treatment worldwide. Due to decreased susceptibility to Ceftriaxone and to Azithromycin the German guidelines recommend Ceftriaxone 1x1g IM/IV plus Azithromycin 1x1,5 g PO for dual treatment of GO</p>

	<p>positive for gonorrhoea should be tested for other STDs, including Chlamydia, syphilis, and HIV.</p>	<p>enter the bloodstream, the disease can affect the joints, heart and brain. Asymptomatic infection of the urethra is rare in males (10%), but typical among women (80%).</p>	<p>sites are superior to culture, but only culture provides antimicrobial susceptibility results. Special non-nutritive swab transport systems and a CO₂-atmosphere are needed to maintain gonococcal viability. GO cultures before treatment and thereafter as a test-of-cure are recommended by some guidelines given the growing rate of antimicrobial resistance of GO.</p>	<p>covering the frequent co-infection with Chlamydia trachomatis [9]. Recommendations for the need of a test-of-cure with NAAT or GO culture are inconsistent in different national guidelines [9]. Recent sex partners should be referred for evaluation, testing and presumptive dual treatment. Sex partners should abstain from unprotected sexual intercourse until therapy completed.</p>
<p>Chancroid</p>	<p>Bacterial disease caused by Haemophilus ducreyi, which is transmitted by direct sexual contact. Uncircumcised men are more likely to contract the disease than circumcised men. Confections with Treponema pallidum or HSV occur in 10% of persons who have chancroid.</p>	<p>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 (buboes), and often burst through the skin, scarring can result.</p>	<p>Usually diagnosed by clinical presentation (combination of painful genital ulcer and tender suppurative inguinal adenopathy) and 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 may be helpful but is not FDA-cleared. Test for HSV performed on the ulcer exudates usually is negative. Always test for HIV infection.</p>	<p>Chancroid has become resistant to Penicillin, Tetracycline and Erythromycin and Ciprofloxacin in some cases. Preferred treatments now involve Azithromycin (1x 1 g PO), Ceftriaxone (1x 0.25 g IM) or Ciprofloxacin (2x 500 mg PO for 3 days) or Erythromycin 3x500mg PO for 7 days. Bubos may need to be drained. Patients need re-examination 1 week after treatment. All sex partners have to be treated.</p>

<p>Donovanosis/ Granuloma inguinale</p>	<p>A chronic, mildly contagious STD caused by an intracellular gram-negative bacterium, <i>Klebsiella</i> (formerly <i>Calymmatobacterium</i>) granulomatis. Donovanosis lesions coexist with secondary bacterial infection other STIs.</p>	<p>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 typically are painless and progress slowly, but can spread throughout the groin and cause abscesses. In extreme cases, their dissemination can give rise to cancer. Lymphadenopathy is unusual.</p>	<p>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 (vacuolated inclusions within leucocytes) are found in macrophages on tissue crush preparation or biopsy. Confections with other STDs are known.</p>	<p>Azithromycin (1x 1 g PO per week, for at least 3 weeks) or Erythromycin (4x 500 mg PO for at least 3 weeks) or Doxycycline (2x 100 mg PO for at least 3 weeks) or Trimethoprim-Sulfamethoxazole (2x1 (800/160 mg) daily PO for at least 3 weeks) or Ciprofloxacin 2x 750mg PO 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.</p>
--	---	---	--	---

<p>Chlamydial and mycoplasmal infection of the urethra</p>	<p>Non-gonococcal urethritis (NGU) is caused by <i>Chlamydia trachomatis</i> (serotypes D-K) in 15–40% and <i>Mycoplasma genitalium</i> in 15–25%, 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>Ureaplasma urealyticum</i>, <i>Trichomonas vaginalis</i>, HSV, EBV and adenovirus. Enteric bacteria have been identified as an uncommon cause of NGU and might be associated with insertive anal sex.</p>	<p>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 epididymo-orchitis. Important sequelae can result from <i>Chlamydia trachomatis</i> infection in women (e.g. PID, infertility, and ectopic pregnancy). Asymptomatic infection is common among women. National screening programs for GO and NGU detections differ greatly, and should include certain men at risk (e.g., MSM) [9].</p>	<p>The diagnosis of urethritis can be clinically confirmed by demonstrating polymorphonuclear leucocytes in Gram-stained urethral smears or first pass urine specimens. Methylene blue or gentian violet stain microscopy of urethral secretions can be used alternatively. NAATs are the most sensitive tests for first-catch urine (men) or collecting swab specimens (women) searching for urogenital chlamydial infection. Rectal and oropharyngeal chlamydial infection require swab specimens for detection. NAAT testing of urine and swab specimens exist for mycoplasmal infections, but are not FDA approved.</p>	<p>Single dose Azithromycin 1,5 g PO or Doxycycline (2x 100 mg PO for 7 days) for chlamydial urethritis; <i>Mycoplasma genitalium</i> is already resistant to Azithromycin in approximately 50%, and Doxycycline is largely ineffective. Moxifloxacin (400 mg PO for 7–14 days) is recommended for mycoplasmal urethritis. Erythromycin (4x 500 mg PO for 7 days); Ofloxacin (2x 300 mg PO for 7 days); Levofloxacin 1x500 mg PO for 7 days. Abstinence from sexual intercourse for 7 days is recommended. Sex partners (within 60 days) should be evaluated, tested and treated. Test-of-cure (NAAT) no earlier than 6 weeks after chlamydial therapy!</p>
---	---	---	---	---

<p>Lympho- granuloma venereum (LGV) or Lympho- granuloma inguinale</p>	<p>Caused by Chlamydia trachomatis (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.</p>	<p>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 mostly unilateral, creating a painful, pus-filled bulge. The disease progresses slowly causing fever, throbbing pain and breaking of the skin, leaving masses of scar tissue. Proctocolitis and genital elephantiasis may result from chronic infection.</p>	<p>The Chlamydia have to be cultured in special cell cultures (Mc Coy cells) and can be diagnosed by direct Immunofluorescence or NAAT (not FDA-cleared) differentiating LGV and non-LGV chlamydial infections. Complement fixation titres $\geq 1:64$ are consistent with the diagnosis of Lymphogranuloma venereum in Chlamydia serology.</p>	<p>Doxycycline (2x 100 mg PO for 3 weeks) Second choice: Erythromycin (4x 500 mg PO for 3 weeks) or Azithromycin (1x 1,5g PO per week for 3 weeks) which may be ineffective in the treatment of rectal chlamydial infections! Buboes may require drainage. Sex partners should be presumptively treated with a Chlamydia regime.</p>
---	--	---	--	--

Viral STDs (Table 2) [1], [2], [3], [4], [5], [6], [7], [8]

Here sexually transmitted viral infections that typically cause genital tract lesions such as HPV, MCV and HSV infections are focussed on. Other viral STDs, i.e. Acquired Immunodeficiency Syndrome (AIDS), hepatitis, cytomegalic inclusion body disease, and Epstein-Barr virus-associated kissing disease may be looked up in the guidelines of other specialities. Enormous progression could be reached in prevention of HPV-associated genital warts and cancer introducing the HPV vaccines worldwide. Indeed, safe and highly effective vaccines are available for 2 STIs now: hepatitis B and HPV. The vaccine against hepatitis B is included in infant immunization programmes in 93% of countries and has already prevented a WHO estimated 1.3 million deaths from chronic liver disease and cancer [10]. Although several HSV candidate vaccines have been promising in animal models, prophylactic and therapeutic HSV vaccines have not been effective in clinical trials thus far; and also research to develop a vaccine against HIV is right at the beginning. Fortunately, HIV treatment is highly effective; persons provided early medical treatment can expect to live a near normal lifespan. Definitely, new vaccines for all STIs will be needed for future prevention efforts.

Human papillomavirus-associated genital warts and cancer

Pertaining to phylogeny the papillomavirus species is known to be older than the human species; therefore the species specific human papillomavirus have to coexist from the beginning of mankind. Meanwhile HPV perfectly adapted to its human host; at least 40 of approximately 200 HPV genotypes of different oncogenic potential can infect the genital area. Especially these anogenital HPV subtypes which may cause the genital warts and genital cancer are extremely wild spread in human population because sexual transmission of HPV guarantees a safe reproduction in all generations, resulting in a 80% lifetime risk for HPV infection [11]. So far there was a simple rule: as long people stay sexually active genital HPV infection will survive and disseminate.

Therefore, Condylomata acuminata caused by HPV infection are not only the most common viral STD worldwide, but probably also they are the oldest STD from human dawn of history. Until the first HPV vaccines have been introduced in 2006 and 2007, obviously, the mankind found no way effectively to get rid of these HPV associated diseases. Today more than 30 million people will develop genital warts every year which are benign on principle and caused by nononcogenic, low-risk HPV types (e.g., HPV 6 and 11). However, HPV can also be closely associated with intraepithelial neoplasia, precancers and cancers in both genders, the so called oncogenic, high-risk HPV types (e.g., HPV 16 and 18). Persistence of the oncogenic HPV infection is the strongest risk factor for development of HPV-associated cancer [11].

Most HPV infections are self-limited, subclinical or latent – that means that they are not directly visible or that they can only be diagnosed by laboratory testing, before possibly being eliminated by the immune system. Visible manifestations of the HPV disease showing low rates of spontaneous resolution include Condylomata acuminata, 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 a genital HPV-associated malignancy (i.e., cervical cancer). Only the community of HIV positive men having sex with men (MSM) are at same or even at higher risk for HPV caused anal cancer recently shown in epidemiologic studies.

Today three licensed prophylactic HPV vaccines are available: a bivalent (HPV 16, 18), a quadrivalent (HPV 6, 11, 16, 18) and recently followed by a nonavalent (HPV 6, 11, 16, 18, 31, 33, 45, 52, 58) vaccine, which prevent (a) HPV infection of the cervical epithelium and other squamous epithelia, (b) the development of premalignant lesions, and in the case of the quadrivalent and the nonavalent vaccines, (c) the development of Condylomata acuminata [12]. All HPV vaccines have shown to be highly effective and proved to be well tolerated. HPV vaccination is administrated as a 2-dose series of IM injection over a 6-month period for children aged 9–13 years and a 3-dose series of IM injection over a 6-month period for children and adults aged 13–26 years. In general, HPV vaccination in men and women through age 26 years is not recommended excepting immunocompromised persons (including persons with HIV infection) and MSM. Note that current national recommendations for HPV vaccination can differ widely in all parts of the world.

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.

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 among young women and MSM. 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. Most cases of recurrent genital herpes are caused by HSV2. There are even more people who have no symptoms. These mild or unrecognized infections may be transmitted to sex partners because HSV is shedded intermittently by the infected person. Promising new vaccines against HSV1 and HSV2 are still under investigation [10].

Table 2: Viral STDs [1], [2], [3], [4], [5], [6], [7], [8], [10], [13]–[14]

STDs	Causes	Symptoms	Diagnosis	Treatment IM=Intramuscularly IV=Intravenously PO=by mouth
Genital warts	HPV low-risk genotypes (i.e. 90% 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, even affecting untypical epithelial tissue (e.g. urinary bladder), and is associated with higher rates of cancer. Precancerous changes in the cervix, vulva, anus, or penis are due to HPV high-risk-types (e.g. HPV 16, 18). HPV	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. In addition to anogenital warts, HPV types 6 and 11 have been associated with conjunctival, nasal oral and laryngeal warts due to sexual practice of	External warts are usually diagnosed clinically. 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 can be used by analogy with the acetic acid test of the outer genitals [12]. Both the acetic acid test and fluorescence urethroscopy are limited in specificity. A tissue	Updates of the guidelines in dermatology, venereology, gynaecology and urology [4], [6], [8], [11], [12] unanimously recommend 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 or Sinecatechins 15% ointment are suitable for therapy at home. Medically applied treatment involves Trichloroacetic acid (TCA), cryotherapy, electro-surgery, laser

	<p>infection can result in anal or genital cancers. MSM are at high risk for genital warts and anogenital precancers and cancer. Partners of patients with genital warts tend to share the disease (70%). Most persons who acquire HPV infection clear the infection by their immune system spontaneously and have no visible health problem. Condoms are not fully protective against HPV transmission.</p>	<p>HPV infected people. Anogenital warts can occur at multiple sites and with multiple lesions, especially if routinely shaving of the pubic hairs is performed. Intra-anal warts are found in persons who have receptive anal intercourse, perianal warts can occur without having anal sexual contact. Therefore, the whole anogenital region, including the mucosa of the distal urethra and of the anal channel must be examined to look for HPV-associated lesions.</p>	<p>biopsy or Pap smear may be taken to determine whether the HPV lesions are cancerous. Generally, both sexual partners should be examined for warts. Routine HPV type analyses are not recommended in genital warts. HPV nucleic acid testing may be used in Cervical Cancer Screening Programs. These tests should not be used for male partners, for diagnosis of genital warts or to indicate vaccination [11], [12].</p>	<p>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. No treatment is superior to another, and no single treatment is ideal for all patients and all locations of anogenital warts. Substantial breakthroughs in the prevention of HPV infection have been made in recent years.</p>
<p>Mollusca contagiosa</p>	<p>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.</p>	<p>Typical blisters or umbilicated, raised papules or nodules can be flesh-colored, white, pink, yellow or clear. Mollusca may appear single or multiple, clusters of lesions may develop. Itching is common, but pain is rare, some patients are completely asymptomatic. In adults HIV co-infection has to be ruled out because mollusca can indicate immunodeficiency.</p>	<p>The blisters, papules or nodules 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. Histopathology will show pathognomonic Molluscum bodies which are inclusions of viral particles in the cytoplasm of cells.</p>	<p>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.</p>

<p>Genital herpes</p>	<p>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. Increasing proportion of anogenital HSV1 infection has been found especially among young women and MSM.</p>	<p>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. Although HSV 1 and HSV 2 persist in the body of infected persons indefinitely symptoms tend to lessen with time. Symptoms are absent in many infected patients. Recurrences and subclinical shedding are much more frequent for genital HSV2 infection. Patient’s prognosis and course of genital herpes depend on the type of herpes infection (HSV1 or HSV2).</p>	<p>Sometimes the diagnosis can be made by physical examination alone. Both type-specific virologic and type-specific serologic tests for HSV are important for diagnosis. Cell culture and PCR are the preferred virologic HSV tests. The sensitivity of viral culture is low due to lability of HSV on transport to the laboratory. NAAT like PCR assays for HSV DNA are more sensitive and determine which type of HSV is causing the infection. In the absence of active HSV lesions viral shedding may be intermittent and culture and NAAT may fail to detect HSV infection. Immunofluorescence tests show only low sensitivity. Type-specific serologic tests are available for testing of type-specific and type-common antibodies to HSV. Because nearly all HSV2 infections are sexually acquired, the presence of type-specific HSV2 antibody implies anogenital infection. Type-specific HSV2 serology might be useful to confirm a clinical diagnosis of genital herpes, especially if culture and NAAT are negative for HSV, or if MSM who are at increased risk for HIV acquisition present for STD evaluation.</p>	<p>Herpes is incurable. Systemic antiviral drugs (Acyclovir 3x 400 mg or 5x200 mg PO, Famciclovir 3x 250 mg PO , Valacyclovir 2x1 g PO) 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 (1x1 g PO/ die), Acyclovir (2x400 mg PO) or Famciclovir (2x250 mg PO), for 16 weeks up to years). 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.</p>
------------------------------	--	---	---	--

STDs caused by protozoa and epizoa [1], [2], [3], [4], [5], [6], [7], [8]

Trichomoniasis

Trichomoniasis is caused by the parasitic protozoon, *Trichomonas vaginalis*, and is often diagnosed in patients that are infected with other STDs. Trichomoniasis increases the risk for HIV acquisition (2–3 fold). *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. Symptoms of epididymitis and prostatitis may be found, however, most infected persons (70–80%) have minimal or no symptoms. Untreated infections might last for month to years. Women aged over 40 years are often affected by *Trichomonas vaginalis*. Therefore Trichomoniasis should not be overlooked in older adults. 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. But sensitivity and specificity of NAAT is still much better compared to microscopy. Generally, treatment should involve both sexual partners. A single dose of Metronidazole (1x2 g PO) or Tinidazole (1x2 g PO) should be effective. An alternative regimen is Metronidazole 2x 500 mg PO for 7 days. To reduce disulfiram-like reaction patients should be abstinent from alcohol for 2–3 days after treatment with Metronidazole. All sex partners need to be treated and should abstain from intercourse until symptoms of both partners have resolved.

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. Permethrin 1% cream rinse or Pyrethrins with piperonyl butoxide applied to affected areas and washed off after 10 minutes or Malathion 0,5% lotion or Ivermectin 250 ug/kg repeated in 2 weeks are also recommended. The scalp is treated with lindane shampoo (cave: toxic!). Patients with pediculosis pubis should be evaluated for other STDs. Sex partners should be treated, bedding and clothing should be decontaminated and reevaluation should be performed.

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, rash and pruritus. 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. Scabies in adults frequently is sexually acquired, although scabies in children usually is not. There are a variety of topical medications that will clear scabies infestations. These include lindane, petroleum jelly and 5% sulfur mixture. Permethrin cream (5%) applied to all areas of the body from the neck down and washed off after 8–14 hours or Ivermectin 200 ug/kg PO repeated in 2 weeks are effective in scabies treatment.

References

1. World Health Organization. Sexual and reproductive health. 2017. Available from: <http://who.int/reproductivehealth/topics/rtis/en/>
- 2.
3. International Union against sexually transmitted infections. IUSTI Regions - Europe: Guidelines. (cited 10 January 2016). Available from: www.iusti.org/regions/europe/euroguidelines.htm
4. AWMF. Leitlinien. (cited 10 January 2016). Available from: www.awmf.org/leitlinien/
5. Australian sexual health alliance. Australian STI Management Guidelines for use in primary care. (cited 10 January 2016). Available from: www.sti.guidelines.org.au
6. Deutsche STI-Gesellschaft. STI-Leitfaden Version 2.1 und STI-Treatment Pocket Guide (englisch). 2014 (cited 10 January 2016). Available from: www.dstig.de/literaturleitlinienlinks/sti-leitfaden.html
7. European Association of Urology. (cited 10 January 2016). www.uroweb.org/nc/professional-resources/guidelines/online
8. Centers for Disease Control and Prevention. 2015 Sexually Transmitted Diseases Treatment Guidelines. 2015 (cited 10 January 2016). Available from: www.cdc.gov/std/tg2015/
9. Schneede P, Weidner W. [Gonococcal and chlamydial infections of the urethra: new German guidelines]. Urologe A. 2014 Oct;53(10):1444-51. DOI: [10.1007/s00120-014-3559-4](https://doi.org/10.1007/s00120-014-3559-4)
10. World Health Organization. Sexually transmitted infections (STIs) – Fact sheet. 2016 (cited 10 January 2016). Available from: www.who.int/mediacentre/factsheets/fs110/en/
11. Schneede P, Waidelich R. [HPV in urology. Basic principles and controversies]. Urologe A. 2013 Sep;52(9):1329-36. DOI: [10.1007/s00120-013-3257-7](https://doi.org/10.1007/s00120-013-3257-7)
12. Schneede P, Waidelich R. [Proven and new methods in the treatment of genital warts]. Urologe A. 2013 Oct;52(10):1416-21. DOI: [10.1007/s00120-013-3174-9](https://doi.org/10.1007/s00120-013-3174-9)
13. Schneede P, Tenke P, Hofstetter AG; Urinary Tract Infection Working Group of the Health Care Office of the European Association of Urology. Sexually transmitted diseases (STDs)—a synoptic overview for urologists. Eur Urol. 2003 Jul;44(1):1-7. DOI: [10.1016/S0302-2838\(03\)00193-3](https://doi.org/10.1016/S0302-2838(03)00193-3)
14. Schneede P, Schlenker B. Sexually transmitted infectious diseases (STDs): updated synopsis for practicing urologists. In: Naber KG, Schaeffer J, Heyns CF, Matsumoto T, Shoskes D, Bjerklund Johansen TE, editors. Urogenital infections. Arnhem: ICUD, EAU; 2010. p. 766-76.

Citation note: Schneede P. Sexually transmitted diseases (STDs) – Updating a concise overview for urologists. Version: 2017-12-19. In: Bjerklund Johansen TE, Wagenlehner FME, Matsumoto T, Cho YH, Krieger JN, Shoskes D, Naber KG, editors. Urogenital Infections and Inflammations. Duesseldorf: GMS; 2017-. DOI: [10.5680/lhiii000006](https://doi.org/10.5680/lhiii000006)

License/Copyright: © 2018 Prof. Dr. med. Schneede, Peter
This chapter is distributed under the terms of the Creative Commons Attribution 4.0 International License. See license information at <https://creativecommons.org/licenses/by/4.0/>