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## Sexually Transmitted Diseases

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## Syphilis

**Definition:** syphilis is a transmittable bacterial disease that predominantly affects the genital area. It is characterized by different clinical stages alternating with long asymptomatic periods.

**Etiology:** it is a sexually transmitted disease caused by *Treponema Pallidum* (TP) *sub species pallidum*, a gram-negative bacterium. Approximately 30% of those exposed become infected.

**Epidemiology:** syphilis has a worldwide spread, and in recent years its incidence has been rising in the western world. This increase has been particularly striking in metropolitan areas and among homosexual men. The disease is more common in males, but its real frequency may be underestimated in women because female genital primary lesions are often unnoticed.

**Clinical appearance:** primary syphilis is characterized by a solitary, reddish, indurated, often eroded and painless nodule localized at the site of TP inoculation. This chancre usually occurs in the genital area, but it has been described on almost any site of the body. Coexistent regional lymphadenopathy, usually healing in about 1 month, is typical.

The clinical manifestations of secondary syphilis include polymorphic cutaneous eruptions, mucous lesions, diffused lymphadenopathy, and systemic symptoms. The most frequent cutaneous

findings include roseola syphilitica and papular syphilis. The former consists of a large number of round or oval erythematous patches, a few millimeters in diameter, symmetrically distributed on both sides of the trunk and upper limbs. Papular syphilis is characterized by an eruption of erythematous or reddish-brown papules, sometimes covered by scales, widely distributed on the skin and frequently involving the palms and soles. Mucosal lesions occurring at this stage include soft, flat vegetations involving the genital and perigenital area.

The third stage of the disease can affect any organ, but it is mainly characterized by neurological involvement. The cutaneous manifestations of tertiary syphilis include nodular syphilis, characterized by painless, indurated, dull red nodules of varying size that may occur on any part of the body, and gummatous syphilis, characterized by deep granulomatous lesions evolving into chronic ulcerations.

**Clinical course:** TP usually enters the skin during sexual contact, as transmission is facilitated by mucosal or skin erosions that may occur during intercourse. After an incubation period of 20-40 days the primary lesion develops at the portal of entry. The primary chancre, if untreated, lasts for 2-4 weeks and heals spontaneously, normally without scarring. After few weeks, or even

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## Suggested Reading

- Cheng S, French P (2008) Unilateral penile swelling: an unusual presentation of primary syphilis? *Int J STD AIDS* 19:640-1
- Coutinho B, Baranowski U, Miller E (2008) Male patient with a genital ulceration. Primary syphilis. *Am Fam Physician* 77:215-6
- Dinotta F, De Pasquale R, Micali G (2009) Secondary syphilis with exclusive peno-scrotal localization. *G Ital Dermatol Venereol* 144:725-8
- Zou H, Fairley CK, Guy R, Chen MY (2012) The efficacy of clinic-based interventions aimed at increasing screening for bacterial sexually transmitted infections among men who have sex with men: a systematic review. *Sex Transm Dis* 39:382-7

during healing of the primary chancre, the secondary stage begins. This phase is characterized by relapsing cutaneous rashes, with damage of skin appendages and internal organs. After a period of latency ranging from 3 months to 3 years, tertiary lesions can develop in the internal organs, the central nervous system, and the skin.

**Diagnosis:** syphilis can be diagnosed by direct and indirect techniques. Direct techniques include dark-field microscopy examination and PCR, both useful for TP detection in the oozing lesions of primary and secondary syphilis. PCR is particularly

suitable for extragenital locations, as it can also be performed on skin specimens. Indirect techniques include treponemal (TPHA, TPPA, EIA-Tp, chemiluminescence immune assay) and non-treponemal (VDRL, RPR) serological tests, both useful in identifying the antibody response to the infection. Histology may be helpful for diagnosis in atypical cases only.

**Therapy:** the first line treatment is systemic penicillin, used at variable dosages depending on the disease stage. In case of penicillin allergy, erythromycin or doxycycline may be used.



**Fig. 4.1** Primary syphilis: reddish and ulcerated nodule on the glans



**Fig. 4.2** Primary syphilis: typical solitary, reddish, and ulcerated nodule on the coronal sulcus



**Fig. 4.3** Primary syphilis: multiple and ulcerated nodules on the shaft and scrotum



**Fig. 4.4** Primary syphilis: multiple ulcerated nodules involving the glans and the shaft in an Afro-American patient



**Fig. 4.5** Primary syphilis: nodule on the glans with atypical psoriasiform presentation



**Fig. 4.6** Secondary syphilis: erosions and flat vegetations involving the scrotum and the glans

## Granuloma Inguinale

**Definition:** granuloma inguinale, also called donovanosis, is a chronic bacterial infection with frequent relapses, affecting the genital area.

**Etiology:** it is a sexually transmitted disease caused by *Klebsiella granulomatis* and *Calymmatobacterium granulomatis*, a rod-shaped gram-negative agent formerly called *Donovania granulomatis*. This microorganism has an incubation period ranging from 8 days to 12 weeks, with an average of 2 to 4 weeks.

**Epidemiology:** it is a very rare disease in Europe and North America. Donovanosis is endemic in tropical or subtropical countries, where it is associated with poverty and poor hygiene. In tropical countries, about 20% of male patients with sexually transmitted diseases have granuloma inguinale. Peak incidence occurs between the ages of 20-40 years; men are more infected than women. There are approximately 100 cases/yr reported in the United States.

**Clinical appearance:** in early stages, asymptomatic papules and nodes develop in the genital or perigenital area. Subsequently, lesions evolve into painless, foul-smelling ulcerations surrounded by a peripheral inflammatory reaction, which bleed easily if traumatized. As the ulcers slowly expand centrifugally and become granulomatous, patients develop subcutaneous granulomas in the inguinal regions, usually without lymph node involvement. Extragenital lesions, notably involving the oral cavity, have been reported. Abdominal visceral

dissemination has been observed, mostly in endemic regions. In such instances, systemic symptoms, such as fever, malaise, anemia, and weight loss, usually occur.

**Clinical course:** the disease has a slow and gradual onset, beginning with an inconspicuous pimple or lumpy eruption on the skin. If untreated, the ulcerative lesions persist, with possible superinfection by other sexually transmitted agents, leading to mutilation and destruction of the genital tissue. In addition, the scar tissue produced by late stage infection may cause urethral stenosis. Local lymphatic damage may lead, less commonly in men than in women, to chronic edema and elephantiasis. A high risk of genital cancer has also been reported.

**Diagnosis:** the diagnosis of granuloma inguinale is made by tissue smears or biopsy or both. The demonstration of intracytoplasmic bacteria (Donovan bodies) in mononuclear cells confirms the diagnosis. More recently, PCR methods have been developed.

**Therapy:** granuloma inguinale is treated with oral antibiotics administered for at least 3 weeks. The use of azythromycin and doxycycline is recommended. Alternative treatments include tetracycline, trimethoprim-sulfamethoxazol, erythromycin, and ciprofloxacin. Although the skin ulcers will start to show signs of healing in about a week, the patient must take the full course of medication to minimize the possibility of relapse.

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## Suggested Reading

- Bezerra SM, Jardim MM, Silva VB (2011) Granuloma inguinale (Donovanosis). *An Bras Dermatol* 86:585-6
- O'Farrell N, Moi H, IUSTI/WHO European STD guidelines Editorial Board (2010) European guideline for the management of donovanosis, 2010. *Int J STD AIDS* 21:609-10
- Roett MA, Mayor MT, Uduhiri KA (2012) Diagnosis and management of genital ulcers. *Am Fam Physician* 85:254-62
- Velho PE, Souza EM, Belda Junior W (2008) Donovanosis. *Braz J Infect Dis* 12:521-5



## Lymphogranuloma Venereum

**Definition:** Lymphogranuloma Venereum (LV), also known as Durand-Nicolas-Favre disease, is a bacterial infection of the lymphatic system characterized by acute inguinal lymphadenitis and genital ulceration.

**Etiology:** the etiological agent of LV is *Chlamydia trachomatis*, serotypes L1, L2, L3. It is a sexually transmitted disease. Its incubation period ranges from 3 to 30 days.

**Epidemiology:** LV is widespread in tropical and subtropical areas of Africa and Asia. It is more frequent in men.

**Clinical appearance:** the initial lesion is often a papule or shallow ulcer in the groin area. A painless sore or lump may be visible in correspondence to the bacteria portal of entry. Because the sore or lump is usually painless and clears up without treatment, it often goes unnoticed. During the second stage, groin lymph nodes may become swollen on one or both sides. Perirectal lymph nodes may also be affected as a result of anal intercourse. When inguinal and femoral nodes are enlarged, they are characteristically separated by Poupart's ligament (sign of Greenblatt). Fever, malaise, headache and arthralgias may sometimes be present. Physical examination may also show drainage of groin lymph nodes through the skin. Diarrhea and lower abdominal pain may ensue.

**Clinical course:** the primary genital lesion is usually transient and painless. After it heals, lymphadenitis occurs, followed by the genitoanorectal syndrome. Lymphadenitis is usually unilateral and affects multiple inguinal nodes. Untreated, LV persists for several months or years. Possible complications include elephantiasis, anal stenosis, and rectal strictures.

**Diagnosis:** it is essentially clinical, and it is confirmed by the LV complement fixation test (LV-CFT) and by laboratory tests devised for Chlamydiae detection. Culture of *C. trachomatis*, although useful for definitive diagnostic confirmation, is technically costly and time-consuming. The best results are obtained using aspirates from an involved inguinal lymph node. Other tests for LV include microimmunofluorescence and polymerase chain reaction. Further tests to rule out other sexually transmitted infections that might have been transmitted at the same time are strongly recommended.

**Therapy:** oral antibiotics are indicated. The treatment of choice is doxycycline, although tetracycline, erythromycin, and azithromycin are also effective. Incision and surgical drainage of the purulent discharge above the inguinal ligament may minimize symptoms.

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## Suggested Reading

- Cusini M, Boneschi V, Arancio L et al (2009) Lymphogranuloma venereum: the italian experience. *Sex Trans Infect* 85:171-2
- Greene L, Rubinstein L, Gaffney J et al (2008) Lymphogranuloma venereum in the UK in 2003. *Int J STD AIDS* 19:139-40
- Kapoor S (2008) Re-emergence of lymphogranuloma venereum. *J Eur Acad Dermatol Venereol* 22:409-16
- Roett MA, Mayor MT, Uduhiri KA (2012) Diagnosis and management of genital ulcers. *Am Fam Physician* 85:254-62
- Vargas-Leguas H, Garcia de Olalla P, Arando M et al (2012) Lymphogranuloma venereum: a hidden emerging problem, Barcelona, 2011. *Euro Surveill* 17



**Fig. 4.7** Unilateral inguinal lymphadenitis with evidence of drainage

## Chancroid

**Definition:** chancroid is a highly contagious bacterial infection characterized by the presence of painful ulcers and inflammatory inguinal adenopathy in the groin area.

**Etiology:** it is caused by *Haemophilus ducreyi*, a small gram-negative streptobacillus transmitted during sexual intercourse. In men the incubation period ranges from 5 to 14 days.

**Epidemiology:** chancroid is very common in Africa and it is becoming more common in other countries. Its real incidence is difficult to determine and probably underestimated, due to the unavailability of diagnostic resources in underdeveloped countries where the disease is prevalent, and because of the difficulties in culturing *H. ducreyi* even when laboratory facilities are available. The disease is more frequent in men than in women. Uncircumcised men seem to be at higher risk than circumcised ones.

**Clinical appearance:** it usually begins as a small papule that rapidly becomes pustular and erodes, leading to the development of a painful ulcer 1 to 2 cm in diameter with sharply defined, undermined irregular borders. The ulcerations, soft and covered by a grayish material, can be single or multiple, but in the majority of cases two clustered lesions of variable size (5-50 mm) may develop. They are very painful and bleed easily, and in men they are generally localized on the penis. Lymphadenopathy is usually unilateral, and in

50% of cases the lymph nodal swelling is followed by a break in the skin which causes draining abscesses. The enlarged lymph nodes and abscesses are called buboes.

**Clinical course:** without therapy, chancroid is self-healing in about 1-2 months. In a few cases it can persist for some years with a relapsing course. Complications include urethral fistulas and foreskin scarring in uncircumcised males. Patients with chancroid should also be checked for other sexually transmitted diseases, including syphilis, HIV, and genital herpes. The disease does not confer immunity, so that reinfection is frequent.

**Diagnosis:** it may easily be misdiagnosed in Western countries due to its rare occurrence and difficulties in detecting the causative pathogen (*H. ducreyi* is difficult to cultivate). Diagnosis is made by the demonstration of *H. ducreyi* in the ulcerative lesions using microbial cultures or nucleic acid amplification techniques. In doubtful cases, histopathological examination can be useful.

**Therapy:** antibiotic treatment with azithromycin, ceftriaxone or erythromycin cures the infection, resolves symptoms and prevents transmission to others. Large lymph node swellings need to be drained, either with a needle or local surgery. If treatment is successful, ulcers usually improve in about a week. The time required for complete healing is generally related to the size of the ulcer.

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## Suggested Reading

- Bhunu CP, Mushayabasa S (2011) Chancroid transmission dynamics: a mathematical modeling approach. *Theory Biosci* 130:289-98
- Hope-Rapp E, Anyfantakis V, Fouéré S et al (2010) Etiology of genital ulcer disease. A prospective study of 278 cases seen in an STD clinic in Paris. *Sex Transm Dis* 37:153-8
- Kemp M, Christensen JJ, Lautenschlager S et al (2011) European guideline for the management of chancroid, 2011. *Int J STD AIDS* 22:241-4
- Li W, Janowicz DM, Fortney KR et al (2009) Mechanism of human natural killer cell activation by *Haemophilus ducreyi*. *J Infect Dis* 200:590-8
- Roett MA, Mayor MT, Uduhiri KA (2012) Diagnosis and management of genital ulcers. *Am Fam Physician* 85:254-62





**Fig. 4.8** Sharply defined ulcer, covered by a grayish material, of the foreskin in an Afro-American patient



**Fig. 4.9** Multiple ulcers located on the proximal shaft

## Gonorrhoea

**Definition:** gonorrhoea is a bacterial infection characterized by acute inflammation at the site of inoculation, with possible local and systemic complications.

**Etiology:** the etiological agent is *Neisseria gonorrhoeae* (a small gram-negative diplococcus). It infects predominantly the noncornified epithelium of the urogenital tract, rectum, oropharynx and conjunctivae. Gonorrhoea is generally transmitted by sexual contact or perinatally. Indirect transmission is very unusual as *N. gonorrhoeae* dies rapidly in the outside environment. The incubation period is 2-7 days.

**Epidemiology:** it is a common infectious disease, affecting both sexes with a higher prevalence in males. The highest incidence of gonorrhoea is in young adults (15-29 years). Incidence has fallen substantially in the last decade, perhaps due to gonorrhoea control programs. It is the cause of approximately 1/3 of all urethritis in the United States.

**Clinical appearance:** the most common presentation of gonorrhoea is acute anterior urethritis, with mucopurulent urethral discharge and dysuria. Burning and pain on urination are also present. A few days later, the discharge usually becomes more profuse and, at times, blood-tinged. Acute epididymitis may also occur. Rectal and pharyngeal infections are possible, usually paucisymptomatic or completely asymptomatic.

**Clinical course:** it most often remains localized to the inoculation site, but, if untreated, it can

involve the upper urogenital tract in males, causing complications such as urethral stricture, prostatitis, epididymitis, and cowperitis. A systemic involvement is possible but it is very rare. Disseminated gonococcal infections (bacteremia) occur in about 1-3% of cases, with fever, arthralgia, acute arthritis and tenosynovitis. Typically, these patients often do not report urogenital or pharyngeal complaints.

**Diagnosis:** traditionally, laboratory diagnosis of gonococcal infection depends on identification of *N. gonorrhoeae* at an infected site with Gram stain and microbial culture. The presence of typical Gram-negative intracellular diplococci after Gram stain establishes the diagnosis. Isolation through culture is the standard diagnostic clue, and should be used whenever practical. It should be performed if symptoms persist following treatment. However, newer polymerase chain reaction-based testing methods are becoming more common. All those testing positive for gonorrhoea should be tested for other sexually transmitted diseases.

**Therapy:** gonorrhoea is effectively treated with penicillin. Because of increasing rates of antibiotic resistance, this issue needs to be taken into account when deciding on treatment. In the UK, the Health Protection Agency has recommended the use of a combination of a single dose of oral azithromycin and intramuscular ceftriaxone as alternative treatment, since injectable ceftriaxone appears to be one of the few effective antibiotics.

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## Suggested Reading

- Bignell C, Fitzgerald M, Guideline Development Group British Association for Sexual Health and HIV UK (2011) UK national guideline for the management of gonorrhoea in adults, 2011. *Int J STD AIDS* 22:541-7
- Bignell C, Ison CA, Jungmann E (2006) Gonorrhoea. *Sex Transm Infect* 82(Suppl 4):6-9
- Newman LM, Moran JS, Workowski KA (2007) Update on the management of gonorrhoea in adults in the United States. *Clin Infect Dis* 44(Suppl 3):S84-101



**Fig. 4.10** Typical urethritis characterized by mucopurulent discharge



**Fig. 4.11** Urethritis with marked mucopurulent discharge



**Fig. 4.12** Balanitis characterized by marked erythema and discharge

## Nongonococcal Urethritis

**Definition:** Nongonococcal Urethritis (NGU) is an infectious disease characterized by discharge and/or urethral symptoms not caused by *Neisseria gonorrhoeae*.

**Etiology:** it may be caused by different organisms, although the most frequent causes are *Chlamydia trachomatis* (subtypes from D to K) and *Mycoplasma genitalium*. Other agents include *Ureaplasma urealyticum*, *Haemophilus vaginalis*, Herpes simplex virus, Adenovirus and *Trichomonas vaginalis*.

**Epidemiology:** it is a common disease; it has been estimated that about 50% of cases of urethritis are nongonococcal. According to the World Health Organization data, every year 92,000,000 cases of chlamydial infections are registered worldwide, and chlamydial infection is considered one of the most important causes of sterility.

**Clinical appearance:** the signs and symptoms of NGU are urethral discharge, burning or pain during micturition, itching, irritation or tenderness, and stained underwear. A history of genital infection in the sexual partner is often reported.

**Clinical course:** if untreated, the disease can

spread along the genitourinary tract leading to complications such as prostatitis in men and inflammatory pelvic disease in women. Moreover, irreversible complications such as sterility due to fibrotic evolution can be observed.

**Diagnosis:** all patients who have confirmed or suspected urethritis should be tested for *N. gonorrhoeae* and *Chlamydiae*. A microscopic and/or culture test of the discharge or of a urine sample can reveal the infection. Microscopic examination is mandatory for differential diagnosis with gonorrhoea. In NGU it reveals more than 5 polymorphonuclear leukocytes (x1000) in a Gram- or methylene blue-stained urethral smear, in the absence of *Neisseria* identification. The most reliable method to differentiate chlamydial from mycoplasma infections is the use of nucleic acid amplification techniques. Urethritis due to mechanical injury and irritating factors should be considered in the differential diagnosis.

**Therapy:** the most common antibiotics used to treat NGU are doxycycline or azithromycin. NGU from *T. vaginalis* should be treated with metronidazole or tinidazole plus azithromycin.

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## Suggested Reading

- Azariah S, Reid M (2000) Adenovirus and non-gonococcal urethritis. *Int J STD AIDS* 11:548-50
- Seña A, Lensing S, Rompalo A et al (2012) Chlamydia trachomatis, Mycoplasma genitalium, and Trichomonas vaginalis infections in men with non-gonococcal urethritis: predictors and persistence after therapy. *J Infect Dis* 206:357-65
- Shahmanesh M, Moi H, Lassau F, Janier M, IUSTI/WHO (2009) 2009 European guideline on the management of male non-gonococcal urethritis. *Int J STD AIDS* 20:458-64





**Fig. 4.13** Erythema of the meatus



**Fig. 4.14** Evidence of urethral discharge