Syphilis

Syphilis, also called Lues, is caused by Treponema pallidum. The risk of transmission is greatest in the early stages of the disease, especially if skin or mucosal ulcers are present. For a single unprotected sexual contact, the risk of transmission is about 30 to 60%. Like other STDs, syphilis favors the transmission of HIV due to lesions in the genital mucosa. In some European and North-American areas, the incidence of syphilis, which was relatively constant during the 1980s and early 1990s, increased to levels last seen in the mid twentieth century. In some large cities, the number of newly diagnosed infections doubled or tripled. Germany had the highest incidence of syphilis in Western Europe in 2003.

Symptoms

Classic syphilis progresses in four stages, listed in Table 1:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Typical clinical appearances</th>
<th>Time since infection</th>
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<tbody>
<tr>
<td>Lues I Ulcus durum / chancre</td>
<td>approx. 3 weeks</td>
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<tr>
<td>Lues II Disseminated exanthemas</td>
<td>approx. 6-8 weeks</td>
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<tr>
<td>Lues III Tuberous syphilis, gumma</td>
<td>several years</td>
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<tr>
<td>Lues IV Tabes dorsalis, progressive paralysis</td>
<td>decades</td>
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In patients coinfected with HIV, the latency period between stage II and the late stages III and IV may be significantly shorter than usual. In some cases, symptoms of the different stadiums may be present at the same time.

Furthermore, unusual manifestations with dramatic skin ulcers or necrosis, high fever and fatigue are described. Occurrence of these clinical symptoms is called Lues maligna.

Another unusual aspect in HIV-infected patients is a possible endogenous reactivation after prior Treponema pallidum infection.

Diagnosis

Routine screening for syphilis with TPHA, TPPA or VDRL may not be reliable in HIV-infected patients. False-negative results can be explained by inadequate production of antibodies or by suppression of IgM production due to exorbitant IgG levels. In case of doubt, specific tests such as FTA-ABS (IgG and IgM) or cardiolipin tests should be carried out.

In erosive skin or mucosal lesions, dark field microscopy should be performed to demonstrate Treponema pallidum directly.
In cases where infection has been proven serologically, a neurological examination should be performed, especially on HIV-infected patients because of the merging of clinical stages. Patients with neurological symptoms should undergo cerebrospinal fluid examination, which is particularly important for making decisions regarding the type of therapy (intramuscular or intravenous).

**Therapy**

Therapy of syphilis should be adapted to the stage of disease.

Recommendations for the early stages of syphilis include three intramuscular injections of benzathine penicillin 2.4 MU administered in weekly intervals (Anglo-American recommendations: only twice). In some countries, clemizol-penicillin is still available. It should be administered intramuscularly at a dose of 1 MU daily for 2 weeks.

In cases of penicillin intolerance, doxycycline (2 x 100 mg), tetracycline (4 x 500 mg) or erythromycin (4 x 500 mg) can be administered orally for 4 weeks, but these drugs are considered to be less effective than penicillin. Consequently, patients should be treated with the same scheme used in neurosyphilis.

Neurosyphilis is usually treated with 5 MU benzylpenicillin given intravenously every 4 hours for 21 days. Other recommendations prefer administration of benzylpenicillin for 14 days, followed by three intramuscular doses of 2.4 MU benzathine penicillin given at weekly intervals.

In cases of penicillin intolerance, neurosyphilis can also be treated with 2 g intravenous ceftriaxone once daily for 14 days. Some guidelines prefer an initial dose of 4 g ceftriaxone. Observational studies in small groups suggest ceftriaxone to be as effective as penicillin in the treatment of syphilis. However, cross-sensitivity may occur.

Alternative treatment options are doxycycline 2 x 100-200 mg per day or erythromycin 4 x 500 mg per day for at least 3 weeks. When treating with macrolides, the possible development of resistance should be considered.

On initiation of syphilis therapy, one should be aware of a possible Jarisch-Herxheimer reaction. This reaction is caused by a massive release of bacterial toxin due to the first dose of antibiotic given. By triggering inflammation mediators, patients may experience shivering, fever, arthritis or myalgia. The symptoms of the Jarisch-Herxheimer reaction may be avoided, or at least reduced, by administering 25-50 mg of prednisolone prior to the first dose of antibiotic.

Serological controls should be performed at 3, 6 and 12 months after syphilis therapy. Because of a possible endogenous reactivation or reinfection in some patients, annual controls should be considered.

**References**


Gonorrhea

Gonorrhea, also called the clap, is caused by Neisseria gonorrhea, a diplococcal bacterium. It is typically localized in the genitourinary mucosa, but infection may also occur orally or anally. Transmission is almost exclusively through sexual activity (exception: neonatal conjunctivitis), and the incubation period is about 2 to 10 days. Co-infection with Chlamydia occurs frequently.

Symptoms

In men, primary symptoms are dysuria and urethral pain. A typical symptom is purulent secretion from the urethra, especially in the morning (“bonjour-drop”). Without treatment, the infection can ascend and cause prostatitis or epididymitis, leading to symptoms such as pain in the perineal region or scrotum or swelling of the scrotum.

In women, the course of gonorrhea is often asymptomatic, although vaginal discharge or purulent dysuria may occur. Involvement of the cervix and adnexa is rare,
but if left untreated, may lead to pelvic inflammatory disease with subsequent infertility.
Extragenital manifestations of gonorrhea occasionally cause pharyngitis or proctitis. Systemic infections with symptoms such as shivering, fever, arthritis or endocarditis are rare.

**Diagnosis**

The diagnosis of gonorrhea is confirmed by microscopy. In a dye-staining test with methylene blue or gram stain, the intracellular diplococci of Neisseria gonorrhoea are traceable. This kind of diagnosis can directly be performed within several minutes at many sites. Other methods, such as serological examination, PCR or laboratory culture are also accurate, but are more complex and more expensive.

**Therapy**

An isolated gonorrhea is usually treated with a single dose of ciprofloxacin 500 mg orally. Other effective antibiotics are Levofloxacin 250 mg or Ofloxacin 400 mg. Recently, the American Centers for Disease Control and Prevention reported an increasing number of fluoroquinolone-resistant bacterial isolates. Consequently, the CDC suggests a single dose of cefixime 400 mg orally or ceftriaxone 125 mg as intramuscular injection for the treatment of gonorrhea in high-risk patients. Intramuscular administration of spectinomycin has been an option, but it is effective only in urogenital and anorectal infection, not in pharyngeal gonorrhea. For these reasons, a pragmatic and sufficient therapy seems to be a single dose of azithromycin 1 g or doxycycline 100 mg twice daily for 7 days. These therapeutic options also treat a possible co-infection with chlamydia species (see following chapter). In all cases of gonorrhea, the sexual partners should also be screened for infection and treated if necessary.

**References**

Chlamydia infection

Infections with Chlamydia trachomatis are nearly twice as prevalent as gonococcal infections. The serovars D–K cause genitourinary infections and, if vertically transmitted, conjunctivitis or pneumonia in the newborn.

The serovars L1–3 cause Lymphogranuloma venereum. This disease is usually considered to be a tropical disease, rarely occurring in industrialized countries. However, for several years, Lymphogranuloma venereum has undergone a renaissance in Europe and USA: actually, the described outbreaks are under investigation by national and international surveillance authorities, which are working on management strategies.

Symptoms

In men, a genital infection with Chlamydia is usually asymptomatic. If symptoms occur, they may be present as urethral discharge, burning or unspecific pain in the genital region. As in gonorrhea, an epididymitis, prostatitis or proctitis may occur. Reiter's syndrome with the triad reactive arthritis, conjunctivitis and urethritis is also possible.

In women, a chlamydial infection often does not cause any symptoms. But in about 20% of female patients, unspecific symptoms such as discharge, burning or, more often, polyuria may occur as an expression of urethritis or cervicitis. Some of the patients also suffer from pelvic inflammatory disease involving the adnexa. This disease pattern can lead to later complications such as infertility or ectopic pregnancy due to tubal occlusions.

In Lymphogranuloma venereum, a primary lesion occurs at the entry location. Some weeks later, a tender lymphadenopathy develops which is mainly unilateral. These swollen lymph nodes may grow into large bubo that tend to ulcerate, possibly leading to scars and lymphedema.

Diagnosis

A chlamydial infection may be suspected based purely on clinical symptoms. Gene amplification methods (PCR, LRC) are the best procedures for confirming the diagnosis. Sensitivity is superior to, while specificity is nearly equal to results obtained by culture. To achieve optimum results, a dry cotton wool wad should be used to collect some epithelioid cells, which should be sent to the laboratory in dry storage. This procedure is now a routine test in most labs.

Other direct tests such as ELISA or direct immunofluorescence are also possible, but there is a lack of sensitivity in populations with low prevalence.

Therapy

The therapy of choice is doxycycline, 2 x 100 mg for 7 days. International guidelines also recommend 1 g azithromycin, given as a single dose, which is an equally potent therapy, but which costs nearly twice as much as doxycycline in many countries. Alternatively, ofloxacin 2 x 200 mg or erythromycin 4 x 500 mg for 7 days can be given.
Lymphogranuloma venereum requires a longer treatment, with doxycycline being administered for a minimum of 3 weeks.

References


Chancroid

Chancroid, also called *Ulcus molle*, is caused by Haemophilus ducreyi, a gram-negative bacterium. It is an endemic infection found primarily in tropical or subtropical regions of the world. In the industrialized countries, it appears to be mainly an imported disease, with only a few cases being reported by the national authorities.

Symptoms

Usually, the incubation period is about 2–7 days. After transmission, one or more frayed-looking ulcers may appear at the entry location, usually in genitourinary or perianal locations. These ulcers are typically not indurated, unlike the primary ulcers of syphilis (therefore the Latin name *Ulcus molle*). Characteristically, they cause massive pain. In about half of the patients the inguinal lymph nodes are swollen and painful, mostly unilaterally. Balanitis or phimosis occurs less frequently.
Condylomata acuminata

**Diagnosis**

Suspected chancroid is difficult to confirm. Clinically, other ulcer-causing STDs such as syphilis or herpes simplex infections have nearly the same symptoms. Microscopy of ulcer smears may demonstrate gram-negative bacteria, but diagnosis should be confirmed from a culture of scrapings from the ulcer or pus from a bubo. Sometimes, a biopsy from the ulcer becomes necessary to differentiate it from a malignoma.

**Therapy**

Therapy should be conducted using a single dose of 1 g oral azithromycin. Ceftriaxone 250 mg intramuscularly, as a single dose, is equally potent. Alternative therapies are ciprofloxacin 2 x 500 mg for three days or erythromycin 4 x 500 mg for 4-7 days. In fluctuant buboes, needle-aspiration of pus may be indicated.

**References**


Condylomata acuminata

Condylomata acuminata are caused by human papillomaviruses (HPV). They are usually present as genital warts, but other locations (oral) are known to be involved. HIV-infected patients have a higher risk of acquiring genital warts.

The typical pathogens, human papillomavirus type 6 or type 11, are not normally considered to be cancerogenic. Although, in both male and female HIV-infected patients, epithelial atypia is seen more often than in uninfected persons.

Besides sexual intercourse, transmission of papillomavirus may be possible via smear infection and perhaps through contaminated objects. But the primary risk factor remains the number of sexual partners.

**Symptoms**

Generally, genital warts remain asymptomatic. Pruritus, burning or bleeding is rare and generally caused by mechanical stress.
Malignant degeneration of genitourinary papillomavirus infections (HPV 16, 18, etc.) is the most important complication. In contrast to HPV-associated cervical carcinoma, genital or anal carcinoma rarely develops on underlying Condylomata.

**Diagnosis**

Condylomata acuminata is a clinical diagnosis. Further diagnostic tests should be considered in case of persistence despite therapy or an early relapse. In addition to histological examination, direct HPV detection, including subtyping, is possible to differentiate between high and low risk types. Actually, this procedure is instrumental in gynecology in case of ambiguous histologies.

**Therapy**

Treatment of genital warts is performed surgically by electrosurgery, cryotherapy, curettage, or laser. Chemical interventions with podophyllin or trichloroacetic acid are also possible. Other methods have been recommended. In daily clinical practice, a surgical intervention followed by adjuvant immunotherapy with interferon beta or (possibly more effective) with imiquimod reduces the rate of relapse and seems to be the best choice for patients.

**References**