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«ГОМЕЛЬСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ»

Кафедра поликлинической терапии и общеврачебной практики
с курсом дерматовенерологии

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ИНФЕКЦИИ, ПЕРЕДАВАЕМЫЕ ПОЛОВЫМ ПУТЕМ

Учебно-методическое пособие
для студентов 4 и 6 курсов факультета по подготовке специалистов
для зарубежных стран медицинских вузов

SEXUALLY TRANSMITTED INFECTIONS

Teaching workbook for 4th and 6th year students of the Faculty
on preparation of experts for foreign countries
of medical higher educational institutions

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Учебно-методическое пособие содержит курс лекций по дерматологии, который составлен в соответствии с типовой учебной программой, включающей основные разделы по венерологии.

Предназначено для студентов 4 и 6 курсов факультета по подготовке специалистов для зарубежных стран медицинских вузов, обучающихся на английском языке.

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CONTENT

SYPHILIS

Synopsis

Etiology: Treponemapallidum.

Transmission: Most frequently sexual; less frequently through blood transfusion and transplacentally (congenital syphilis).

Stages: Primary, secondary, latent, and tertiary.

Incubation period: 9–90 days.

Primary stage: Single, indurated, clean, painlessulcer, oozes serum on pressure. Shotty regionallymphadenopathy.

Secondary stage: Generalized rash (maculopapular, pustular), alopeciia. Mucosal lesions (mucous patches and snail trackulcers), intertriginouscondylomalata and shotty, generalized lymphadenopathy.

Latent stage: A latent period of varied duration, characterized by the absence of signs or symptoms of disease, with only reactive serologic tests as evidence of infection.

Tertiary stage: Cutaneous, mucosal and bone gummata. And cardiovascular and central nervous systeminvolvement.

Investigations: T. pallidum (on dark ground microscopy) from chancre. Serologicaltests for syphilis of two types: Nontreponemal tests(VDRL, RPR-test) which are more sensitive, so used for screening. And treponemal tests (FTA-abs, TPHA, FTA-Abs, CLIA) which aremore specific, so used to confirm diagnosis.

Treatment: The recommended treatment for mosttypes of syphilis is benzathine penicillin G, with dose and administration schedule determined by disease stage.

Etiology

Causative agent–Treponemapallidum.

- Phylum:Spirochaetes.
- Order:Spirochaetales.
- Family:Spirochaetaceae.
- Genus:Treponema.
- Species:T. pallidum.

Treponemapallidum, a spirochete which is:

- Corkscrew shaped.
- Motile with characteristic movements, like.
- angulation, bending, rotatory motion, and
- back and forth squiggle.

The bacterium is surrounded by a cytoplasmic membrane, which is itself enclosed by a loosely associated outer membrane. Between those membranes lies a thin layer of peptidoglycan, which provides structural stability and houses

endoflagella, organelles that are responsible for T. pallidum's characteristic corkscrew motility. Microscopically the bacterium is indistinguishable from other pathogenic treponemes that cause nonvenereal diseases.

The bacterium has very limited metabolic capabilities, making it reliant on host pathways for many of its metabolic needs. T. pallidum does not survive more than a few hours to days outside its host and cannot be cultured in vitro for sustained periods, complicating efforts to understand the organism. Instead, it must be propagated in mammals, with rabbits the preferred species because, following testis inoculation, rabbits experience disease manifestations, unlike mice. T.pallidum divides slowly, taking from 30 to 50 hours invitro. That slow reproduction rate has important implicationsfor treatment, which must be present in thebody for a long period in order to assure effectiveness against the bacterium. Following inoculation, T. pallidum attaches to hostcells, including epithelial, fibroblast-like, and endothelialcells, likely by binding to fibronectin, laminin,or other components of host serum, cell membranes,and the extracellular matrix. It can invade rapidlyinto the bloodstream — within minutes of inoculation,based on rabbit models — and can cross many barriersin the body, such as the blood – brain barrier and theplacental barrier, to infect many tissues and organs.

That dissemination leads ultimately to manifestations of syphilis distant from the site of the initial chancre(s)in an infected person and in a developing fetus.T. pallidum lacks virulence factors common to manyother bacteria, including lipopolysaccharide endotoxin. It does, however, produce a brisk immuneresponse, mediated by membrane lipoproteins, thatbegins shortly after infection. Infection at all stagesleads to infiltration by lymphocytes, macrophages, and plasma cells. CD4+ T cells predominate in chancres,and CD8+ T cells predominate in lesions of secondary syphilis. Infection leads also to elaboration of Th1 cytokines, including IL-2 and IFN-γ, although downregulationof the Th1 response during secondary syphilis, coincident with the peaking of antibody titers, might contribute to the organism's ability to evade the host immune response. Subtyping studies ofT. pallidum have linked certain strains of the organismto neurosyphilis.

The humoral immune response begins with productionof IgM antibodies approximately 2 weeks afterexposure, followed 2 weeks thereafter by IgG antibodies. IgM in addition to IgG continues to be producedduring infection and can lead to immune-complex formation. Antibody titers peak during bacterialdissemination, in secondary syphilis. Some antibodiescrossreactwith other treponemalspecies, andsome are specific for T. pallidum subspecies pallidum.The immune response is somewhat active against the organism, helping block attachment of the organism tohost cells, conferring passive immunity in rabbit models, and enhancing phagocytosis in vitro. The immune response is sufficient to prevent syphilisreinfection in persons who have untreated syphilis. In other words, in what is called Colles' law or "chancreimmunity," persons with untreated sy-

philis willnot experience another episode of primary syphilis as long they remain untreated. However, the immune response is insufficient to eradicate T. pallidum from the host. In addition to suppressing the Th1 response, the organism is thought to evade those host defensesby taking harbor in immune-privileged tissues (e.g., central nervous system, eye, and placenta), failing tobe present in sufficient quantities (e.g., during latentinfection) to trigger a host response, varying its surfaceproteins during infection through gene conversion, and overcoming host attempts to prevent bacterial access toiron, which is necessary for bacterial growth. Theimmune response is also not adequate to prevent reinfectionafter a person is cured of syphilis, although itmight modify the course of reinfection. Compared withpersons with syphilis for the first time, for example,reinfected persons are less likely to have manifestationsof primary or secondary syphilis and more likely to bediagnosed with latent syphilis. The immune response is also likely responsible forthe tissue damage caused in syphilis. Damage to axonslocated near the site of a chancre might explain why thatlesion, although ulcerative, is typically painless.

Transmission

Transmission of syphilis can be:

✓ Acquired:

- Sexual: through unprotected sexual contact,this being the predominant method of transmission.
- Blood: through contaminated blood andblood products.
- Accidental: in health care workers, e.g.,through needle prick injury.
- Congenital: Vertical transmission occurs inutero (transplacentally) or at the time of delivery. Infectivity of mother is higher if she hasearly stage of syphilis; before the fifth monthof gestation, the fetus even if infected escapessevere damage due to its inability to mount aninflammatory response.

Epidemiology

The prevalence of syphilis depends on manyfactors:

- Sexual promiscuity.
- Population explosion.
- Urbanization
- HIV-pandemic.

In developing countries, especially in the rural areas, syphilis is still the commonest cause of ulcerative STD. In developed countries, the prevalence of syphilis had wanedbut resurged with HIV pandemic.

Age: Affects sexually active age group. Congenital syphilis in newborn.

Gender: Women are infected more easily than men, but tend to be asymptomatic for primary syphilis and so often first present with secondary syphilis.

Classifcation

Syphilis can be classified into:

Early syphilis:

Infection < 24 months old.
Lesions teeming with *T. pallidum*and so highly infectious.

Late syphilis:
Infection > 24 months old.
*T. pallidum*sparse and so not infectious.

International Classification of Diseases, Revision 10 (1990)

A50 — Congenital syphilis.
A50.0 — Early congenital syphilis, symptomatic.
A50.1 — Early congenital syphilis, latent.
A50.2 — Early congenital syphilis, unspecified.
A50.3 — Late congenital syphilitic oculopathy.
A50.4 — Late congenital neurosyphilis [juvenile neurosyphilis].
A50.5 — Other late congenital syphilis, symptomatic.
A50.6 — Late congenital syphilis, latent.
A50.7 — Late congenital syphilis, unspecified.
A50.9 — Congenital syphilis, unspecified.
A51 — Early syphilis.
A51.0 — Primary genital syphilis.
A51.1 — Primary anal syphilis.
A51.2 — Primary syphilis of other sites.
A51.3 — Secondary syphilis of skin and mucous membranes.
A51.4 — Other secondary syphilis.
A51.5 — Early syphilis, latent.
A51.9 — Early syphilis, unspecified.
A52 — Late syphilis.
A52.0 — Cardiovascular syphilis.
A52.1 — Symptomatic neurosyphilis.
A52.2 — Asymptomatic neurosyphilis.
A52.3 — Neurosyphilis, unspecified.
A52.7 — Other symptomatic late syphilis.
A52.8 — Late syphilis, latent.
A52.9 — Late syphilis, unspecified.
A53 — Other and unspecified syphilis.
A53.0 — Latent syphilis, unspecified as early or late.
A53. — Syphilis, unspecified.

Clinical Features. Syphilis can present in one of four different stages: primary, secondary, latent, and tertiary, and may also occur congenitally. It was referred to as "the great imitator" by Sir William Osler due to its varied presentations *Incubation period* — 9–90 days (average 21 days).

Clinical course. The natural history of syphilis is presented in Table1.

Table1 — Stages of Syphilis

Stages of Syphilis	
Contact (⅓ become infected) ↓ (10–90 days)	
Primary (chancre) ↓ (3–12 weeks)	
Secondary (mucocutaneous lesions, organ involvement) ↓ (4–12 weeks)	
Early latent → Relapsing (1/4) (2 year from contact)	
Late latent (more than 2 year)	
Remission (⅔)	Tertiary (⅓) Late benign Cardiovascular Neurosyphilis Other symptomatic late syphilis

Primary syphilis. In 50 % of patients with primary syphilis, the typical lesion is called **a chancre, appears at the point of contact.**This is classically (40 % of the time) a single, firm, painless, non-itchy skin ulceration with a clean base and sharp borders between 0.3 and 3.0 cm in size. The ulcer has a clean floor and oozes clear serum on pressure. The lesion, however, may take on almost any form. In the classic form, it evolves from a macule to a papule and finally to an erosion or ulcer. Occasionally, multiple lesions may be present (~ 40 %). Multiple lesions are more common when coinfected with HIV. Rarely lesions may be painful or tender, and they may occur outside of the genitals.

Uncommon presentations include giant necrotic chancre, phagedenic chancre (a deep, bright-red, necrotic ulcer with a soft base and exudate, resulting from secondary bacterial infection associated with immunosuppression), phimosis resulting from adherence of a chancre on the foreskin to the glans, and balanitis. Chancres in women can be more edematous than indurated. Edema indurativum is a unilateral labial swelling with rubbery consistency and intact surface, indicative of a deep-seated chancre.

The lesion may persist for three to six weeks without treatment. Heals spontaneously (4–6 weeks) or on treatment, usually with a slightly atrophic scar.

Location of ulcers

Males: Coronalsulcus, glans, prepuce, and shaft of penis. Perianal area in homosexual males.

Females: Labia minora, labia majora, and mons pubis.Sometimes in cervix or vagina, when disease is asymptomatic.

Extragenital lesions: Also seen on mouth, lips, tonsils, nipples, anusand finger.

Lymphangitis — inflammation of the regional lymph vessels which connects the chancre to the regional lymph nodes. It is mostly visible on the lymph vessels connecting the chancre on the glans penis to the base of the penis in male patients.

Lymphadenopathy. Lymph node enlargement frequently (80 %) occurs around the area of infection, occurring seven to 10 days after chancre formation. Inguinal lymphadenopathy. Lymph nodes are multiple, small, shotty, firm (like lead shots).

Secondary syphilis (SS). SS is a systemic disease with cutaneous as well as extracutaneous manifestations. Secondary syphilis occurs approximately four to ten weeks after the primary infection. While secondary disease is known for the many different ways it can manifest, symptoms most commonly involve the skin, mucous membranes, and lymph nodes. Skin lesions of SS may be few or numerous. Lesions are symmetrical initially, becoming asymmetrical later. There may be a reddish-pink, non-itchy rash on the trunk and extremities, including the palms and soles. The rash may become maculopapular or pustular. It may form flat, broad, whitish, wart-like lesions known as condylomalatum on mucous membranes. All of these lesions harbor bacteria and are infectious. Other symptoms may include fever, sore throat, malaise, weight loss, hair loss, and headache. Rare manifestations include liver inflammation, kidney disease, joint inflammation, periostitis, inflammation of the optic nerve, uveitis, and interstitial keratitis. The acute symptoms usually resolve after three to six weeks; however, about 25 % of people may present with a recurrence of secondary symptoms. Many people who present with secondary syphilis (40–85 % of women, 20–65 % of men) do not report previously having had the classic chancre of primary syphilis.

The different morphological forms of *cutaneous lesions*seen are:

Roseolarsyphilide: symmetrical erythematous macular rash, often just perceptible.

Papularsyphilide: most common rash of SS. Dull red papules, initially discrete. Over a period of time may coalesce to form annular lesions , which may be lichenoid.

Psoriasiform lesions: when scaling is predominant, the lesions appear psoriasiform.

Malignant syphilide: pustular, necrotic, and rupioid lesions may be seen in immunocompromised patients.

Palm and sole lesions: Hyperpigmented, coppery red, scaly lesions. Or hyperkeratoticpapules.

Condylomalata. In intertriginous area, the papules may erode superficially. Sometimes at commissures, the papules split (**split papules**). Also highly infectious are condylomalata, which present as moist, flat, well-demarcated papules or plaques with macerated or eroded surfaces in intertriginous areas, commonly in the labial folds in females or in the perianal region in all. However, any moist intertriginous area of the body can harbor condylomalata, including the axillae, web spaces between toes, and the folds under breasts or an abdominal panniculus.

Mucous patches: Dull erythematous plaques with grayish slough. Mucous patches are white-to yellow erosions on the tongue that efface lingual papillae. Confluence of mucous patches on the tongue has been termed plaques fauches en prairie. Mucous patches can be present elsewhere in the oral cavity, on other mucous membranes, or at the corners ofthe mouth, where they appear as "split papules," withan erosion traversing the center. Mucouspatches are teeming with spirochetes and, hence, highlyinfectious.

Other dermatologic manifestations include a patchy*nonscarring alopecia*, described as "moth-eaten" or, less commonly, a diffuse alopecia of the scalp. Loss of lateral third of the eyebrows can occur.

Without treatment, the secondary stage typically recedes in 4–12 weeks. Scarring typically does not occur although pigmentary changes (leukodermacolli syphiliticum or, if on the neck, "necklace of Venus") can result from inhibition of melanogenesis. Patients with secondary syphilis can experience systemic symptoms that include (in roughly descending order of prevalence) sore throat, malaise, headache, weight loss,fever, musculoskeletal aches, visual disturbances, and hoarseness. Pharyngitis and tonsillitis, laryngitis, uveitis, gastritis, hepatitis, renal disease (membranous glomerulopathy), and periostitis have all beenreported in secondary syphilis, as have hematologicabnormalities including lymphopenia, anemia, and elevated erythrocyte sedimentation rate.

Lymphadenopathy

Generalized, symmetrical, and rubbery lymphadenopathy. Axillary, cervical, and inguinal groups invariably enlarged. Lymph node groups like suboccipital, posterior cervical, and epitrochlear which are normally not enlarged in other diseases may also be enlarged, so a diagnostic clue. Systemic involvementSS is a systemic disease with involvement of many organ systems:

Musculoskeletal system: Periostitis and arthritis

Ocular: Iridocyclitis, uveitis, and choroidoretinitis.

Renal: Nephrotic syndrome due to an immunecomplex glomerulonephritis.

Central nervous system: Cerebrospinal fluid abnormalities.

Latent syphilis is the stage of syphilis where there is persistent seroreactivity in the absence of any clinical evidence of syphilis. It is further described as ei-

ther early (less than 2 year after secondary syphilis) or late (more than 2 year after secondary syphilis and latent syphilis of unknown duration. Early latent syphilis may have a relapse of symptoms. Late latent syphilis is asymptomatic, and not as contagious as early latent syphilis.

Clinical management of patients with late latent syphilis and latent syphilis of unknown duration is identical and differs from clinical management of patients with early latent syphilis. Early latent syphilis can be diagnosed if, within the year preceding discovery of the reactive serologic test, a person had one of the following:

1. Documented seroconversion or fourfold or greater increase in titer of a nontreponemal test.
2. Unequivocal symptoms of primary or secondary syphilis.
3. A sex partner documented to have primary, secondary, or early latent syphilis; o
4. Reactive nontreponemal and treponemal tests from a person whose only possible exposure occurred within the previous 12 months.

Tertiary syphilis. Tertiary syphilis may occur approximately 3 to 15 years after the initial infection, and may be divided into three different forms: gummatous syphilis, late neurosyphilis, and cardiovascular syphilis. Without treatment, a third of infected people develop tertiary disease. People with tertiary syphilis are not infectious.

Gummatous syphilis or late benign syphilis usually occurs 2 to 46 years after the initial infection, with an average of 15 years. This stage is characterized by the formation of chronic gummas, which are soft, tumor-like balls of inflammation which may vary considerably in size. They typically affect the skin, bone, and liver, but can occur anywhere, may diffusely infiltrate an organ or tissue; they grow and heal slowly and leave scars. It is a form of granuloma. Gummas are most commonly found in the liver (gummahepatis), but can also be found in brain, heart, skin, bone, testis, and other tissues, leading to a variety of potential problems including neurological disorders or heart valve disease.

Benign tertiary syphilis of bone results in either inflammation or destructive lesions that cause a deep, boring pain, characteristically worse at night.

Neurosyphilis refers to an infection involving the central nervous system. It may occur early, being either asymptomatic or in the form of syphilitic meningitis, or late as meningovascular syphilis, general paresis, or tabesdorsalis, which is associated with poor balance and lightning pains in the lower extremities. Late neurosyphilis typically occurs 4 to 25 years after the initial infection. Meningovascular syphilis typically presents with apathy and seizure, and general paresis with dementia and tabesdorsalis.

Cardiovascular syphilis usually manifests 10 to 25 years after the initial infection as aneurysmal dilation of the ascending aorta, insufficiency of the aortic valve, or narrowing of the coronary arteries. Pulsations of the dilated aorta may cause symptoms by compressing or eroding adjacent structures in the chest.

Symptoms include brassy cough, and obstruction of breathing due to pressure on the trachea, hoarseness due to vocal cord paralysis resulting from compression of the left laryngeal nerve, and painful erosion of the sternum and ribs or spine.

Congenital syphilis is syphilis present in utero and at birth, and occurs when a child is born to a mother with syphilis. Untreated early syphilis infections results in a high risk of poor pregnancy outcomes, including saddle nose, lower extremity abnormalities, miscarriages, premature births, stillbirths, or death in neonates. Some infants with congenital syphilis have symptoms at birth, but many develop symptoms later. Babies exposed, in utero, can have deformities, delays in development, or seizures along with many other problems such as rash, fever, hepatosplenomegaly, anemia, and jaundice. Newborns will typically not develop a primary syphilitic chancre, but may present with signs of secondary syphilis (i.e. generalized body rash). Often these babies will develop syphilitic rhinitis ("snuffles"), the mucus from which is laden with the T. pallidum bacterium, and therefore highly infectious. Rarely, the symptoms of syphilis go unseen in infants so that they develop the symptoms of latent syphilis, including damage to their bones, teeth, eyes, ears, and brain.

Classification

Early. By definition, early congenital syphilis occurs in children between 0 and 2 years old.

Symptomatic newborns, if not stillborn, are born premature, with hepatosplenomegaly, skeletal abnormalities, pneumonia and a bullous skin disease. If not identified and treated, these newborns develop poor feeding and rhinorrhea.

Symptoms in newborns may include:

- Failure to gain weight or failure to thrive, fever, irritability.
- Rinitis, snuffles, aka "syphilitic rhinitis", which appears similar to the rhinitis of the common cold, except it is more severe, lasts longer, often involves bloody rhinorrhea, and is often associated with laryngitis.
- Rash and infiltration of the mouth, genitals, and anus.
- Rash — starting as small blisters on the palms and soles, and later changing to copper-colored, flat or bumpy rash on the face, palms, and soles.
- Skeletal lesions: Osteochondritis, osteomyelitis (diaphyseal), periostitis. Osteochondritis occurs at metaphysis, widens the zone of provisional calcification until there is epiphyseal separation (usually before age 3 moths). X-ray shows lucent metaphyseal band. It heals after 6 months of age.

Late congenital syphilis is a subset of cases of congenital syphilis. By definition, it occurs in children at or greater than 2 years of age who acquired the infection trans-placentally.

Symptoms. Frequently-found group of symptoms is Hutchinson's triad, which consists of Hutchinson's teeth (notched incisors), keratitis and deafness and occurs in 63 % of cases.

1. Blunted upper incisor teeth known as Hutchinson's teeth. Patients with this have teeth that are smaller and more widely spaced than normal and which have notches on their biting surfaces. It is named after Sir Jonathan Hutchinson, an English surgeon and pathologist, who first described them. Hutchinson's teeth form part of Hutchinson's triad.

2. Inflammation of the cornea known as interstitial keratitis. Keratitis is a condition in which the eye's cornea, the front part of the eye, becomes inflamed. The condition is often marked by moderate to intense pain and usually involves any of the following symptoms: pain, impaired eyesight, photophobia, red eye and a 'gritty' sensation.

3. Deafness from auditory nerve disease.

Less the symptoms can be:

- Frontal bossing (prominence of the brow ridge).
- Saddle nose (collapse of the bony part of nose). It is characterized by a loss of height of the nose, because of the collapse of the bridge. The depressed nasal dorsum may involve bony, cartilaginous or both bony and cartilaginous components of nasal dorsum.
- Hard palate defect.
- Swollen knees.
- Saber shins. Saber shin is a malformation of the tibia. It presents as a sharp anterior bowing of the tibia. The Saber shin is a sharp-edged anteriorly convex tibia.
- Short maxillae.
- Protruding mandible.

Diagnosis. *Syphilis should be suspected in patients with typical mucocutaneous lesions or unexplained neurologic disorders, particularly in areas where the infection is prevalent. In such areas, it should also be considered in patients with a broad range of unexplained findings. Because clinical manifestations are so diverse and advanced stages are now relatively rare in most developed countries, syphilis may escape recognition. Patients with HIV and syphilis may have atypical or accelerated disease.*

Blood tests are divided into nontreponemal and treponemal tests. Nontreponemal tests are used initially, and include venereal disease research laboratory (VDRL) and rapid plasma reagin tests. However, as these tests are occasionally false positives, confirmation is required with a treponemal test, such as treponemalpallidum particle agglutination (TPHA) or fluorescent treponemal antibody absorption test (FTA-Abs), chemoluminescence immunoassays (CLIA). False positives on the nontreponemal tests can occur with some viral infections such as varicella and measles, as well as with lymphoma, tuberculosis, malaria, endocarditis, connective tissue disease, and pregnancy. Treponemal tests detect antitreponemal antibodies qualitatively and are very specific for syphilis. Neither reaginic

nor treponemal tests become positive until 3 to 6 wks. after the initial infection. Thus, a negative result is common in early primary syphilis and does not exclude syphilis until after 6 wk. Reaginic titers decline after effective treatment, becoming negative by 1 yr in primary and by 2 yr in secondary syphilis. Treponemal tests usually remain positive for many decades, despite effective treatment and thus cannot be used to assess effectiveness.

Neurosyphilis is diagnosed by finding high numbers of leukocytes (predominately lymphocytes) and high protein levels in the cerebrospinal fluid in the setting of a known syphilis infection.

Darkfield microscopy directs light obliquely through a slide of exudate from a chancre or lymph node aspirate to directly visualize spirochetes. Although the skills and equipment required are not usually available, darkfield microscopy is a specific test for early primary syphilis. The spirochetes appear against a dark background as bright, motile, narrow coils that are about 0.25 μm wide and 5 to 20 μm long. They must be distinguished morphologically from nonpathogenic spirochetes, which may be part of the normal flora, especially of the mouth.

Two other tests can be carried out on a sample from the chancre: direct fluorescent antibody testing and nucleic acid amplification tests. Direct fluorescent testing uses antibodies tagged with fluorescein, which attach to specific syphilis proteins, while nucleic acid amplification uses techniques, such as the polymerase chain reaction, to detect the presence of specific syphilis genes. These tests are not as time-sensitive, as they do not require living bacteria to make the diagnosis.

Treatment

Early infections. The first-choice treatment for uncomplicated syphilis remains a single dose of intramuscular benzathine penicillin G. Doxycycline and tetracycline are alternative choices for those allergic to penicillin; however, due to the risk of birth defects these are not recommended for pregnant women. Resistance to macrolides, rifampin, and clindamycin is often present. Ceftriaxone, a third-generation cephalosporin antibiotic, may be as effective as penicillin-based treatment. It is recommended that a treated person avoid sex until the sores are healed.

Late infections. For neurosyphilis, due to the poor penetration of penicillin G into the central nervous system, those affected are recommended to be given large doses of intravenous penicillin. If a person is allergic, ceftriaxone may be used or penicillin desensitization attempted. Other late presentations may be treated with once-weekly intramuscular penicillin G for three weeks. If allergic, as in the case of early disease, doxycycline or tetracycline may be used, albeit for a longer duration. Treatment at this stage limits further progression, but has only slight effect on damage which has already occurred.

Jarisch-Herxheimer reaction (JHR)

Most patients with primary or secondary syphilis, especially those with secondary syphilis, have a JHR within 6 to 12 h of initial treatment. It typically mani-

fests as malaise, fever, headache, sweating, rigors, anxiety, or a temporary exacerbation of the syphilitic lesions. The mechanism is not understood, and JHR may be misdiagnosed as an allergic reaction. JHR usually subsides within 24 h and poses no danger. However, patients with general paresis or a high CSF cell count may have a more serious reaction, including seizures or strokes, and should be warned and observed accordingly. Unanticipated JHR may occur if patients with undiagnosed syphilis are given antitreponemal antibiotics for other infections.

Posttreatment surveillance. After treatment, patients should have. Examinations and reaginic tests at 3, 6, and 12 mo and annually thereafter until the test is nonreactive. For neurosyphilis, CSF testing every 6 mo until CSF cell count is normal.

GONORRHEA

Synopsis

Etiology: Neisseria gonorrhoeae, transmitted sexually; sometimes vertically (from mother to child) causing ocular infection in neonates.

Incubation period: 1–5 days.

Males: Urethritis manifesting as profuse urethral discharge and dysuria.

Females: Usually asymptomatic carriers; may have vaginal discharge.

Complications: Include infection of adjoining structures and glands. And late complications like urethral stricture (males) and pelvic inflammatory disease andinfertility (females).

Diagnosis: Clinical suspicion confirmed in males by demonstration of Gram-negative intracellular diplococcic on Gram stain. And in females by culturing theorganism.

Treatment: Uncomplicated gonococcal infection: singleoral dose of cefixime (400 mg) or ciprofloxacin (500 mg) or intramuscular ceftriaxone (125 mg);complicated infections need longer treatment.

Gonnococcal infection, also known as gonorrheais one of the two most common sexually transmitted infections. This infection is caused by the bacterium Neisseria gonorrhoeae, is a species of Gram-negative coffee bean-shaped diplococci bacteria. N. gonorrhoeae are non-motile. gonorrhoeae has surface proteins called Opa proteins, which bind to receptors on immune cells. In so doing, N. gonorrhoeae is able to prevent an immune response. The host is also unable to develop an immunological memory against N. gonorrhoeae – which means that future reinfection is possible. N. gonorrhoeae can also evade the immune system through a process called antigenic variation, in which the N. gonorrhoeae bacterium is able to alter the antigenic determinants (sites where

antibodies bind) such as the Opaproteins and Type IV pili that adorn its surface. The many permutations of surface proteins make it more difficult for immune cells to recognize N. gonorrhoeae and mount a defense. N. gonorrhoeae is naturally competent for DNA transformation as well as being capable of conjugation. These processes allow for the DNA of N. gonorrhoeaeto acquire or spread new genes. Especially dangerous from the aspect of healthcare is the ability to conjugate, since this can lead to antibiotic resistance.

The infection is transmitted from one person to another through vaginal, oral, or anal sex. A mother may transmit gonorrhea to her newborn during childbirth; when affecting the infant's eyes, it is referred to as ophthalmianeonatorum. It can be spread by toilets or bathrooms to girls.

International Classification of Diseases, Revision 10 (1990)

A54 — Gonococcal infection.

A54.0 — Gonococcal infection of lower genito-urinary tract without periurethral or accessory gland abscess.

A54.1 — Gonococcal infection of lower genito-urinary tract with periurethral and accessory gland abscess.

A54.2 — Gonococcalpelviperitonitis and other gonococcalgenito-urinary infections.

A54.3 — Gonococcal infection of eye.

A54.4 — Gonococcal infection of musculoskeletal system.

A54.5 — Gonococcal pharyngitis.

A54.6 — Gonococcal infection of anus and rectum.

A54.8 — Other gonococcal infections.

A54.9 — Gonococcal infection, unspecified.

Signs and symptoms

In men, symptoms usually appear two to 14 days after infection.Most infected men with symptoms have inflammation of the penile urethra associated with a burning sensation during urination and greenish yellow or whitish discharge from the penis. In men, discharge with or without burning occurs in half of all cases and is the most common symptom of the infection.

Rare complications of gonococcal urethritis can include penile lymphangitis, penile edema («bull-headed clap»), periurethral abscesses, and postinflammatory urethral strictures (this last complication is especially rare in the antibiotic era).

Prostatitis. Most commonly there is painful urination, (dysuria), frequency, voiding small amounts, getting up more frequently at night. Other common symptoms include: pain in the head of the penis or in the testicles; pain in the groins or lower abdomen, pain behind the scrotum; discomfort or pain on erection or orgasm, decrease in sexual desire or function, tiredness or lethargy; chronic low back pain; blood in the urine, (hematuria), or semen, (hematospermia).

Epididymitis — Acute unilateral epididymitis can be a complication of gonococcal infection. Unilateral testicular pain and swelling may be the sole

presenting complaints of men with epididymitis, with concomitant urethritis often discovered during the history and physical examination. The clinical manifestations of acute infectious epididymitis are the onset of testicular pain is often accompanied by inflammation, redness, and warmth in the scrotum. If the inflammation spreads to the testicle, the condition may be reclassified as epididymo-orchitis or orchiepididymitis.

Gonorrhea symptoms in women. Gonorrhea is a major cause of urethritis and cervicitis in women; the latter can result in pelvic inflammatory disease (PID), infertility, ectopic pregnancy, and chronic pelvic pain. In some women, symptoms are so mild that they go unnoticed.

Cervicitis — The uterine cervix is the most common site of mucosal infection with N. gonorrhoeae in women. Most women with cervical gonococcal infection are asymptomatic. Thus, the incubation period of gonorrhea is less well characterized in women than men. When present, genital symptoms develop in most women within 10 days of exposure. Symptomatic infection typically manifests as vaginal pruritus and or a mucopurulent discharge. Some women may complain of intermenstrual bleeding or menorrhagia. Pain is atypical in the absence of upper tract infection. On examination, the cervix may appear normal or show signs of frank discharge. The cervical mucosa is often friable.

Urethritis — N. gonorrhoeae can be isolated from the, although urethral infection can uncommonly occur without concomitant cervical involvement. Among sexually active adolescent females, urinary symptoms alone, such as dysuria, urgency, or frequency, may be the presenting complaint. As with gonococcal cervicitis, urethral involvement is typically asymptomatic. The main symptom, when present, is dysuria.

Bartholinitis — Symptomatic involvement of Bartholin's glands, located behind the labia. Symptoms, when present, include perilabial pain and discharge, and signs may include edema of the labia and enlargement and tenderness of the gland.

Pelvic inflammatory disease — Pelvic inflammatory disease (PID) occurs in approximately 10 to 20 percent of women with cervical gonorrhea. Given the high incidence of asymptomatic gonococcal infection in women, PID can be the first presenting complaint. Symptoms of PID include pelvic, abdominal pain, abnormal vaginal bleeding, and dyspareunia. Often these symptoms occur with the onset of menses. Women with PID due to gonorrhea may appear more acutely ill and may be more likely to be febrile than women with nongonococcalsalpingitis. Signs of PID on examination include abdominal tenderness, uterine tenderness, adnexal or cervical motion tenderness.

Perihepatitis (Fitz-Hugh-Curtis syndrome) — Perihepatitis is an inflammation of the Glisson's capsule surrounding the liver and can be associated with PID. Symptoms and signs include sharp pleuritic pain localized to the right upper quadrant, which may be accompanied by nausea, vomiting, and fever. A

friction rub may be heard along the right anterior costal margin. Liver function tests are frequently normal or only mildly elevated.

Complications of pregnancy — Urogenitalgonococcal infections have been associated with chorioamnionitis, premature rupture of membranes, preterm birth, and spontaneous abortions in pregnant women. Infants born to infected mothers may have lower mean birth weight, neonatal conjunctivitis ("ophthalmianeonatorum"), pharyngitis, arthritis, and gonococcemia.

Newborns and children. Neonates may acquire N. gonorrhoeae during passage through the birth canal from contact with infected secretions. Such ocular infections are known as ophthalmianeonatorum, and are characterized by profuse, purulent ocular discharge and can lead to severe corneal perforationor scarring.

Extragenital infection — N. gonorrhoeae can infect the rectum and pharynx, although infections at these sites are typically asymptomatic. Rarely, bacteremic spread from a mucosal site and resultant disseminated infection can occur. Additionally, N. gonorrhoeae can cause an aggressive conjunctivitis in adults and adolescents that can be transmitted through non-sexual contact.

Proctitis — In men, anorectalgonococcal infections typically occur among men who have sex with men (MSM) who engage in anal receptive intercourse; they are uncommon in heterosexual men.

In women, N. gonorrhoeae can be transmitted to the anal canal via a genital infection due to the proximity of the vagina, even in the absence of receptive anal intercourse.

In both men and women, most cases of anorectalgonococcal infection are asymptomatic. Symptoms and signs of proctitis, when present, include tenesmus, anorectal pain, rectal fullness, constipation, anorectal bleeding, and mucopurulent discharge.

Pharyngitis — Gonococcal infection of the pharynx is usually acquired by oral sexual exposure. The majority of oropharyngeal infections with N. gonorrhoeae are asymptomatic, although sore throat, pharyngeal exudates, and/or cervical lymphadenitis are present in some cases.

Conjunctivitis — Gonococcal conjunctivitis mainly affects infants born to untreated mothers. In adults and adolescents, sporadic cases can occur as a result of autoinoculation from an anogenital source. Gonococcal conjunctivitis ranges from mild pauci-symptomatic infections to aggressive infections characterized by conjunctival injection, purulent discharge, and periorbital edema, which, if untreated, can progress to corneal ulceration, perforation, and blindness.

Disseminated gonococcal infection. Dissemination often leads to one of two clinical syndromes: purulent arthritis or a triad of tenosynovitis, dermatitis, and polyarthralgias. Other manifestations of disseminated bacterial infection, such as endocarditis, meningitis, and osteomyelitis, are rare.

Diagnosis. Traditionally, gonorrhea was diagnosed with gram stain and culture.

Because of its high specificity (> 99 %) and sensitivity (> 95 %), a Gram stain of a male urethral specimen that demonstrates polymorphonuclear leukocytes with intracellular Gram-negative diplococci can be considered diagnostic for infection with N. gonorrhoeae in symptomatic men. However, because of lower sensitivity, a negative Gram stain should not be considered sufficient for ruling out infection in asymptomatic men. However, newer polymerase chain reaction (PCR)-based testing methods are becoming more common. In those failing initial treatment, culture should be done to determine sensitivity to antibiotics.

Gonorrhea is ***treated*** with antibiotics. Treatment is recommended for:

- A person who has a positive gonorrhea test.
- Anyone who has had sexual contact in the past 60 days with a person diagnosed with gonorrhea, whether or not they have symptoms or used condoms.
- A newborn whose mother has gonorrhea at the time of delivery.

Resistance of Neisseria gonorrhoeae to antimicrobial agents continues to spread and intensify; the agents involved are cefixime, cefodizime, cefotaxime, cefoxitin, ceftizoxime, ceftriaxone, cefuroxime, cefuroxime axetil, ciprofloxacin, fleroxacin, norfloxacin, ofloxacin, pefloxacin, temafloxacin, azithromycin, aztreonam, netilmicin, rifampin plus erythromycin stearate, sisomicin, and spectinomycin.

CHLAMYDIA INFECTION

Synopsis

Etiology: Chlamydia trachomatis, serovars D–K.

Epidemiology: In developed countries, more common thangonococcal genital tract infection.

Clinical features: About 50 % of patients are asymptomatic; mucoid discharge in the rest.

Treatment: Azithromycin 1 g SOD14. Or doxy cycline 200 mg daily × 7 days.

Chlamydia infection is a common sexually transmitted infection in humans caused by the bacterium Chlamydia trachomatis. The term Chlamydia infection can also refer to infection caused by any species belonging to the bacterial family Chlamydiaceae. C. trachomatis is found only in humans. Chlamydia is a major infectious cause of human genital and eye disease. Chlamydia infection is one of the most common sexually transmitted infections worldwide.

C. trachomatis is naturally found living only inside human cells. Chlamydia can be transmitted during vaginal, anal, or oral sex, and can be passed from an infected mother to her baby during childbirth. Between half and three-quarters of all women who have a chlamydia infection of the cervix (cervicitis) have no symptoms and do not know that they are infected.

Both sexes can display urethritis, proctitis (rectal disease and bleeding), trachoma, and infertility. In men, infection of the urethra (urethritis) is usually symptomatic, causing a white discharge from the penis with or without pain on urinating (dysuria).Occasionally, the condition spreads to the upper genital tract (causing prostatitis and epididymitis in men, in women, cervicitis, pelvic inflammatory disease (PID), ectopic pregnancy, and acute or chronic pelvic pain are frequent complications).

Neonates born to infected mothers are also susceptible to infections of the eye (conjunctivitis) and lung.

Chlamydia trachomatis, an obligate intracellular human pathogen. C.trachomatis is a gram-negative bacterium.

C. trachomatis includes three human biovars: serovars Ab, B, Ba, or C–cause trachoma: infection of the eyes, which can lead to blindness; serovars D-K — cause urethritis, pelvic inflammatory disease, ectopic pregnancy, neonatal pneumonia, and neonatal conjunctivitis; serovars L1, L2 and L3 — lymphogranulomavenereum (LGV). Chlamydia can exchange DNA between its different strains, thus the evolution of new strains is common.

The bacteria have a two-phase life cycle (figure 1). The infectious form is known as the elementary body, which enters host cells through endocytosis. Replication through binary fission occurs inside the host cell, using host-derived adenosine triphosphate, with formation of reticulate bodies. Large intracytoplasmic inclusions inside cells are made up of hundreds of reticulate bodies, which then convert back to infectious elementary bodies to be released from the cell.

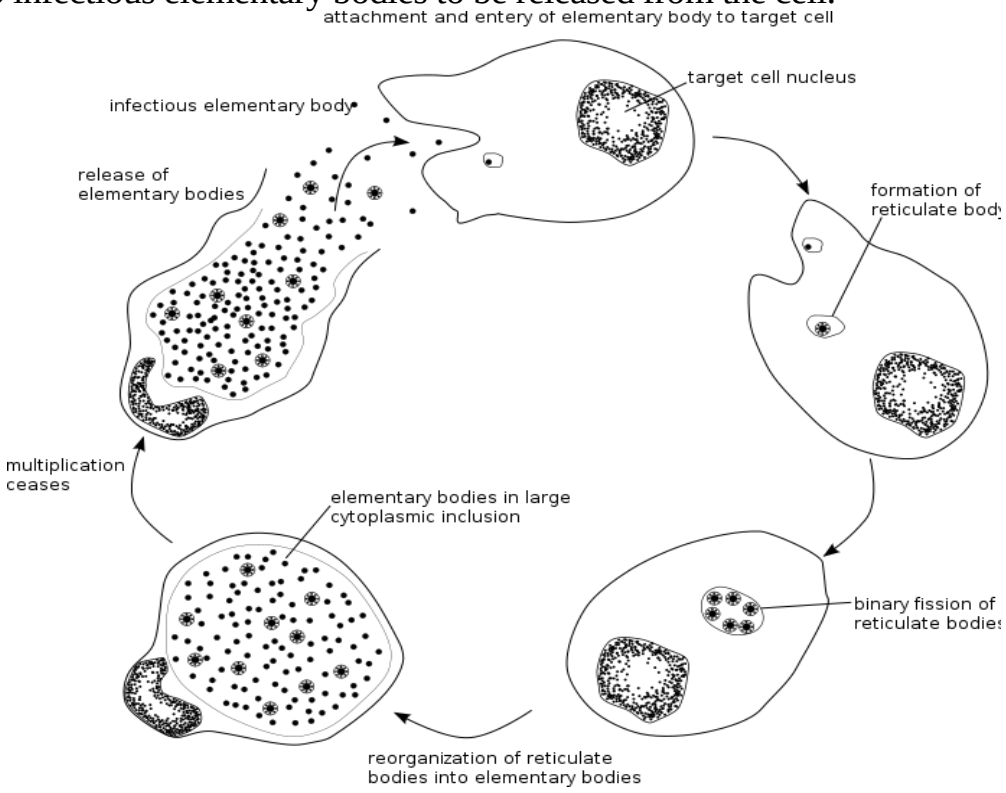

Figure 1 — Life-cycle of Chlamydia (Wikipedia)

International Classification of Diseases, Revision 10 (1990)

A56 — Other sexually transmitted chlamydial diseases.
A56.0 — Chlamydial infection of lower genito-urinary tract.
A56.1 — Chlamydial infection of pelviperitoneum and other genito-urinary organs.
A56.2 — Chlamydial infection of genito-urinary tract, unspecified.
A56.3 — Chlamydial infection of anus and rectum.
A56.4 — Chlamydial infection of pharynx.
A56.8 — Sexually transmitted chlamydial infection of other sites.
(A70-A74) — Other diseases caused by chlamydiae.
A70 — Chlamydia psittaci infection.
A71 — Trachoma.
A71.0 — Initial stage of trachoma.
A71.1 — Active stage of trachoma.
A71.9 — Trachoma, unspecified.
A74 — Other diseases caused by chlamydiae.
A74.0 — Chlamydial conjunctivitis.
A74.8 — Other chlamydial diseases.
A74.9 — Chlamydial infection, unspecified.

Signs and symptoms

Incubation period — 1–5 weeks.Chlamydial cervicitis in a female patient characterized by mucopurulent cervical discharge, erythema, and inflammation. Male patients may develop a white, cloudy or watery discharge (shown) from the tip of the penis.

Women. Chlamydial infection of the neck of the womb (cervicitis) is a sexually transmitted infection which is asymptomatic for about 50–70 % of women infected with the disease. The infection can be passed through vaginal, anal, or oral sex. Of those who have an asymptomatic infection that is not detected by their doctor, approximately half will develop pelvic inflammatory disease (PID), a generic term for infection of the uterus, fallopian tubes, and/or ovaries. PID can cause scarring inside the reproductive organs, which can later cause serious complications, including chronic pelvic pain, difficulty becoming pregnant, ectopic (tubal) pregnancy, and other dangerous complications of pregnancy.

Chlamydia is known as the «Silent Epidemic» because in women, it may not cause any symptoms in 70–80 % of cases, and can linger for months or years before being discovered. Symptoms that may occur include unusual vaginal bleeding or discharge, pain in the abdomen, painful sexual intercourse (dyspareunia), fever, painful urination or the urge to urinate more frequently than usual (urinary urgency).

Men. In men, chlamydia shows symptoms of infectious urethritis (inflammation of the urethra) in about 50 % of cases. Symptoms that may occur include: a

painful or burning sensation when urinating, an unusual discharge from the penis, swollen or tender testicles, or fever. Discharge, or the purulent exudate, is generally less viscous and lighter in color than for gonorrhea. If left untreated, it is possible for chlamydia in men to spread to the testicles causing epididymitis, which in rare cases can cause sterility if not treated within 6 to 8 weeks. Chlamydia is also a potential cause of prostatitis in men, although the exact relevance in prostatitis is difficult to ascertain due to possible contamination from urethritis.

Eye disease. The infection can be spread from eye to eye by fingers, shared towels or cloths, coughing and sneezing and eye-seeking flies. Newborns can also develop chlamydia eye infection through childbirth.

Newborns may develop conjunctivitis and pneumonia after being infected from passage through the birth canal of an infected mother. Signs of ophthalmianeonatorum may include injected conjunctivae, purulent discharge, or swollen eyelids. Subacute, afebrile pneumonia as a consequence of neonatal chlamydialinfection usually presents after 1–3 months. Symptoms include cough and wheezing. Animal experiments suggest that neonatal respiratory chlamydial infection predisposes to asthma later in life.

Perinatal infections. As many as half of all infants born to mothers with chlamydia will be born with the disease. Chlamydia can affect infants by causing spontaneous abortion; premature birth; conjunctivitis, which may lead to blindness; and pneumonia. Conjunctivitis due to chlamydia typically occurs one week after birth.

Rheumatological conditions. Chlamydia may also cause reactive arthritis (**REITER'S SYNDROME**) — the triad of arthritis, conjunctivitis and urethritis (inflammation of the urethra) — especially in young men.

Laboratory tests

- Nucleic acid amplification tests (NAAT). These tests find the genetic material (DNA) of Chlamydia bacteria. These tests are the most sensitive tests available, meaning that they are very accurate and that they are very unlikely to have false-negative test results. A polymerase chain reaction (PCR) test is an example of a nucleic acid amplification test. This test can also be done on a urine sample.
- Nucleic acid hybridization tests (DNA probe test). A probe test also finds chlamydia DNA. A probe test is very accurate but is not as sensitive as nucleic acid amplification tests.
- Enzyme-linked immunosorbent assay (ELISA, EIA) is a test that uses antibodies and color change to identify chlamydia.
- Direct fluorescent antibody test (DFA). This quick test also finds Chlamydia antigens.
- Chlamydia cell culture. A test in which the suspected chlamydia sample is grown in a vial of cells. The pathogen infects the cells and after a set incubation time (48 hours) the vials are stained and viewed on a fluorescent light mi-

croscope. Cell culture is more expensive and takes longer (two days) than the other tests. The culture must be grown in a laboratory.

Treatment. C. trachomatis may be treated with any of several bacteriostatic antibiotics: macrolides (azithromycin, clarithromycin, erythromycin, etc) or tetracyclines (doxycycline, tetracycline, etc).

REITER'S DISEASE

Reactive arthritis is classified as an autoimmune condition that develops in response to an infection in another part of the body (cross-reactivity). Coming into contact with bacteria and developing an infection can trigger the disease. By the time the patient presents with symptoms, often the "trigger" infection has been cured or is in remission in chronic cases, thus making determination of the initial cause difficult. The arthritis often is coupled with other characteristic symptoms; this is called Reiter's syndrome, Reiter's disease or Reiter's arthritis. The manifestations of reactive arthritis include the following triad of symptoms: an inflammatory arthritis of large joints, inflammation of the eyes in the form of conjunctivitis or uveitis, and urethritis in men or cervicitis in women. Arthritis occurring alone following sexual exposure or enteric infection is also known as reactive arthritis. Patients can also present with mucocutaneous lesions, as well as psoriasis-like skin lesions such as circinatebalanitis, and keratodermablennorrhagicum. Enthesitis can involve the Achilles tendon resulting in heel pain. Not all affected persons have all the manifestations.

The clinical pattern of reactive arthritis commonly consists of an inflammation of fewer than five joints which often includes the knee or sacroiliac joint. The arthritis may be «additive» (more joints become inflamed in addition to the primarily affected one) or «migratory» (new joints become inflamed after the initially inflamed site has already improved).

Reactive arthritis is an RF-seronegative, HLA-B27-linked arthritis often precipitated by genitourinary or gastrointestinal infections. The most common triggers are intestinal infections (with Salmonella, Shigella or Campylobacter) and sexually transmitted infections (with Chlamydia trachomatis). It most commonly strikes individuals aged 20–40 years of age, is more common in men than in women, and more common in white than in black people. This is owing to the high frequency of the HLA-B27 gene in the white population. It can occur in epidemic form. Patients with HIV have an increased risk of developing reactive arthritis as well.

Signs and symptoms

Because common systems involved include the eye, the urinary system, and the hands and feet, one clinical mnemonic in reactive arthritis is «Can't see, can't pee, can't climb a tree». The classic triad consists of:

- Nongonococcal urethritis.

- Asymmetric oligoarthritis.
- Conjunctivitis.

Symptoms generally appear within 1–3 weeks but can range from 4 to 35 days from the onset of the inciting episode of the disease.

The classical presentation of the syndrome starts with urinary symptoms such as burning pain on urination (dysuria) or an increased frequency of urination. Other urogenital problems may arise such as prostatitis in men and cervicitis, salpingitis and/or vulvovaginitis in women.

It presents with monoarthritis affecting the large joints such as the knees and sacroiliac spine causing pain and swelling. An asymmetrical inflammatory arthritis of interphalangeal joints may be present but with relative sparing of small joints such as the wrist and hand.

Patient can have enthesitis presenting as heel pain, Achilles tendinitis or plantar fasciitis, along with balanitiscircinata (circinatebalanitis), which involves penile lesions present in roughly 20 to 40 percent of the men with the disease.

A small percentage of men and women develop small hard nodules called keratodermablennorrhagicum on the soles of the feet and, less commonly, on the palms of the hands or elsewhere. The presence of keratodermablennorrhagica is diagnostic of reactive arthritis in the absence of the classical triad. Subcutaneous nodules are not a feature.

Ocular involvement (mild bilateral conjunctivitis) occurs in about 50% of men with urogenital reactive arthritis syndrome and about 75% of men with enteric reactive arthritis syndrome. Conjunctivitis and uveitis can include redness of the eyes, eye pain and irritation, or blurred vision. Eye involvement typically occurs early in the course of reactive arthritis, and symptoms may come and go.

Mucocutaneous lesions can be present. Common findings include oral ulcers that come and go. In some cases, these ulcers are painless and go unnoticed. In the oral cavity, the patients may suffer from recurrent aphthous stomatitis, geographic tongue and migratory stomatitis in higher prevalence than the general population.

Some patients suffer serious gastrointestinal problems similar to those of Crohn's disease.

About 10 percent of people with reactive arthritis, especially those with a prolonged course of the disease, will develop cardiac manifestations, including aortic regurgitation and pericarditis. Reiter's syndrome has been described as a precursor of other joint conditions, including ankylosing spondylitis.

Diagnosis

- There are few clinical symptoms, but the clinical picture is dominated by arthritis in one or more joints, resulting in pain, swelling, redness, and heat sensation in the affected areas.
- The diagnosis of genital chlamydial infections.

• Tests for C-reactive protein and erythrocyte sedimentation rate are nonspecific tests that can be done to corroborate the diagnosis of the syndrome.

• A blood test for the genetic marker HLA-B27 may also be performed.

Treatment. The main goal of treatment is to identify and eradicate the underlying infectious source with the appropriate antibiotics if still present. Otherwise, treatment is symptomatic for each problem. Nonspecific urethritis may be treated with a short course of tetracycline. Analgesics, particularly NSAIDs, are used. Steroids, sulfasalazine and immunosuppressants may be needed for patients with severe reactive symptoms that do not respond to any other treatment. Local corticosteroids are useful in the case of iritis.

MYCOPLASMA INFECTION

Synopsis

Etiology: genera Mycoplasma and Ureaplasma.

Epidemiology: In developed countries, more common thangonococcal genital tract infection.

Clinical features: About 50 % of patients are asymptomatic; mucoid discharge in the rest.

Treatment: Azithromycin ,doxycycline, levofloxacin.

The Mycoplasmataceae is a family of bacteria in the order Mycoplasmatales. This family comprises the genera Mycoplasma and Ureaplasma.

Mycoplasma is a genus of bacteria that lack a cell wall around their cell membrane. Without a cell wall, they are unaffected by many common antibiotics such as penicillin or other beta-lactam antibiotics that target cell wall synthesis. They can be parasitic or saprotrophic. Several species are pathogenic in humans, including M. pneumoniae, which is an important cause of atypical pneumonia and other respiratory disorders, and M. genitalium, which is believed to be involved in pelvic inflammatory diseases.

Mycoplasma are the smallest bacterial cells yet discovered, can survive without oxygen and are typically about 0.1 μm in diameter.

Ureaplasma is a genus of bacteria belonging to the family Mycoplasmataceae. As the name imples, ureaplasma is urease positive.

Mycoplasma hominis is a species of bacteria in the genus Mycoplasma. Along with ureaplasmas, mycoplasmas are the smallest free-living organisms known. They have no cell wall and therefore do not Gram stain. M. hominis is associated with pelvic inflammatory disease and bacterial vaginosis. This species causes a sexually transmitted infection.

Mycoplasma genitalium is a small pathogenic bacterium that lives on the ciliated epithelial cells of the urinary and genital tracts in humans. It is a sexual-

ly transmitted pathogen which can cause significant morbidity in men and women, and is a co-factor in HIV transmission.

International Classification of Diseases, Revision 10 (1990)
A49.3 — Mycoplasma infection, unspecified.

Signs and symptoms. Four genital mycoplasmas, M. hominis, M. genitalium and Ureaplasma spp. have been associated with a large variety of illnesses but have been demonstrated as a cause only for a few clinical conditions.

M. hominis has been associated with various pathological conditions. The most frequent are genital infections in women but not in men. M. hominis is not responsible for cervicitis. It can be involved in pelvic inflammatory disease but PID are usually considered to be a multibacterial infection in which M. hominis is probably acting as a secondary agent.

M. hominis is one of the organisms that proliferate during the course of bacterial vaginosis, associated with Gardnerellavaginalisand anaerobes, but its contribution to the pathological process is unknown.

M. hominis is responsible for infections related to pregnancy. It has been isolated from the amniotic fluid of women with chorioamnionitis and there is strong evidence of involvement in post-partum or post-abortum fever generally secondary to endometritis.

M. hominis has also been associated with extragenital infections.

Ureaplasmaspp., particularly U. urealyticum, are causes of non-gonococcal urethritis (NGU) in men. They play a minimal and uncertain role in prostatitis and epididymitis as well in cystitis, pyelonephritis and urinary calculi.Ureaplasma spp. can be found in the mucosal surfaces of the cervix or vagina of sexually mature asymptomatic women.

Ureaplasmas and mycoplasmas can be important pathogens in individuals with immunodeficiency. Ureaplasma spp. can cause invasive disease of the joints, especially in individuals with antibody deficiencies but non only. There is also some evidence that Ureaplasma spp. are involved in reactive arthritis.

Infection with M. genitalium generally produces severe clinical symptom, or a combination of symptoms; but sometimes can be asymptomatic. It causes inflammation in the urethra (urethritis) both in men and women, which is associated with mucopurulent discharge in the urinary tract, and burning while urinating. In women, it causes cervicitis and pelvic inflammatory diseases, including endometritis and salpingitis. It is also supected with tubal factor infertility. Unlike other Mycoplasma, the infection is not associated with bacterial vaginosis. It is highly associated with the intensity of HIV infection. It is also suspected to play a role in the development of prostate and ovarian cancers and lymphomas. There is a consistent association of M. genitalium infection and female reproductive tract syndromes. M. genitalium infection was significantly associated with increased risk of preterm birth, spontaneous abortion, cervicitis, and pelvic inflammatory disease. Infertility risk is also strongly associate with infection with M. gentalium.

Laboratory examinant. Mycoplasma cells are physically small — less than 1 μm — and they are therefore difficult to detect with a conventional microscope. Both M hominis and U urealyticum can be detected in culture using specialized media and techniques within 2–5 days. These organisms can also be detected by PCR assays. M genitalium requires a PCR assay due to its slow.

Treatment. The U.S. Centers for Disease Control and Prevention has one specific recommended regimen, with azithromycin and another specific recommended regimen with doxycycline. As alternative regimens, the agency has specific regimens each with erythromycin or erythromycin ethylsuccinate or ofloxacin or levofloxacin.

TRICHOMONIASIS

Synopsis

Etiology: protozoan parasite Trichomonasvaginalis.

Epidemiology: Worldwide, it has beenestimated to affect more than 180 million women.

Clinical features: Men are usually asymptomatic. Women — vaginal discharge, vulvar pruritus,swelling and erythema, dyspareunia, lower abdominal discomfort, or dysuria.

Treatment: Nitroimidazoles — metronidazole and tinidozoleare.

Trichomoniasis is a common cause of vaginitis. It is a sexually transmitted infection, and is caused by the single-celled protozoan parasite Trichomonasvaginalis producing mechanical stress on host cells and then ingesting cell fragments after cell death. Trichomoniasis is primarily an infection of the urogenital tract; the most common site of infection is the urethra and the vagina in women.

Unlike other parasitic protozoa, Trichomonasvaginalis exists in only one morphological stage, a trophozoite, and cannot encyst. The T. vaginalistrophozoite is oval as well as flagellated, or «pear» shaped as seen on a wet-mount. It is slightly larger than a white blood cell, measuring 9 × 7 μm. Five flagella arise near the cytostome. While T. vaginalis does not have a cyst form, organisms can survive for up to 24 hours in urine, semen, or even water samples.

International Classification of Diseases, Revision 10 (1990)
A59 — Trichomoniasis.
A59.0 — Urogenital trichomoniasis.
A59.8 — Trichomoniasis of other sites.
A59.9 — Trichomoniasis, unspecified.

Signs and symptoms. Women who are infected may complain of a malodorous, yellow–green vaginal discharge, vulvar pruritus, swelling and erythema, dyspareunia, lower abdominal discomfort, or dysuria. Infection tends to occur in

sexually active women and men. Men are usually asymptomatic, although some may complain of urethral discharge and dysuria or urinary frequency. Both men and women may be asymptomatic carriers. Newborns may become infected from passage through the birth canal of an infected mother. Infection in a child may be a sign of sexual abuse.

Complications.

- Trichomoniasis is associated with increased risk of transmission and infection of HIV.
- Trichomoniasis may cause a woman to deliver a low-birth-weight or premature infant.
- Evidence implies that infection in males potentially raises the risks of prostate cancer development and spread due to inflammation.

Laboratory examinant. There are three main ways to test for Trichomoniasis.

- The first is known as saline microscopy. This is the most commonly used method and requires an endocervical, vaginal, or penile swab specimen for examination under a microscope. The presence of one or multiple trichomonads constitutes a positive result. This method is cheap but has a low sensitivity often due to an inadequate sample, resulting in false negatives.
- The second method includes the nucleic acid amplification tests.
- The thirddiagnostic method is culture; however, sensitivity is still somewhat low.

Treatment for both pregnant and non-pregnant patients usually utilizes metronidazole (metronidazole tablets must not be taken during the first 3 months of pregnancy), but with caution especially in early stages of pregnancy 2000 mg by mouth once. Sexual partners, even if asymptomatic, should be treated concurrently.

LYMPHOGRANULOMA VENEREUM

Synopsis

Etiology: Chlamydia trachomatis serovars L1, L2, and L3.

Clinical features: Genital lesion not noticed. Presenting feature is enlargement of inguinal, femoral, and sometimes external iliac group of lymp nodes. Sign of groove characteristic.

Complications: Esthiomene.

Treatment: Doxycycline (200 mg) or erythromycin base (2 g) daily for 21 days. Aspiration of buboes.

Lymphogranulomavenereum LGV(also known as "Climatic bubo,") is a sexually transmitted disease caused by the invasive serovars L1, L2, L2a or L3 of Chlamydia trachomatis.

LGV is primarily an infection of lymphatics and lymph nodes. Chlamydia trachomatis is the bacterium responsible for LGV. It gains entrance through breaks in the skin, or it can cross the epithelial cell layer of mucous membranes. The organism travels from the site of inoculation down the lymphatic channels to multiply within mononuclear phagocytes of the lymph nodes it passes.

LGV was first described by Wallace in 1833 and again by Durand, Nicolas, and Favre in 1913. Since the 2004 Dutch outbreak many additional cases have been reported, leading to greater surveillance. Soon after the initial Dutch report, national and international health authorities launched warning initiatives and multiple LGV cases were identified in several more European countries (Belgium, France, the UK, Germany, Sweden, Italy and Switzerland) and the US and Canada. All cases reported in Amsterdam and France and a considerable percentage of LGV infections in the UK and Germany were caused by a newly discovered Chlamydia variant, L2b, a.k.a. the Amsterdam variant. The L2b variant could be traced back and was isolated from anal swabs of MSM who visited the STI city clinic of San Francisco in 1981. This finding suggests that the recent LGV outbreak among MSM in industrialised countries is a slowly evolving epidemic. The L2b serovar has also been identified in Australia.

International Classification of Diseases, Revision 10 (1990)

A55 — Chlamydial lymphogranuloma (venereum).

Signs and symptoms. The clinical manifestation of LGV depends on the site of entry of the infectious organism (the sex contact site) and the stage of disease progression.

Inoculation at the mucous lining of external sex organs (penis and vagina) can lead to the inguinal syndrome named after the formation of buboes or abscesses in the groin (inguinal) region where draining lymph nodes are located. These signs usually appear by 3 days to a month after exposure.

The rectal syndrome arises if the infection takes place via the rectal mucosa (through anal sex) and is mainly characterized by proctocolitis symptoms.

The pharyngeal syndrome is rare. It starts after infection of pharyngeal tissue, and buboes in the neck region can occur.

Primary stage. LGV may begin as a self-limited painless genital ulcer that occurs at the contact site 3–12 days after infection. Women rarely notice a primary infection because the initial ulceration where the organism penetrates the mucosal layer is often located out of sight, in the vaginal wall. In men fewer than 1/3 of those infected notice the first signs of LGV. This primary stage heals in a few days. Erythema nodosum occurs in 10 % of cases.

The secondary stage most often occurs 10–30 days later, but can present up to six months later. The infection spreads to the lymph nodes through lymphatic drainage pathways. The most frequent presenting clinical manifestation of LGV among males whose primary exposure was genital is unilateral (in 2/3 of cases) lymphadenitis and lymphangitis, often with tender inguinal and/or femoral lym-

phadenopathy because of the drainage pathway for their likely infected areas. Lymphangitis of the dorsal penis may also occur and resembles a string or cord. If the route was anal sex the infected person may experience lymphadenitis and lymphangitis noted above. They may instead develop proctitis, inflammation limited to the rectum (the distal 10–12 cm) that may be associated with anorectal pain, tenesmus, and rectal discharge, or proctocolitis, inflammation of the colonic mucosa extending to 12 cm above the anus and associated with symptoms of proctitis plus diarrhea or abdominal cramps.

In addition, symptoms may include inflammatory involvement of the perirectal or perianal lymphatic tissues. In females, cervicitis, perimetritis, or salpingitis may occur as well as lymphangitis and lymphadenitis in deeper nodes. Because of lymphatic drainage pathways, some patients develop an abdominal mass which seldom suppurates, and 20–30 % develop inguinal lymphadenopathy. Systemic signs which can appear include fever, decreased appetite, and malaise. Diagnosis is more difficult in women and men who have sex with men (MSM) who may not have the inguinal symptoms.

The third stage of LGV. Over the course of the disease, lymph nodes enlarge, as may occur in any infection of the same areas as well. Enlarged nodes are called buboes. Buboes are commonly painful. Nodes commonly become inflamed, thinning and fixation of the overlying skin. These changes may progress to necrosis, fluctuant and suppurative lymph nodes, abscesses, fistulas, strictures, and sinus tracts. During the infection and when it subsides and healing takes place, fibrosis may occur. This can result in varying degrees of lymphatic obstruction, chronic edema, and strictures. These late stages characterised by fibrosis and edema are also known as the third stage of LGV and are mainly permanent.

The diagnosis usually is made serologically (through complement fixation) and by exclusion of other causes of inguinal lymphadenopathy or genital ulcers. Serologic testing has a sensitivity of 80 % after 2 weeks. Serologic testing may not be specific for serotype (has some cross reactivity with other chlamydia species) and can suggest LGV from other forms because of their difference in dilution, 1:64 more likely to be LGV and lower than 1:16 is likely to be other chlamydia forms.

For identification of serotypes, culture is often used. Culture is difficult. Requiring a special medium, cycloheximide-treated McCoy or HeLa cells, and yields are still only 30–50 %. DFA, or direct fluorescent antibody test, PCR of likely infected areas and pus, are also sometimes used.

If polymerase chain reaction (PCR) tests on infected material are positive, subsequent restriction endonuclease pattern analysis of the amplified outer membrane protein A gene can be done to determine the genotype.

Recently a fast realtime PCR (Taqman analysis) has been developed to diagnose LGV.With this method an accurate diagnosis is feasible within a day. It has been noted that one type of testing may not be thorough enough.

Differential diagnosis

The bubo of LGV should be differentiated from chancroid (table 2).

Table 2 — Differential diagnosis The bubo of LGV and chancroid

	Chancroid	LGV
Genital ulcer	Present	Transient or absent
Number of groups	Usually single group enlarged	Multiple groups of lymph nodes enlarged; enlargement of inguinal and femoral groups results in sign of groove
Sinus mouth	Ruptures to form chancroidal ulcer at the mouth	Ruptures to form multiple sinuses with undermined edge
Constitutional symptoms	Occasional	Frequent

Treatment involves antibiotics and may involve drainage of the buboes or abscesses by needle aspiration or incision. Further supportive measure may need to be taken: dilatation of the rectal stricture, repair of rectovaginal fistulae, or colostomy for rectal obstruction.

Common antibiotic treatments include: tetracycline (doxycycline) (all tetracyclines, including doxycycline, are contraindicated during pregnancy and in children due to effects on bone development and tooth discoloration), and erythromycin.

CHANCROID

Synopsis

Etiology: Haemophilusducreyi.

Incubation period: 3–5 days.

Morphology: Multiple, tender, ragged ulcers which bleed on manipulation.

Lymphadenopathy: Tender, inflammatory inguinal nodes (buboes) which may suppurate to form chancroid-like ulcers.

Investigations: Diagnosis based on clinical features as laboratory tests neither specific nor sensitive.

Treatment: Azithromycin, 1 g single dose. Or ceftriaxone, 250 mg intramuscular, single dose. Or ciprofloxacin, 1 g daily × 3 days; erythromycin base, 1.5 g daily × 7 days.Aspiration or incision and drainage (nondependent) of fluctuant buboes.

Chancroid (also known as soft chancre and ulcusmolle) is a bacterial sexually transmitted infection characterized by painful sores on the genitalia. Chan-

croid is known to spread from one individual to another solely through sexual contact.

Causes. Chancroid is a bacterial infection caused by the fastidious Gram-negative streptobacillusHaemophilusducreyi. It is a disease found primarily in developing countries, most prevalent in low socioeconomic groups, associated with commercial sex workers.

Infection levels are very low in the Western world, typically around one case per two million of the population (Canada, France, Australia, UK and US). Most individuals diagnosed with chancroid have visited countries or areas where the disease is known to occur frequently, although outbreaks have been observed in association with crack cocaine use and prostitution.

Chancroid is a risk factor for contracting HIV, due to their ecological association or shared risk of exposure, and biologically facilitated transmission of one infection by the other.

Pathogenesis. H. ducreyi enters skin through microabrasions incurred during sexual intercourse. A local tissue reaction leads to development of erythomatous papule, which progresses to pustule in 4–7 days. It then undergoes central necrosis to ulcerate.

International Classification of Diseases, Revision 10 (1990)

A57 — Chancroid

Signs and symptoms. Buboes in a male. These are only local and no systemic manifestations are present. The ulcer characteristically:

- Ranges in size dramatically from 3 to 50 mm (1/8 inch to two inches) across.
- Is painful.
- Has sharply defined, undermined borders.
- Has irregular or ragged borders.
- Has a base that is covered with a gray or yellowish-gray material.
- Has a base that bleeds easily if traumatized or scraped.
- Pinful lymphadenopathy occurs in 30 to 60 % of patients.
- Dysuria (pain with urination) and dyspareunia (pain with intercourse) in females.
- About half of infected men have only a single ulcer. Women frequently have four or more ulcers, with fewer symptoms.
- The initial ulcer may be mistaken as a "hard" chancre, the typical sore of primary syphilis, as opposed to the "soft chancre" of chancroid.
- Approximately one-third of the infected individuals will develop enlargements of the inguinal lymph nodes.
- Half of those who develop swelling of the inguinal lymph nodes will progress to a point where the nodes rupture through the skin, producing draining abscesses.

Location of ulcers

Males:

- Internal and external surface of prepuce.
- Coronal sulcus.
- Frenulum.
- Shaft of penis.
- Prepucial orifice.
- Urethral meatus.
- Glans penis.

Females:

- Labia majora is most common site. "Kissing ulcers" may develop. These are ulcers that occur on opposing surfaces of the labia.
- Labia minora.
- Fourchette.
- Vestibule.
- Clitoris.
- Perineal area.
- Inner thighs.

Complications:

• Extensive adenitis may develop.

• Large inguinal abscesses may develop and rupture to form draining sinus or giant ulcer.

• Superinfection by Fusarium and Bacteroides. These later require debridement and may result in disfiguring scars.

• Phimosis can develop in long standing lesion by scarring and thickening of foreskin, which may subsequently require circumcision.

Laboratory findings. From bubo pus or ulcer secretions, H. ducreyi can be identified. PCR-based identification of organisms is available. Simple, rapid, sensitive and inexpensive antigen detection methods for H. ducreyi identification are also popular. Serologic detection of H. ducreyi is and uses outer membrane protein and lipooligosaccharide.

Differential diagnosis. Ulcer of chancroid should be differentiated from:

- Primary syphilis.
- Donovanosis (table 5).
- Herpes genitalis (table 3).

Bubo of chancroid should be differentiated from:

- Bubo of lymphogranulomavenereum (table 2).

Comparison with primarysyphilis. There are many differences and similarities between the conditions syphilitic chancre and chancroid.

- Similarities.
- Both originate as papules at the site of inoculation, and progress to ulcerated lesions.

- Both lesions are typically 1–2 cm in diameter.
- Both lesions are caused by sexually transmissible organisms.
- Both lesions typically appear on the genitals of infected individuals.
- Both lesions can be present at multiple sites and with multiple lesions.

✓ Differences

- Chancre is a lesion typical of infection with the bacterium that causes syphilis, Treponemapallidum.
- Chancroid is a lesion typical of infection with the bacterium Haemophilusducreyi.
- Chancres are typically painless, whereas chancroid are typically painful.
- Chancres are typically non-exudative, whereas chancroid typically have a grey or yellow purulent exudate.
- Chancres have a hard (indurated) edge, whereas chancroid have a soft edge.
- Chancres heal spontaneously within three to six weeks, even in the absence of treatment.
- Chancres can occur in the pharynx as well as on the genitals.

Table 3 — Differential diagnosis chancroid from Herpes genitalis

	Chancroid	Herpes genitalis
History	No history of vesiculation But of tiny pustules	Grouped vesicles which rupture to form polycyclic erosions
Lymphadenopathy	Inflammatory bubo which ruptures	Lymph nodes enlarged. Do not rupture

Treatment. A single oral dose (1 gram) of azithromycin, or a single IM dose of ceftriaxone, or oral erythromycin for seven days.

H. ducreyi is resistant to sulfonamides, tetracyclines, penicillins, chloramphenicol, ciprofloxacin, ofloxacin, trimethoprim and aminoglycosides. Recently, several erythromycin resistant isolates have been reported.

DONOVANOSIS

Synonyms: Granuloma venereum, granuloma inguinale.

Synopsis

Etiology: Klebsiellagranulomatis.

Morphology: Single or few, asymptomatic ulcers with an elevated, serpiginous edge, and beefy red floor.

Subcutaneous nodules (pseudobuboes) in inguinal region may ulcerate. No lymphadenopathy.

Sites: Genital and perianal areas.

Complications: Large deforming lesions; malignant transformation.

Investigations: Tissue smear and histopathology show organisms as bipolar intracellular inclusions.

Treatment: Doxycycline (200 mg daily) or azithromycin (1 g once a week) for 3 weeks.

Donovanosis (granuloma inguinale)is a bacterial disease caused by Klebsiella (Calymmatobacterium) granulomatis characterized by ulcerative genital lesions.

Transmission. The microorganism spreads from one host to another through contact with the open sores.

International Classification of Diseases, Revision 10 (1990).

A58 — Granuloma inguinale.

Symptoms. Small, painless nodules appear aft about 10–40 days of the contact with the bacteria. Later the nodules burst, creating open, fleshy, oozing lesionsfnd ulcers.

Morphology of lesions

- Single (sometimes multiple), asymptomaticulcer(s).
- Floor is made of beefy, exuberant granulationtissue which bleeds easily on manipulation.
- Border is elevated and has a serpiginous outline.

Location of ulcers. The lesions occur at the region of contact typically found on the glans, prepuce shaft of the penis, perianal area, and penoscrotal junction by males; the labiamajora, monsveneris, and perianal area by females. Rarely, the vaginal wall or cervix is the site of the lesion. At least one case in India led to partial auto-amputation of the penis.

Lymphadenopathy not seen. Sometimes subcutaneous swellings appear in the inguinal region (pseudobuboes) and these may ulcerate to form typical ulcers of donovanosis.

The infection spreads, mutilating the infected tissue. The infection will continue to destroy the tissue until treated.

Complications

- Giant ulcers.
- Destruction and deformity of genitalia.
- Rarely, malignant transformation.

The disease often goes untreated because of the scarcity of medical treatment in the countries in which it is found. In addition, the painless genital ulcers can be mistaken for syphilis. The ulcers ultimately progress to destruction of internal and external tissue, with extensive leakage of mucus and blood from the

highly vascular lesions. The destructive nature of donovanosis also increases the risk of superinfection by other pathogenic microbes.

Diagnosis. The diagnosis is based on the patient's sexual history and on physical examination revealing a painless, "beefy-red ulcer" with a characteristic rolled edge of granulation tissue. In contrast to syphilitic ulcers, inguinal lymphadenopathy is generally mild or absent.

Tissue biopsy and Wright-Giemsa stain (made from a piece of crushed ulcer tissue) is used to aid in the diagnosis. The presence of Donovan bodies in the tissue sample confirms donovanosis. Donovan bodies are rod-shaped, oval organisms that can be seen in the cytoplasm of mononuclear phagocytes or histiocytes in tissue samples from patients with granuloma inguinale. They appear deep purple when stained with Wright's stain.These intracellular inclusions are the encapsulated gram-negative rods of the causative organisms. They were discovered by Charles Donovan.

Differential diagnosis.

Donovanosis should be differentiated from:

1. Chancre (table 4).
2. Chancroid (table 5).

Table 4 — Differential diagnosis donovanosis from chancre

	Chancre	Donovanosis
Base	Indurated	Firm
Floor	Clean floor	Beefy red floor of granulation tissue
On pressure	Oozes serum	Bleeds on manipulation
Edge	Well-defined	Elevated and serpiginous
Lymphadenopathy	Shotty	No lymphadenopathy

Table 5 — Differential diagnosis donovanosis from chancroid

	Chancroid	Donovanosis
Symptoms	Painful	Asymptomatic
Number	Multiple lesions	Single–few lesions
Base	Soft	Firm
Floor	Dirty looking, which bleeds on touch	Beefy red floor, which bleeds on touch
Lymphadenopathy	Bubo	No lymphadenopathy

Treatment. Three weeks of treatment with erythromycin, streptomycin, or tetracycline, or 12 weeks of treatment with ampicillin are standard forms of therapy. Normally, the infection will begin to subside within a week of treatment, but the full treatment period must be followed in order to minimize the possibility of relapse.

CUTANEOUS MANIFESTATIONS OF HUMAN IMMUNODEFICIENCY VIRUS DISEASE

Synopsis

• As of 2008, more than 30 million people were living with HIV infection/AIDS.

• HIV-1 and HIV-2 are human lymphotropic retroviruses that principally infect CD4+ T lymphocytes and CD4+ cells of monocytic lineage.

• An individual is deemed to have AIDS if he or she is HIV-seropositive with a CD4+ T cell count < 200/μL, a CD4+ T cell percentage < 14, or anyof several diseases deemed to be indicative of a severe defect in cell mediated immunity.

• The broad and diverse spectrum ofdermatologic disease in HIV infection/AIDS includes inflammatory, infectious, neoplastic, and medication-related disorders.

• Specific stages of HIV disease (acute HIV syndrome, immune reconstitution, clinically latent disease, and advanced disease) tend to be associated with different dermatologic disorders.

• Dermatologic disease may help to estimate the level of immunosuppression in HIV infection/ AIDS, particularly in resource-limited settings.

• As there are many dermatologic disorders thatare seen in HIV infection/AIDS, this chapter focuses on those diseases that are the most closely associated.

THE HUMAN IMMUNODEFICIENCY VIRUS (HIV) is a lentivirus (a subgroup of retrovirus) that causes HIV infection and acquired immunodeficiency syndrome (AIDS). AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Without treatment, average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells.

International Classification of Diseases, Revision 10 (1990):

(B20-B24) Human immunodeficiency virus [HIV] disease

B20 — Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases.

B20.0 — HIV disease resulting in mycobacterial infection.

B20.1 — HIV disease resulting in other bacterial infections.

B20.2 — HIV disease resulting in cytomegaloviral disease.

B20.3 — HIV disease resulting in other viral infections.

B20.4 — HIV disease resulting in candidiasis.

B20.5 — HIV disease resulting in other mycoses.

B20.6 — HIV disease resulting in Pneumocystis carinii pneumonia.

B20.7 — HIV disease resulting in multiple infections.

B20.8 — HIV disease resulting in other infectious and parasitic diseases.

B20.9 — HIV disease resulting in unspecified infectious or parasitic disease.

B21 — Human immunodeficiency virus [HIV] disease resulting in malignant neoplasms.

B21.0 — HIV disease resulting in Kaposi's sarcoma.

B21.1 — HIV disease resulting in Burkitt's lymphoma.

B21.2 — HIV disease resulting in other types of non-Hodgkin's lymphoma.

B21.3 — HIV disease resulting in other malignant neoplasms of lymphoid, haematopoietic and related tissue.

B21.7 — HIV disease resulting in multiple malignant neoplasms.

B21.8 — HIV disease resulting in other malignant neoplasms.

B21.9 — HIV disease resulting in unspecified malignant neoplasm.

B22 — Human immunodeficiency virus [HIV] disease resulting in other specified diseases.

B22.0 — HIV disease resulting in encephalopathy.

B22.1 — HIV disease resulting in lymphoid interstitial pneumonitis.

B22.2 — HIV disease resulting in wasting syndrome.

B22.7 — HIV disease resulting in multiple diseases classified elsewhere.

B23 — Human immunodeficiency virus [HIV] disease resulting in other conditions.

B23.0 — Acute HIV infection syndrome.

B23.1 — HIV disease resulting in (persistent) generalised lymphadenopathy.

B23.2 — HIV disease resulting in haematological and immunological abnormalities, not elsewhere classified.

B23.8 — HIV disease resulting in other specified conditions.

B24 — Unspecified human immunodeficiency virus [HIV] disease.

PATHOGENESIS. HIV infects vital cells in the human immune system such as helper T cells (specifically CD4+ T cells), macrophages, and dendritic cells. HIV infection leads to low levels of CD4+ T cells through a number of mechanisms, including apoptosis of uninfected bystander cells, direct viral killing of infected cells, and killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4+ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections.

Incubation period — two to three weeks, though may be much longer.

Transmission.

HIV transmission takes place through the following routes:

1. Sexual intercourse (vaginal/anal/oral): With an infected partner:

- Man with woman (heterosexual).
- Man with man (homosexual).

2. Transfusion: With infected blood and blood products, transplantation of organ/tissue, andthrough artificial insemination.

3. Contaminated needles and syringes: Seenmost frequently in intravenous drug users(IDUs) when they share unsterilized needlesand syringes.

4. Vertical transmission: From an infected mother to child, i.e., perinatal transmission (before,during and after delivery).

5. Nosocomial infection: In hospital/health caresettings on account of accidental needle stickinjury or sharp instrument cuts, etc., whiletreating an HIV/AIDS patient, though rare, doesoccur.

Natural History of HIV Infection. The course of HIV infection from the time of initial infection to the development of full blown AIDS is divided into five stages.

Primary HIV infection: which may manifest as acute retroviral syndrome or be asymptomatic.

- Clinical stage 1: which may manifest as persistent generalized lymphadenopathy or be asymptomatic.
- Clinical stage 2: which may manifest with unexplained symptoms, infections, oral lesions or itchy dermatoses.
- Clinical stage 3: which may manifest with unexplained symptoms, infections, oral lesions itchy dermatoses or 'penic' hematological changes.
- Clinical stage 4: which may manifest with wasting disease, infections, neoplasms and neurological disease.

Clinical Features.

The illness lasts 1–3 weeks and manifests as:

- Symptoms: Fever, pharyngitis, vomiting, headache, arthralgia, and myalgia.
- Cutaneous manifestations: Maculopapular rash, mucosal (mouth, esophagus, and genital) ulceration.
- Lymphoreticular system: Lymphadenopathy and hepatosplenomegaly.
- Neuropsychiatric manifestations: Meningoencephalitis, neuropathies (peripheral neuropathy, facial palsy, Guillain–Barré syndrome, brachial neuritis, radiculopathy), and psychosis.

Dermatological manifestations of HIV infection.

- **Infectious**

— Mycobacterial infection.
— Cytomegalovirus.
— Viral hepatitis.
— Varicella zoster virus.
— Herpes simplex virus.

— Human papillomavirus.
— Cryptococcosis.
— Histoplasmosis.
— Leishmaniasis.

• **Inflammatory**

— Sarcoidosis.
— Rheumatoid arthritis.
— Systemic lupus erythematosus.
— Tumid lupus.
— Dyshidrotic eczema.
— Eosinophilic folliculitis.

• **Neoplastic**

— Kaposi sarcoma.
— Dermatofibroma.

INFLAMMATORY DERMATOSES

Seborrheic dermatitis is one of the most common dermatologic manifestations of HIV disease, affecting as many as 83 % of HIV-infected individuals during the course of their disease. Seborrheic dermatitis may occur during all stages of HIV disease, and frequently occurs early in HIV-infection (CD4+ T cell count > 500/μL). As is the case in immunocompetent adults, HIVinfected individuals with seborrheic dermatitis typically present with erythema and greasy scale involving the scalp, eyebrows, nasolabial folds, and posterior auricular regions. However, more disseminated formsofseborrheic dermatitis are often seen in advanced HIV disease. The forehead and malar areas, as well as the chest, back, axillae, and groin may be involved. In fact, erythroderma arising from seborrheic dermatitis may be an initial presenting sign of HIV infection.

Psoriasis Vulgaris. Although psoriasis may develop at any stage of HIV infection, the severity of psoriasis tends to correlate with worsening immune function. For some individuals, psoriasis may be the initial presenting symptom of HIV infection, and new onset psoriasis in an individual at risk for HIV is an indication for HIV testing. All clinical subtypes of psoriasis are observed in HIVinfected individuals, though guttate, inverse and erythrodermic psoriasis are the most common.

Pruritus is a common complaint in individuals with late symptomatic and advanced HIV disease. In the majority of cases, primary or secondary dermatoses rather than metabolic disorders are the cause of pruritus. An atopic-like diathesis may become manifest in individuals with advanced HIV disease and pruritus, even in the absence of a prior history of atopy. Changes secondary to chronic rubbing and scratching are often seen, including excoriations, lichen simplex chronicus, and prurigonodularis. Secondary S. aureus infection (impeti-

ginization, furunculosis, or cellulitis) may also occur in traumatized lesions. Ichthyosis vulgaris and xerosis are common in advanced HIV disease and may be associated with mild pruritus.

Eosinophilic folliculitis is a chronic pruritic dermatosis occurring in persons with advanced HIV disease. In one retrospective study of HIV-infected individuals, low CD4+ T cell counts (< 200/μL) were associated with the development of eosinophilic folliculitis, independent of ART status. Clinically, eosinophilic folliculitis presents with extremely pruritic small pink to red edematous, folliculocentric papules, and less commonly pustules. Lesions tend to develop symmetrically above the nipple line on the chest, proximal arms, head, and neck. Secondary changes are common, and include excoriations, lichen simplex chronicus, and prurigonodularis, as well as secondary infection with S. aureus. In individuals with darker skin, postinflammatory hyperpigmentation often produces significant cosmetic disfigurement.

Papular Pruritic Eruption of HIV has been considered to be within the spectrum of pruritic papular disorders in HIV, which includes eosinophilic folliculitis and nonspecific pruritus. The primary lesion is a firm urticarial papule, though sterile pustules have been described as well. The eruption is usually symmetric and distributed primarily on the extremities, and less commonly on the trunk and face. Lesions are occasionally but not always folliculocentric. Because the eruption is intensely itchy, the eruption is typically associated with multiple excoriations, marked postinflammatory hyperpigmentation, and scarring.

Erythroderma in HIV disease may be related to drug hypersensitivity, atopic dermatitis, psoriasis, seborrheic dermatitis, photosensitivity dermatitis, coexisting human T-cell lymphotrophic virus-1 infection, pityriasisrubrapilaris, or cutaneous T cell lymphoma.

OPPORTUNISTIC INFECTIONS

HPVinfections are commonly seen at all stages of HIV disease, and anogenital and oral HPV infections have been reported to occur at a higher rate in HIV-infected individuals compared to that in the general population.

Common Warts. As immunodeficiency progresses, common warts may become larger, more numerous, confluent, and more refractory to treatment. HPV-5 can cause an unusual pattern of extensive verruca planaand pityriasis (tinea) versicolor-like lesions, similar to that seen in epidermodysplasiaverruciformis.

Anogenital Warts. Clinically, anogenital warts appear similar to those seen in immunocompetent individuals; however, condyloma may be more numerous or extensive, and are often less responsive to therapy. As in immunocompetent individuals, anogenital warts in HIV-infected individuals most commonly result from infection by HPV-6 and HPV-11. Althoughanogenitalwarts are commonly considered to be benign lesions, anogenital warts in HIV-infected individuals are morelikely to reflect infection with multiple HPV types, includ-

ing high-risk oncogenic types -16, -18, -31, -51,-53, -56, and -58 as well as low-risk types -6 and -11.

Oral HPV Infections. HPV-induced oropharyngeal lesions typically present as pink or white verrucous papules, resembling anogenitalcondyloma. If lesionsare extensive, they may coalesce to form multiple large plaques, which may transform to verrucous carcinoma (oral florid papillomatosis). Oral HPV infection has also been associated with a subset of oropharyngealSCC, which sometimes arises from the base of the tongue and tonsils.

HPV-Induced Dysplasia and Invasive SCC. The risk of HPV-induced dysplasia and malignancy is significantly higher in HIV-infected individuals compared to that in the general population.

Herpes Simplex Virus 1 and 2 Infections is commonly associated with HIV disease. Chronic herpetic ulcers of greater than 1 months' duration are an AIDS defining condition. HSV infection in HIV disease may present with severe, painful ulcerations of the perioral region, anogenital region, and digits. Atypical morphologies, such as hyperkeratotic, verrucous papules and nodules, are sometimes observed in advanced HIV disease. In more advanced HIV disease, lesions typically respond less promptly to oral antiviral therapy and recur more frequently.

Varicella Zoster Virus Infections. In HIV-infected individuals, varicella zoster virus infection (VZV) may present as severe varicella (primary VZV infection), persistent varicella, dermatomal herpes disseminated herpes zoster, and chronic or recurrent herpes zoster. In advanced HIV disease, herpes zoster may present atypically. Disseminated herpes zoster infection may manifest with scattered vesicles in the absence of dermatomallesions. Persistent ecthymatousulcerations and verrucous papules in the absence of a vesicular stage have also been described.

Molluscumcontagiosum lesions are caused by poxvirus infection, and are a cutaneous marker for advanced HIV disease. Commonly seen in children, molluscuminfections in HIV-infected individuals may bpresent with pearly skin-colored umbilicated papules characteristically seen in immunocompetentindividuals. However, lesions that are large, confluent and predominantly facial are characteristic of advanced HIV disease. Atypical lesionsare also common, and may resemble folliculitis,abscesses, warts, furuncles, and cutaneous horns. In HIV-infected individuals, molluscum infections tend to be progressive and recurrent.

Oral hairy leukoplakia is a benign infection of epithelial cells of oral mucosa with Epstein–Barr virus. A common oral manifestation of HIV disease, oral hairy leukoplakia is marker of moderate to advanced immunosuppression.

Clinically, oral hairy leukoplakia presents with asymptomatic hyperplastic, whitish plaques on the bilateral aspects of the lateral tongue. Lesions are typically asymmetric, and have corrugations accentuating the normal tongue ridges.

Staphylococcus aureus is a common bacterial pathogen causing cutaneous and systemic infections at all stages of HIV disease. No unique staphylococcal infections occur in HIV disease. Rather, HIV-infected individuals tend to present a wide range of primary skin and soft tissue infections that are normally seen in immunocompetent individuals. S. aureus infections in HIV-infected individuals are most commonly severe and recurrent.

Cutaneous Tuberculosis is caused by Mycobacterium tuberculosis, Mycobacterium bovis, and theBCG vaccine. Various manifestations of cutaneous tuberculosis have been described in HIV-infectedindividuals, including scrofuloderma, lichen scrofulosorum, disseminated miliary tuberculosis, gummatous tuberculosis, and tuberculous abscess. Cutaneous miliary tuberculosis — a previously rare form of cutaneous tuberculosis that arises from hematogenous spread of bacilli to the skin from an internal focus of infection. Clinically, cutaneous miliary tuberculosis may initially present with red–brown pinpoint macules, papules, and papulovesicles. Lesions often develop into small flat-topped papules that crust over centrally. The eruption tends to be asymmetrically distributed, and favors the buttocks, thighs, and extensor surfaces. The cutaneous findings of cutaneous military tuberculosis are nonspecific, and may resemble a bacterial folliculitis. Pulmonary symptoms may be present, though radiographic findings may be nonspecificas well.

Candidiasis. Candida colonization of the oropharynx is common in HIV-infected individuals, and has been reported in up to 90 % of individuals with advanced disease. Oropharyngealcandidiasis typically presents in four different clinical patterns: (1) pseudomembranous (thrush), (2) hyperplastic, (3) erythematous (atrophic), and (4) angular cheilitis. Pseudomembranous candidiasis typically involves the tongue, and presents with yellow–white plaques that are removable by scraping. Hyperplastic candidiasis usually involves the buccal mucosa, and consists of white plaques that are not removable by scraping. Erythematous candidiasis commonly presents with erythematous patches of the palate and the dorsal tongue with associated depapillation. Angular cheilitis manifests as erythema with curdlike flecks or painful fissures at the angles of the lips. A number of studies have documented a higher incidence of vulvovaginal candidiasis in HIV-infected women, particularly in those with advanced HIV disease.

Dermatophyte infections. As is the case for immunocompetent individuals, Trichophytonrubrum and Trichophytonmentagrophytes are the most common dermatophytes seen in HIVinfected individuals. In HIV disease, dermatophyteinfections of the epidermis, commonly caused by T. rubrum may be more extensive, and are often asymptomatic. Disseminated disease may sometimes present atypically. Infectionsof the nails are also common. T. rubrum frequentlycauses distal and lateral subungualonychomycosis inboth HIV-infected and immunocompetent individuals.However, T. rubrum also causes proximal subungualonychomycosis (infection of the undersurface ofthe proximal nail plate), which is seen

almost exclusivelyin individuals infected with HIV. Unless immunocompetence is restored, dermatophyte infections are often chronic and recurrent.

Invasive Fungal Infections. Disseminated fungal infections in advanced HIV disease may arise either by local invasion of the skin or mucosa with secondary lymphatic or hematogenous dissemination or reactivation of a latent pulmonary focus of infection. Cryptococcosis, Coccidioidomycosis, Histoplasmosis, Penicilliosis, Aspergillosis are most common life-threatening fungal infection associated with advanced HIV disease.

Sexually Transmitted Diseases. Given that the vast majority of HIV infections are sexually transmitted, individuals with HIV infection should also be screened for other sexually transmitted diseases such as Chlamydia, gonorrhea, and genital ulcerative diseases (e.g., syphilis, herpes, and chancroid).

Sexually transmitted diseases STDs and HIV make a lethal combination and have several interactions:

• Presence of STDs amplifies the risk of transmission of HIV. The ulcerative STDs (syphilis, herpes genitalis, and chancroid) increase the transmission of HIV almost ten times, while the STDs associated with discharges (gonorrhea, chlamydial infection) amplify the transmission of HIV by four to five times.

• In the early phase of HIV infection, the course of STDs is normal but as the immunosuppression nprogresses, the STDs may present atypically, run a fulminant course and may be resistant to conventional treatment.

• Presence of STDs may modify the course of HIV, e.g., human papilloma virus may have a higher oncogenic potential in presence of HIV infection.

OPPORTUNISTIC NEOPLASMS

Individuals with HIV disease have been reported to have a higher prevalence of the AIDS-defining malignancies, Kaposi sarcoma (, in situ and invasive cervical SCC, and non-Hodgkin lymphoma. However, HIV-infected individuals have also been noted to have an increased incidence of in situ and invasive anal SCC, vulvar/vaginal SCC, Hodgkin lymphoma, primary liver cancer, lung cancer, melanoma, nonmelanoma skin cancers, oropharyngeal cancer, and leukemia. The etiology of the higherincidence of malignancy among HIV-infected individuals is likely multifactorial. Contributing factors may include diminished immune-mediated tumor surveillance, concomitant infection with oncogenic viruses (such as Epstein–Barr, HPV, and human herpesvirus-8), and associated behavior and lifestyle factors.

AIDS-related Kaposi's Sarcoma KS-rapidly progressive form in HIV-infected patients with early involvement of extracutaneous sites.

Clinically, AIDS KS differs from classical KS by its more rapid course and its rapid multifocal dissemination: early AIDS-KS lesions that appear as small oval violaceous macules develop rapidly into plaques and small nodules, which

frequently are present at multiple locations at disease onset and have a tendency for rapid progression. In contrast to other variants of KS, the initial lesions in AIDS patients frequently develop on the face, especially on the nose, eyelids, ears, and on the trunk, where the lesions follow the relaxed skin tension lines. If untreated, disseminated AIDS-KS lesions may coalesce to form large plaques involving large parts of the face, the trunk, or the extremities leading to functional impairment. The oral mucosa is frequently involved and represents the initial site of a 10–15 % of AIDS KS. Involvement of the pharynx is not uncommon and may result in difficulty in eating, speaking, and breathing. The involvement of extracutaneous sites occursmore rapidly and more dramatically in patients with AIDS KS than those with classical KS. Besides theoral mucosa, KS lesions are most frequently found in the lymph nodes, the gastrointestinal tract, and the lungs. Although gastrointestinal KS is usually found when cutaneous lesions are present, exclusive gastrointestinal involvement is possible as is noted intransplantation-associated KS. KS lesions have a predilectionfor the stomach and duodenum and can causebleeding and ileus. Although visible by gastroscopy, such lesions are underdiagnosed histologically because they are located in the submucosa and may escape the biopsy forceps. Pulmonary KS can cause respiratory symptoms such as bronchospasm, coughing, and progressive respiratory insufficiency.

Laboratory tests in a patient suspected of having HIV infection.

- Tests for HIV-specific antibodies:

Screening tests

✓ *ELISA.*
✓ *Rapid tests.*
✓ *Supplemental tests.*
✓ *Western Blot assay.*
✓ Immunofluorescence test.

- Tests to identify HIV (Confirmatory tests):

✓ *Viral isolation.*
✓ *HIV-specific core antigen.*
✓ *PCR for RNA copies.*

Specific Treatment

Drugs available based on mechanism of action, two classes of antiretroviral drugs are available.

- Reverse transcriptase inhibitors: Which are of two types:

— Nucleoside reverse transcriptase inhibitors(NRTIs).

— Non-nucleoside reverse transcriptase inhibitors (NNRTIs).

- Protease inhibitors.

Drug regimens

- Use of a single drug often results in resistance, so monotherapy should be avoided.
- Studies using two to three antiretroviral drugs have shown encouraging results (lowering of HIV-RNA to < 50 copies/ml, i.e., not detectable).
- The use of highly active antiretroviral therapy (HAART) involves use of two NRTI along with one NNRTI or PI.

Indications for antiretroviral therapy. Eradication of HIV infection cannot be achieved with currently available regimens because a pool of latently infected CD4+ cells is established very early in the infection and this persists in the body. However, antiretroviral therapy is helpful because it:

- Restores immune function.
- Reduces morbidity and mortality in HIV patients.
- Improves the quality of life.

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