CONTINUING MEDICAL EDUCATION

The Presentation, Diagnosis, and Treatment of Sexually Transmitted Infections

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SUMMARY

Background: The reported incidence of sexually transmitted infections (STIs) in Germany is rising. For example, the number of new reported cases of syphilis rose from 3034 in 2010 to 4410 in 2012.

Methods: This review is based on pertinent articles retrieved by a selective search in MEDLINE, and on guidelines and systematic reviews from Germany and abroad.

Results: We discuss sexually transmitted infections presenting with genital, anal, perianal, or oral ulcers, urethritis, cervicitis, urethral or vaginal discharge, or genital warts. We also discuss sexually transmitted infection with HIV and the hepatitis C virus (HCV). Acquired sexually transmitted infections elevate the risk of transmission of other sexually transmitted infections; thus, patients presenting for the diagnosis or treatment of any kind of sexually transmitted infection should be evaluated for others as well. For most of these diseases, treatment of the patient's sexual partner(s) is indicated. Diagnostic nucleic acid amplification techniques are over 90% sensitive and specific and are generally the best way to detect the responsible pathogen. Factors impeding effective treatment include antibiotic resistance (an increasing problem) and the late diagnosis of HIV and HCV infections.

Conclusion: Sexually transmitted infections are common around the world, and any such infection increases the patient's risk of contracting other types of sexually transmitted infection. Molecular genetic diagnostic techniques should be made widely available.

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Sexually transmitted infections are caused by a wide variety of bacteria, viruses, and parasites that are communicated from one human being to another primarily by vaginal, anal, or oral sexual contact. Different sexually transmitted infections (STIs) can be present or be transmitted simultaneously, and the presence of any such infection increases the risk of contracting other types of STI. Sexually transmitted infections are often oligo- or asymptomatic.

According to the World Health Organization (WHO), sexually transmitted infections are one of the five types of disease for which adults around the world most commonly seek medical help (1). The current state of the data on the prevalence of sexually transmitted infections in Germany does not permit any reliable conclusions about infection rates, except for those of two diseases: human immunodeficiency virus (HIV) and syphilis (2).

Sexually transmitted infections can cause severe fetal and neonatal damage, genital neoplasia, and infertility. A number of diagnostic strategies and tests, of variable quality, are available for the individual pathogens.

The diagnostic and therapeutic algorithms can generally be tailored to the leading clinical manifestations (if the patient is symptomatic). Thus, sexually transmitted infections can usefully be classified by their presenting features, as follows:

- Genital, anal, perianal, or oral ulcers
- Urethral or vaginal discharge
- Genital warts
- HIV or hepatitis C virus (HCV) infection.

If the availability of diagnostic tests is limited, effective treatment can also be initiated without any testing on the basis of the clinical findings alone, if these are clearly typical of a particular sexually transmitted disease. Asymptomatic infections are

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Definition

According to the WHO, sexually transmitted infections are one of the five types of disease for which adults around the world most commonly seek medical help.

Figure 1: Acute herpes simplex virus infection in the area of the mons pubis

common, however, and only detectable by testing.

Up to 90% of sexually transmitted infections are asymptomatic. The likelihood that an infection will be asymptomatic depends both on the site of infection and on the responsible pathogen. For example, the probability of asymptomatic rectal infection with *C. trachomatis* and *N. gonorrhoeae* is 85% in men who have sex with men (MSM) (e1). 30% of pregnant girls in Tanzania have an asymptomatic type 2 herpes simplex virus (HSV-2) infection (3). In the United States, about 85% of *T. vaginalis* infections in women are asymptomatic; so are 77% in men (4).

The treatment of sexually transmitted infections has the following objectives:

- To cure the infection in the individual patient as rapidly as possible, and to eliminate contagiousness as rapidly as possible in order to interrupt the chain of transmission;
- To prevent reinfection and recurrent infection.

The treatment of sexual partners is important as well. Bacterial infections and trichomoniasis can now be cured with systemic treatment (1, 5, 6). Viral infections due to HIV, HSV, and human papillomaviruses cannot be cured, but they can be weakened or modulated with systemic treatment (1, 5, 6).

Methods

We selectively searched the MEDLINE database for pertinent publications and guidelines (7–12, e2–e4). Hepatitis B infections, scabies, pubic lice, cytomegalovirus infections, lymphogranuloma venereum, ulcer molle, and inguinal granuloma will not be discussed here.

Learning objectives

Readers of this article should be able to:

- Recognize the clinical features of selected common sexually transmitted diseases
- Apply the currently recommended diagnostic tests for these diseases
- Know their appropriate treatment in the light of current antibiotic resistance rates.

Sexually transmitted infections presenting with genital, anal, perianal, or oral ulcers

Herpes simplex virus (HSV) infection

Infectious ulcers in the genito-anal region are commonly due to HSV. HSV-1 accounts for 20% of cases, HSV-2 for 80%. HSV infection is the most common sexually transmitted infection that causes ulcers. Herpes simplex virus persists in the human host for his or her entire lifetime. Painful vesicles may develop into erosions or ulcers that secrete a hyaline infectious fluid (Figure 1). The ulcers generally heal completely in two to three weeks. HSV infection can manifest itself initially with regional lymphadenopathy and fever; on the other hand, it can also be asymptomatic.

HSV infection can be transmitted by sexual contact (including oral sex) as well as perinatally from mother to child. Persons with an acute HSV-1 infection should refrain from unprotected oral sex. Unprotected sexual contact in the setting of HSV infection promotes the acquisition of HIV infection (odds ratio [OR] 1.7) (e5) and other sexually transmitted diseases. Moreover, studies have shown that HSV-2 infection triples the risk of HIV infection through unprotected sexual intercourse (e6). HSV infection is diagnosed by the analysis of vesicular fluid or genital secretions, generally with the aid of nucleic acid amplification techniques, which are the most sensitive method (over 95%) and nearly 100% specific (e7). The virus can also be revealed by antigen-detection techniques, but these are much less sensitive. Genital herpes infections are treated systemically with aciclovir, valaciclovir, or famciclovir; the dose depends on whether the episode is an initial infection or a recurrence, and on whether the patient is immunocompromised (Table). In patients who have HSV infections that recur four or more times a year, long-term viral suppression therapy with aciclovir, valaciclovir, or famciclovir should be considered (13). The treatment of sexual partners may be indicated (5). Treatment during pregnancy is important (e8, e9, 14) (treatment recommendations of the German STI Society [Deutsche STI-Gesellschaft – Gesellschaft zur Förderung der Sexuellen Gesundheit, DSTIG]: www.dstig.de/literaturleitlinien/links/sti-leitfaden.html).

Systemic treatment

Bacterial infections and trichomoniasis can now be cured with systemic treatment.

The goals of treatment

- To cure the infection and eliminate contagiousness as rapidly as possible, in order to interrupt the chain of transmission
- To prevent reinfection and recurrent infection.

TABLE

The treatment of sexually transmitted diseases*

Clinical features	Pathogens	Primary microbiological diagnostic test(s)	Treatment
Urethritis	Unknown or <i>N. gonorrhoeae</i>	Not performed or NAT	Empiric treatment: ceftriaxone 1 g i.m./i.v. (single dose) plus azithromycin 1.5 g p.o. (single dose)
	<i>N. gonorrhoeae</i>	Culture	Specific treatment (based on detected organism & sensitivity): cefixime 400 mg p.o. (single dose) or ciprofloxacin 500 mg (single dose) or ofloxacin 400 mg (single dose) or azithromycin 1.5 g p.o. (single dose)
	<i>C. trachomatis</i>	NAT	Doxycycline 100 mg p.o. b.i.d. for 7 days or azithromycin 1.5 g p.o. (single dose) (less effective for anal involvement)
	<i>M. genitalium</i>	NAT	Azithromycin 0.5 g p.o., followed by azithromycin 0.25 g p.o. for 7 days or moxifloxacin 400 mg p.o. for 10 to 14 days
	<i>T. vaginalis</i>	Microscopy, NAT, (culture)	Metronidazole 2 g p.o. (single dose) or tinidazole 2 g p.o. (single dose) or metronidazol 0.5 g p.o. b.i.d. for 7 days
Cervicitis	Unknown	Not performed	Empiric treatment: azithromycin 1 g p.o. (single dose) or (in case of elevated likelihood of <i>N. gonorrhoeae</i>) ceftriaxone 1 g i.m./i.v. (single dose) plus azithromycin 1.5 g p.o. (single dose)
	<i>C. trachomatis</i>	See above	See above
	<i>N. gonorrhoeae</i>	See above	See above
	<i>T. vaginalis</i>	See above	See above
	Herpes simplex virus	NAT	See below
Herpes simplex viruses (HSV), primary infection	Herpes simplex virus	NAT	Aciclovir 400 mg p.o. t.i.d. for 7–10 days or aciclovir 200 mg p.o. 5x/d for 7–10 days or valaciclovir 500 mg p.o. b.i.d. for 7–10 days or famciclovir 250 mg p.o. t.i.d. for 7–10 days or in severe cases: aciclovir 5 mg/kg BW i.v. t.i.d. for 5–7 days (for 10 days in immunosuppressed patients) in pregnant women: aciclovir 200 mg p.o. 5x/d for 10 days

The antibiotic treatment of *N. gonorrhoeae*

Ceftriaxone plus azithromycin is the treatment of first choice.

The antibiotic treatment of *M. genitalium*

A 7-day course of azithromycin is the treatment of choice.

Clinical features	Pathogens	Primary microbiological diagnostic test(s)	Treatment
HSV, reactivation	Herpes simplex virus	NAT	Aciclovir 800 mg p.o. b.i.d. for 5 days or aciclovir 400 mg p.o. t.i.d. for 5 days or aciclovir 800 mg p.o. t.i.d. for 2 days or famciclovir 125 mg p.o. b.i.d. for 5 days or famciclovir 1.0 g p.o. b.i.d. for 1 day or valaciclovir 500 mg p.o. b.i.d. for 3 days or valaciclovir 1.0 g p.o. q.d. for 5 days If indicated, topical treatment with aciclovir or foscarnet sodium (not sufficient in pregnancy!) Start interventional treatment as soon as the first sign of reactivation appears. In pregnant women: aciclovir 400 mg p.o. t.i.d. for 10 days
HSV, long-term suppression			Aciclovir 400 mg p.o. b.i.d. for no more than 6 months or famciclovir 250 mg p.o. b.i.d. for no more than 6 months or valaciclovir 500 mg p.o. q.d. for no more than 6 months
Syphilis, early (<1 year)	<i>Treponema pallidum</i>	Serology	Benzathine penicillin G 2.4 million IU i.m. once (1.2 million IU in each buttock) or ceftriaxone 2 g i.v. q.d. for 10 days (in case of penicillin allergy) or doxycycline 100 mg p.o. b.i.d. for 14 days (in case of penicillin allergy; not for pregnant women)
Syphilis, late (>1 year) or unknown date of exposure			Benzathine penicillin G 2.4 million IU i.m. (1.2 million IU in each buttock) three times at 7-day intervals, i.e., on days 1, 8, and 15 or ceftriaxone 2 g i.v. q.d. for 10–14 days or doxycycline 100 mg p.o. b.i.d. for 28 days (in case of penicillin allergy; not for pregnant women) or erythromycin 500 mg p.o. q.i.d. for 28 days

* see also the treatment recommendations of the German STI Society (DSTIG): www.dstig.de/literaturleitlinienlinks/sti-leitfaden.html
NAT, nucleic acid test

Treponema pallidum infection (syphilis)

Syphilis is caused by *Treponema pallidum*. Sentinel analysis in Germany revealed a fluctuating reported incidence of the disease in the range of 1.1 to 1.9 cases per 100 000 persons per year from 2003 to 2008 (2). There were 3034 reported cases in 2010, and 4410 in

2012 (7). Syphilis in clinical stage I, II, or III is called “early syphilis” for the first year after the date of infection and “late syphilis” at later times. Half of all infected persons develop a painless ulcer with an indurated edge (ulcus durum) after an average interval of three weeks; this heals in 4–6 weeks with or without treatment (Figure 2) (7). Painless lymphadenopathy

Genital herpes simplex virus infection

Genital herpes simplex virus infections should always be treated systemically.

The treatment of syphilis

Benzathine penicillin is the drug of first choice.

develops regionally. Hematogenous spread (stage II; secondary syphilis) leads to systemic symptoms arising six weeks to six months later, including fever, myalgia, bone and joint pain, transaminase elevation, and, typically, a maculopapular rash (roseola syphilitica). Other, polymorphic types of rash (Figure 2) can arise through involvement of the mucous membranes (*plaques muqueuses*), the palms and soles (palmoplantar syphilid); intertriginous condylomata lata can be distinguished visually from condylomata acuminata by experienced clinicians (Figures 3b and c). Treponemes are present in these skin lesions, which can therefore transmit infection by contact (7). 75% of untreated patients have no further symptoms after the end of stage II (7), but 25% develop tertiary syphilis (stage III) in 12 months to 10 years (7). Stage III syphilis causes a wide variety of general medical, neurological, and psychiatric morbidity and may be life-threatening if untreated.

The pathogen is generally revealed serologically by antibody detection in the framework of the diagnostic algorithm. First, a pathogen-specific screening test is performed, e.g., a *Treponema pallidum* particle agglutination test (TPPA). If this test is positive, it is followed by a specific confirmation test employing a different antigen strategy, e.g. an enzyme-linked immunosorbent assay (ELISA). If this test is positive as well, the activity level of syphilis is assessed in a third stage of evaluation (e.g., cardiolipin antibodies or treponeme-specific IgM), in order to distinguish syphilis in need of treatment from residual seropositivity in inactive disease. With appropriate equipment, an experienced examiner can see *Treponema pallidum* directly on dark-field microscopy of vesicular fluid or genital secretions in primary syphilis (caution: the specimens are infectious). In Germany, all positive laboratory tests for syphilis must be reported anonymously to the Robert Koch Institute (the governmental infection control agency). If neurosyphilis is suspected, CSF should be obtained by lumbar puncture and submitted for analysis; this should also be done in any patient with suspected syphilis who is HIV-positive with severe immunodeficiency (< 200 CD4⁺ cells), or in whom the date of exposure is unknown (possible late syphilis) (7).

The disease is transmitted exclusively by direct contact with the genito-anal or oral mucosa (less commonly, the skin) of infected persons, i.e., by sexual contact. Intrauterine transmission is also possible. Syphilis cannot be transmitted by objects such as

Figure 2: Primary infection and secondary stage of syphilis: ulcer durum on the upper lip; maculopapular facial rash

towels, toilet seats, etc., although transmission via “sex toys” is possible in certain situations. The spread of syphilis can be halted by timely diagnosis and rigorous treatment, with regular clinical and serologic monitoring of its effect; patients should be thoroughly informed of the diagnosis and its implications, and all of their sexual partners from the three months prior to the onset of the disease should be tested.

Penicillin is the drug of first choice for syphilis. Early syphilis is treated with a single injection of benzathine penicillin, 2.4 million IU i.m., while late syphilis is treated with three injections of the same drug at the same dose, one each on days 1, 8, and 15 (Table). Patients who are allergic to penicillin can be alternatively given doxycycline 100 mg p.o. b.i.d. for 14 days, or ceftriaxone 1–2 g i.v. for 10 days. The treatment of congenital syphilis will not be discussed here (e8). Treatment failure rates are high—6.9–22.4% in early syphilis, 19.4–31.1% in late syphilis, and 27.3–27.8% in neurosyphilis (7). Thus, all patients need rigorous clinical and serologic follow-up every 3 months for a year (2 years in HIV-positive or immunocompromised patients) (7). All patients with syphilis should be tested for other sexually transmitted diseases, including gonorrhea and HIV (6).

The transmission of herpes simplex viruses

HSV infection can be transmitted by sexual contact (including oral sex) as well as perinatally from mother to child.

Syphilis

Half of all infected persons develop a painless ulcer with an indurated edge (ulcus durum) after an average interval of three weeks; this heals in 4–6 weeks with or without treatment.

Figure 3: Various appearances and localizations of condylomatous warts: **a)** condylomata acuminata, coronal sulcus of the penis; **b)** condylomata acuminata, perianal; **c)** condylomata lata, perianal

Sexually transmitted infections presenting with urethral or vaginal discharge

Urethritis

Urethritis can be of either infectious or non-infectious origin. It is often asymptomatic. If symptomatic, it generally presents with a mucopurulent or purulent discharge, dysuria, or itching. The main pathogens are *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Mycoplasma genitalium* (6, e4); rarer ones include *Trichomonas vaginalis*, *Gardnerella vaginalis*, *Ureaplasma urealyticum*, herpes simplex virus (HSV), and adenoviruses (6, e10).

The following clinical findings suggest the diagnosis of urethritis:

- Mucopurulent or purulent urethral discharge (Figure 4)
- ≥ 2 leukocytes in a smear of the urethral discharge under 1000x magnification
- ≥ 10 leukocytes in the sediment of 3 mL of early-stream urine under 400x magnification
- A positive leukocyte esterase test of early-stream urine.

Mere visual inspection of the discharge is inadequate for a reliable etiologic diagnosis. Gram staining of the urethral discharge should be performed for rapid diagnosis; in men, Gram staining is 95% sensitive and 99.9% specific (10, 15).

Patients are treated empirically with antibiotics covering *N. gonorrhoeae* and *C. trachomatis* (Table) (7). In Germany, *N. gonorrhoeae* has high rates of resistance to penicillin (80%) and fluoroquinolones

(74%) (16–19). Orally administered cefixime has been repeatedly reported to have a high rate of treatment failure and is therefore not recommended for first-line empiric treatment (6, 9). If antibiotic treatment brings no improvement, additional evaluation for *T. vaginalis* (microscopy, nucleic acid test [NAT]) and *M. genitalium* (NAT) should be considered. Doxycycline treatment is generally ineffective against urethritis due to *M. genitalium* (6, 20, e11). Treatment with a single dose of azithromycin 1 g p.o. is associated with the development of macrolide resistance; thus, the currently recommended treatment of urethritis due to *M. genitalium* consists of one dose of azithromycin 500 mg p.o., followed by azithromycin 250 mg p.o. q.d. for 7 days (7, 20). If this is ineffective, moxifloxacin 400 mg p.o. q.d. should be given for 10 to 14 days (7, 20). Insufficient data are available on the efficacy of other fluoroquinolones, such as ciprofloxacin or levofloxacin. The clinical significance of other *Mycoplasma* species and of *Ureaplasma* species is currently debated (21).

Patients with diagnosed urethritis should be tested for other sexually transmitted infections, including HIV and syphilis (6).

The patient's sexual partner(s) of the past 60 days should be evaluated and, if necessary, treated. The patient should remain sexually abstinent until at least 7 days after the end of treatment.

A follow-up evaluation with NAT should be performed four weeks or more after the end of treatment to confirm the eradication of the infection.

The transmission of syphilis

The disease is transmitted exclusively by direct contact with the genito-anal or oral mucosa (less commonly, the skin) of infected persons, i.e., by sexual contact.

Symptoms of urethritis

Urethritis is often asymptomatic; if symptomatic, it generally presents with a mucopurulent or purulent discharge, dysuria, or itching.

Cervicitis

Cervicitis has two main diagnostic hallmarks:

- A purulent or mucopurulent discharge that is visible in the endocervical canal or on an endocervical smear (generally termed “mucopurulent cervicitis” or simply “cervicitis”), and
- Persistent endocervical bleeding, which can be easily induced by the gentle insertion of a swab in the cervix.

Either or both of these signs may be present. Cervicitis is often asymptomatic, but many affected women complain of an abnormal vaginal discharge or intermenstrual bleeding (e.g., after sexual intercourse).

The main pathogens are *C. trachomatis* and/or *N. gonorrhoeae*; rarer ones include *T. vaginalis* and HSV-2 (e12). Limited data suggest that *M. genitalium* can also cause cervicitis. In most cases of cervicitis, however, no pathogen is isolated (10).

Leukorrhea is defined as a vaginal discharge in which there are more than 10 leukocytes per high-power field under 400x magnification. This finding indicates cervicitis as long as there is no clinical evidence of infectious vaginitis. Because cervicitis can also be a sign of endometritis, women with newly diagnosed cervicitis should also be evaluated for a possible pelvic infection with *C. trachomatis* or *N. gonorrhoeae*. NAT is currently the most sensitive test for *T. vaginalis* (6).

The empiric treatment of cervicitis should be directed against *C. trachomatis*, and also against *N. gonorrhoeae* in patients at high risk, i.e., those with multiple sexual partners or a history of prior sexually transmitted infections (for the choice of antibiotic, see the treatment of urethritis, above). Women in whom cervicitis due to *C. trachomatis* and/or *N. gonorrhoeae* is diagnosed should also be tested for other sexually transmitted infections, including HIV and syphilis (6).

Trichomonas infection

In men, infection with *Trichomonas vaginalis* can present with the symptoms and signs of urethritis, epididymitis, or prostatitis; in women, it presents with a vaginal discharge that may be diffuse, ill-smelling, or yellowish-green. 70–85% of all infected persons, however, have minimal or no symptoms, and untreated asymptomatic infection can persist for months or years (e13). *T. vaginalis* infection elevates the risk of acquiring HIV by a factor of 2 to 3 (e14).

Figure 4: Purulent urethral discharge in gonorrheal urethritis

For many years immediate microscopy was the most common diagnostic test for *Trichomonas* infection, despite a low sensitivity of only 50% to 65% (22). NAT, developed recently, is 95% to 100% sensitive and specific (e15). In one study, the use of NAT increased the rate of positive diagnosis from 2.7% to 13.5% (22); thus, NAT is clearly indicated. In general, either a smear of urethral or vaginal origin or the patient's urine is studied. The treatment is with nitroimidazoles (Table).

Persons infected with *T. vaginalis* should also be tested for other sexually transmitted diseases (e.g., chlamydia, gonococci, or human papillomaviruses [HPV]). A follow-up test after treatment is recommended to document the eradication of the infection (5). Sexual partners should be treated as well.

Sexually transmitted infections presenting with genital warts

Human papillomavirus infection

Human papillomaviruses (HPV) are divided into two types on the basis of their oncogenic potential. Low-risk varieties, such as HPV6 and HPV11, give rise to condylomata acuminata (genital warts) (Figure 3a, b); high-risk varieties, such as HPV16 and HPV18, cause neoplasia. The treatment of condylomata acuminata is difficult and often protracted. Recurrence rates of 6–60% after topical treatment, 18–77% after surgery, and 9–69% after surgical treatment have been described (23). Persistent HPV infection (possibly due to

The treatment of urethritis

If antibiotic treatment brings no improvement, additional evaluation for *T. vaginalis* (microscopy, NAT) and *M. genitalium* (NAT) should be considered.

The treatment of sexual partners

The urethritis patient's sexual partner(s) of the past 60 days should be evaluated and, if necessary, treated. The patient should remain sexually abstinent until at least 7 days after the end of treatment.

BOX

HIV testing (e3, e21)

- All patients presenting to a physician for the diagnosis or treatment of a sexually transmitted disease should be tested for HIV.
- HIV testing requires the patient's documented informed consent.
- HIV testing begins with a 4th-generation screening test (e.g., Combostat, Ab+Ag). Positivity can be expected no sooner than 2–3 weeks after exposure.
- If the screening test is positive, a confirmatory test is performed on a second serum sample (e.g., Western blot; can distinguish HIV-1 from HIV-2 with an HIV-2 antigen).
- A test for type-specific HIV-RNA is performed if the above test results are unclear, or if an acute HIV infection is suspected before seroconversion can take place (no sooner than 10 days after exposure).
- 4th generation HIV testing can rule out HIV infection six weeks after exposure, unless the patient has deficient B-cell-mediated immunity.
- Patients found to be HIV-positive should undergo professional counseling and examination, as well as screening for further sexually transmitted diseases, including syphilis, gonorrhea, lymphogranuloma venereum, HBV, and HCV.
- The patient's sexual partner(s) should be offered an HIV test and screening for other sexually transmitted diseases.
- HIV-negative sexual partners should be offered post-exposure prophylaxis within 72 hours of exposure.
- In Germany, positive HIV test results must be reported to the Robert Koch Institute within 14 days, anonymously, on a special reporting form.

Ab, antibody; Ag, antigen; HBV, hepatitis B virus; HCV, hepatitis C virus

an underlying immunodeficiency) increases the risk of dysplasia and tumors. More than 99% of cervical carcinomas and more than 90% of anal carcinomas are HPV positive, and HPV can be demonstrated in up to 70% of penile, vulvar, and vaginal carcinomas (5). Up to 30% of carcinomas of the throat, and tonsillar carcinomas in particular, are caused by HPV (e16). Anal carcinoma is a central problem in HIV medicine today, as it is more common among HIV-positive men who have sex with men (70–100 per 100 000) (23, 24 e17). Genital warts should be treated locally with cryotherapy, trichloroacetic acid, or ablative techniques such as curettage. The surgical treatment of anogenital warts should be followed by adjuvant topical treatment

with 5% imiquimod ointment for 8 weeks. Alternatives include podophylloxylin, 5-fluorouracil and cyclosporine. Precancerous lesions and carcinomas should be treated according to the current guidelines (e18).

HIV and HCV infections

HIV infection

Of the estimated 80 000 persons with HIV in Germany today, roughly 90% acquired the infection through sexual contact (5, 25). Two-thirds are men who have sex with men (MSM). The incidence of HIV infection has risen slightly over the past 10 years. The highest number of new cases in Germany in a single year was 3525, in 2014. 780 of these cases were reported as having been caused by heterosexual transmission (HET); that was 182 more HET cases than had been reported the previous year (e16). If untreated, HIV infection progresses from the acute infection to the latency stage (2–10 years), the symptomatic stage, and death (Centers for Disease Control [CDC] classification). HIV-positive persons who receive timely and appropriate treatment, with good compliance, now have nearly the same life expectancy as HIV-negative persons (26–30, e19). Late diagnosis, however, is still a common and serious problem: 1/3 of all persons with HIV in Germany were diagnosed only in a stage of advanced immunodeficiency (< 200 CD4/ μ L). This markedly worsens the clinical course and increases the risk of transmission (27, e20).

The opportunity to diagnose HIV arises when the patient has an acute HIV infection or suffers from symptoms that may be due to HIV, or from AIDS-defining symptoms or conditions. 50–90% of persons with acute HIV infection have an EBV or flu-like illness (EBV, Epstein-Barr virus), generally of brief duration, within 3–4 weeks of the exposure. Features that indicate a possible HIV infection include a history of possible HIV exposure, fever, rash, and a marked loss of helper T-cells (CD4⁺ lymphocytes). In persons with untreated HIV infection, the gradual loss of cellular immunocompetence causes atypical symptoms and signs (Box). HIV infection can often be suspected from the site, extent, and severity of an infection or condition of a possibly opportunistic type, as well as from its tendency to recur or its resistance to standard treatment. It is important for the physician and the patient to have an open, unprejudiced

Signs and symptoms in *Trichomonas* infection

In men, infection with *Trichomonas vaginalis* can present with the symptoms and signs of urethritis, epididymitis, or prostatitis; in women, it presents with a vaginal discharge that may be diffuse, ill-smelling, or yellowish-green.

Anal carcinoma

Anal carcinoma is a central problem in HIV medicine today, as it is more common among HIV-positive men who have sex with men.

discussion of the patient's sexual orientation and practices (5).

The risk of transmission depends on the concentration of the virus (HIV), the particular sexual practices involved, and any concomitant infection with other sexually transmitted diseases (31, 32, e20, e21).

The concentration of virus particles is highest at the time of primary infection and in the stage of advanced immunodeficiency (10^6 – 10^7 copies/mL in the blood). The higher the viral burden, the higher the risk of transmission by sexual contact; HIV transmission is unlikely if the HIV-positive individual has a consistently low viral count (less than 50 copies/mL) and no other concomitant sexually transmitted diseases (e22). Among all sexual practices, being the receptive partner in unprotected anal intercourse confers the highest risk of contracting HIV—up to 1.4%, depending on the viral count of the HIV-positive person (e23).

The risk of HIV transmission is elevated by a factor of 3 to 10 by the concomitant presence of a florid sexually transmitted infection (33, e23, e24). Such infections are common among persons with HIV (13–16%) (33, e22). Sexually transmitted diseases take a more complicated course in HIV-positive persons than in HIV-negative persons; they also induce a rise in viral counts and progression of the HIV disease (34, e3).

The risk of HIV transmission can be lessened by:

- Rigorous treatment of sexually transmitted infections (42%)
- Condoms (85%)
- Antiretroviral therapy (ART) (96%)
- ART and condoms (99.2%) (e23)
- Pre-exposure prophylaxis of HIV-negative sexual partners (86%) (5, 6).

The CDC stage of HIV depends on the clinical findings and the helper cell count. The key surrogate markers for the assessment of prognosis and for the monitoring of treatment are:

- The helper cell count ($CD4^+$ / μ L). The lower the count, the more severe the cellular immunodeficiency and the higher the risk of AIDS and death.
- The concentration of virus particles in the blood (viral count in RNA copies/mL). The higher the viral count, the more rapid the progression of disease and the higher the risk of

transmission.

Antiretroviral therapy should be offered to the patient as soon as HIV is diagnosed; this is the recommendation of the WHO (35) as well as of the American HIV guidelines (e25). The German and Austrian guidelines are now being revised (e2).

Early treatment, with good compliance, suppresses the virus completely and gives HIV-positive persons a life expectancy comparable to that of HIV-negative persons. The early initiation of treatment saves money compared to later initiation (e23), as well as being an effective preventive measure against disease transmission (36).

HCV infection

Hepatitis C virus (HCV) infection is not a typical sexually transmitted disease. Nonetheless, HIV-infected men who have sex with men and who have many sexual partners, use sexually stimulating drugs, and engage in traumatizing sexual practices have a 17.8% risk of contracting HCV, compared to 0.4% among HIV-negative persons (5, 37, e26). Any man who has sex with men and in whom an HCV infection is newly diagnosed should be evaluated for other sexually transmitted infections, including HIV and syphilis. Double and triple infections are common (up to 15%).

Persons infected with HIV should undergo annual screening tests for HCV (with anti-HCV antibody and HCV-RNA tests). There is no vaccine against HCV, and 80% of HCV infections are chronic (e27, e28). The new, directly acting drugs against HCV enable interferon-free treatment for all types of HCV (e28, e29). As a rule, cure is attained in over 90% of treated patients within 12 weeks (38). Persons co-infected with HIV and HCV are at increased risk of hepatic cirrhosis and should be given antiviral therapy for HCV infection, just as is recommended for HCV mono-infection (e28, e29).

Conflict of interest statement

Prof. Wagenlehner has served as a paid consultant for Astellas, Bionorica Cubist, Galenus, Leo-Pharma, Merlion, OM-Pharma, Pierre Fabre, Perell Research, Rosen Pharma, and Zambon. He has received payment for presenting at continuing medical education events from Astellas, Bionorica Cubist, Galenus, Leo-Pharma, Merlion, OM-Pharma, Pierre Fabre, Rosen Pharma, and Zambon. He has also received payment for carrying out clinical trials on behalf of Astellas, Bionorica, Calixa, Cereza, Cubist, The German Research Foundation (Deutsche Forschungsgemeinschaft), the European Association of Urology, Galenus, The Hessen State Ministry of Higher Education, Research and the Arts, Merlion, OM-Pharma, Rosen Pharma, and Zambon.

Prof. Brockmeyer has received reimbursement of conference participation fees and travel and accommodation costs from Gilead, Jansen, and MSD. He

Acute HIV infection

50–90% of persons with acute HIV infection have an EBV or flu-like illness of, generally, brief duration within 3–4 weeks of the exposure.

The risk of HIV infection can be lessened by:

- Treatment of sexually transmitted infections
- Condoms
- Antiretroviral therapy (ART)
- ART and condoms
- Pre-exposure prophylaxis

has received payment for carrying out clinical trials on behalf of Gilead, MSD, and Janssen.

Prof. Wichelhaus has served as a paid consultant for Teutopharma. He has received payment for preparing continuing medical education events from Pfizer, Bayer, Biomerieux, and Gilead.

Dr. Discher has served as a paid consultant for Gilead, Abbvie, and Roche. He has received reimbursement of conference participation fees and travel and accommodation costs, as well as payment for preparing continuing medical education events, from BMS, Gilead, MSD, Roche, Abbvie, and Janssen.

Prof. Friese states that he has no conflict of interest.

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Hepatitis C virus infection

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Supplementary material
For eReferences please refer to:
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Question 1

What sexually transmitted disease can be cured by systemic treatment?

- a) *Trichomoniasis*
- b) HIV infection
- c) HSV-1 infection
- d) HPV infection
- e) HSV-2 infection

Question 2

What percentage of sexually transmitted infections may remain asymptomatic, depending on the causative organism?

- a) 10%
- b) 30%
- c) 50%
- d) 70%
- e) Up to 90%

Question 3

What organisms most commonly cause cervicitis?

- a) *C. trachomatis* and *T. vaginalis*
- b) *T. vaginalis* and *N. gonorrhoeae*
- c) *N. gonorrhoeae* and *C. trachomatis*
- d) Herpes simplex virus and *T. vaginalis*
- e) Human papillomavirus and *T. vaginalis*

Question 4

Which of the following is a typical finding in urethritis?

- a) Pustules in the urogenital region
- b) ≥ 2 leukocytes in a smear of urethral discharge under 1000x magnification
- c) Ca. 5 leukocytes in the sediment of 3 mL of early-stream urine under 400x magnification
- d) A negative leukocyte esterase test in early stream urine
- e) A painful swelling on the shaft of the penis

Question 5

What is the recommended empiric treatment for urethritis due to *M. genitalium* in Germany?

- a) Doxycycline 200 mg p.o. q.d. for 7 days
- b) Ciprofloxacin 500 mg p.o. q.d. for 3 days
- c) Azithromycin 500 mg p.o. for 1 day followed by azithromycin 250 mg p.o. q.d. for 7 days
- d) Cefixime 400 mg p.o. (single dose)
- e) Penicillin 200 mg p.o. q.d. for 7 days

Question 6

Which of the following findings is a sign of cervicitis if there is no clinical evidence of inflammatory vaginitis?

- a) >10 leukocytes per high-power field under 400x magnification
- b) Erythrocyte sedimentation rate 10 mm/h
- c) Hemoglobin 15 g/dL
- d) Alpha-1-antitrypsin 1.5 g/L
- e) C-reactive protein (CRP) 3 mg/L

Question 7

By what factor does an HSV-2 infection elevate the risk of contracting HIV through unprotected sexual intercourse?

- a) 2
- b) 3
- c) 4
- d) 5
- e) 6

Question 8

What is the earliest time after an HIV exposure that HIV infection can be definitively ruled out, unless the patient has deficient B-cell immunity?

- a) 4 weeks
- b) 6 weeks
- c) 8 weeks
- d) 10 weeks
- e) 12 weeks

Question 9

What is the drug of first choice against syphilis?

- a) Vancomycin
- b) Tetracycline
- c) Aureomycin
- d) Streptomycin
- e) Benzathine penicillin

Question 10

What sexually transmitted infection most commonly causes ulceration?

- a) Herpes simplex infection
- b) HIV infection
- c) *Neisseria gonorrhoeae* infection
- d) *Chlamydia trachomatis* infection
- e) HPV infection

Supplementary material to:

The Presentation, Diagnosis, and Treatment of Sexually Transmitted Infections

by Florian M.E. Wagenlehner, Norbert H. Brockmeyer, Thomas Discher, Klaus Friese, and Thomas A. Wichelhaus

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