

Classification of infections that are transmitted sexually. Course of syphilis infection, major clinical manifestations of primary, secondary, tertiary and congenital syphilis, including on the mucous membranes of the mouth.

*If you have some questions
about lecture you may call to
your lecturer

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* Plan of the lecture

- * 1. Etiology, pathogenesis and transmission of viral and bullous disorders.
- * 2. Classification and features of clinical manifestations of viral and bullous disorders.
- * 3. Diagnostic of viral and bullous disorders.
- * 4. Principles of general and local treatment of viral and bullous disorders.
- * 5. Methods of primary and secondary prevention of viral and bullous disorders.

* Sexually transmitted diseases (STDs, venereal diseases) are among the most common infectious diseases in the world today. STDs are sometimes referred to as sexually transmitted infections, since these conditions involve the transmission of an infectious organism between sex partners. More than 20 different STDs have been identified, and about 19 million men and women are infected each year in the United States, according to the CDC (2010).

SEXUALLY TRANSMITTED DISEASES

Fact Sheet



Stay informed,
be safe, act
smart, and raise
awareness
about Sexually
Transmitted
Diseases
(STDs).

Herpes

Breaking out is hard to do



- More than 500 million people are living with genital herpes infection
- Caused by Herpes simplex virus 2
- There is no cure. However, medicines can prevent or shorten outbreaks

a.k.a. Pox. Don't let the pox into your home, or anyone else's

Syphilis

- 5.6 million new cases reported each year
- Caused by the bacteria *Treponema pallidum*
- Cured with the right antibiotics



Playing doctor is a game you don't want to lose

Chlamydia

- 130 million new infections occur annually in the world
- Caused by the bacteria *Chlamydia trachomatis*
- Chlamydia can be cured with the right treatment



Crab Louse

Don't let these crabs louse up your life



- Pubic louse infestation is found worldwide and can affect anyone
- *Phthirus pubis* is a parasitic insect of humans
- Treated with lice-killing lotions

This virus is 400,000 times smaller than a golf ball, but a nasty killer

HIV

- 43 million people are estimated to be living with HIV
- Human immunodeficiency virus kills cells which help the body fight infections
- No effective cure exists for HIV, but it can be controlled with proper medical care



Gonorrhea

a.k.a. The Clap, from the old French for brothel, "clapier"



- Very common infection among young people (15-24 years)
- Caused by a *Neisseria gonorrhoeae* bacterium infection
- Can be cured with the right treatment, but some drug-resistant strains are developing

A relationship with Trich can be parasitic and hard to handle

Trichomoniasis

- Is the most prevalent non-viral STD, 140 million new infections each year
- Caused by a tiny parasite called *Trichomonas vaginalis*
- It can be treated with antibiotics



HPV

Kissing this frog can give you warts. The HPV vaccine is a true prince!



- Most sexually active women and men will be infected at some point in their lives
- Human papillomavirus is a virus that includes more than 100 different strains or types
- A vaccine is now available which protects against several HPV types



Anyone who is sexually active can get an STD. It's time to take action! Talk, protect, test and treat!

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Depending on the disease, the infection can be spread through any type of sexual activity involving the sex organs, the anus, or the mouth; an infection can also be spread through contact with blood during sexual activity. STDs are infrequently transmitted by any other type of contact (blood, body fluids or tissue removed from an STD infected person and placed in contact with an uninfected person); however, people that share unsterilized needles markedly increase the chance to pass many diseases, including STD's (especially hepatitis B), to others. Some diseases are not considered to be officially an STD (for example, hepatitis types A, C, E) but are infrequently noted to be transferred during sexual activity. Consequently, some authors include them as STD's, others do not. Consequently, lists of STD's can vary, depending on whether the STD is usually transmitted by sexual contact or only infrequently transmitted.

STDs are most often caused by viruses and bacteria. The following is a list of the most common STDs, their causes and other infections (see STDs with asterisk mark*) that may be transmitted on occasion by sexual activity, but are frequently not considered primarily to be an STD by many investigators:

STDs caused by bacteria

- * Chancroid (*Haemophilus ducreyi*)
- * Chlamydia (*Chlamydia trachomatis*)
- * Gonorrhea (*Neisseria gonorrhea*)
- * Granuloma inguinale (*Calymmatobacterium granulomatis*)
- * Lymphogranuloma venereum (*Chlamydia trachomatis*)
- * Syphilis (*Treponema pallidum*)

STDs caused by viruses:

- ❖ Genital herpes (herpes simplex virus)
- ❖ Genital warts (human papillomavirus virus [HPV])
- ❖ Hepatitis B and D, and infrequently, A*, C*, E* (hepatitis viruses, types A-E)
- ❖ HIV/AIDS (human immunodeficiency virus [HIV virus])
- ❖ Molluscum contagious* (poxvirus)

STD caused by protozoan:

- * Trichomoniasis (*Trichomonas vaginalis*)

STD's caused by fungi:

- * Jock itch (*Tenia cruris*)
- * Yeast infections (*Candida albicans*)

STD's caused by parasites

- * Pubic lice or crabs (*Pediculosis pubis*)
- * Scabies (*Sarcoptes scabiei*)



Syphilis

Background

Syphilis is an infectious venereal disease caused by the spirochete *Treponema pallidum*. Syphilis is transmissible by sexual contact with infectious lesions, from mother to fetus in utero, via blood product transfusion, and occasionally through breaks in the skin that come into contact with infectious lesions. If untreated, it progresses through 4 stages: primary, secondary, latent, and tertiary.

Syphilis has a myriad of presentations and can mimic many other reactions and immune-mediated processes in advanced stages. It has earned the nickname “the great impostor.” The complex and variable manifestations of the disease prompted Sir William Osler to remark, “The physician who knows syphilis knows medicine.”

Many famous personages throughout history are thought to have died from syphilis, including Bram Stoker, Henry VIII, and Vincent van Gogh. Since the discovery of penicillin in the mid-20th century, the spread of this once very common disease has been largely controlled, but efforts to eradicate the disease entirely have been unsuccessful.

Syphilis can occur at any age, but it's most often seen in people who are aged or older. It tends to be a long-lasting (chronic) condition, and some types can be life-threatening without treatment. Treatment with medication usually controls it.





Pathophysiology

- * Three genera of spirochetes cause human infection:
 - * • Treponema, which causes syphilis, yaws, and pinta
 - * • Borrelia, which causes Lyme disease and relapsing fever
 - * • Leptospira, which causes leptospirosis
- * The particular spirochete responsible for syphilis is *Treponema pallidum*.
- * *T pallidum* is a fragile spiral bacterium 6-15 micrometers long by 0.25 micrometers in diameter. Its small size makes it invisible on light microscopy; therefore, it must be identified by its distinctive undulating movements on darkfield microscopy. It can survive only briefly outside of the body; thus, transmission almost always requires direct contact with the infectious lesion.
- * Syphilis is usually classified into 4 stages: primary, secondary, latent, and tertiary. It can be either acquired or congenital. That is, it can be transmitted either by intimate contact with infectious lesions (most common) or via blood transfusion (if blood has been collected during early syphilis), and it can also be transmitted transplacentally from an infected mother to her fetus.

Acquired syphilis

- * In acquired syphilis, *T pallidum* rapidly penetrates intact mucous membranes or microscopic dermal abrasions and, within a few hours, enters the lymphatics and blood to produce systemic infection. Incubation time from exposure to development of primary lesions, which occur at the primary site of inoculation, averages 3 weeks but can range from 10-90 days. Studies in rabbits show that spirochetes can be found in the lymphatic system as early as 30 minutes after primary inoculation, suggesting that syphilis is a systemic disease from the outset.
- * The central nervous system (CNS) is invaded early in the infection; during the secondary stage, examinations demonstrate that more than 30% of patients have abnormal findings in the cerebrospinal fluid (CSF). During the first 5-10 years after the onset of untreated primary infection, the disease principally involves the meninges and blood vessels, resulting in meningovascular neurosyphilis. Later, the parenchyma of the brain and spinal cord are damaged, resulting in parenchymatous neurosyphilis. Go to Neurosyphilis for complete information on this topic.

- * Regardless of the stage of disease and location of lesions, histopathologic hallmarks of syphilis include endarteritis (which in some instances may be obliterative in nature) and a plasma cell-rich infiltrate. Endarteritis is caused by the binding of spirochetes to endothelial cells, mediated by host fibronectin molecules bound to the surface of the spirochetes. The resultant endarteritis can heal with scarring in some instances.
- * The syphilitic infiltrate reflects a delayed-type hypersensitivity response to *T pallidum*, and in certain individuals with tertiary syphilis, this response by sensitized T lymphocytes and macrophages results in gummatous ulcerations and necrosis. Antigens of *T pallidum* induce host production of treponemal antibodies and nonspecific reagin antibodies. Immunity to syphilis is incomplete.
- * For example, host humoral and cellular immune responses may prevent the formation of a primary lesion on subsequent infections with *T pallidum*, but they are insufficient to clear the organism. This may be because the outer sheath of the spirochete is lacking immunogenic molecules, or it may be because of down-regulation of helper T cells of the TH1 class.
- * Primary syphilis is characterized by the development of a painless chancre at the site of transmission after an incubation period of 3-6 weeks. The lesion has a punched-out base and rolled edges and is highly infectious.

Histologically, the chancre is characterized by mononuclear leukocytic infiltration, macrophages, and lymphocytes. The inflammatory reaction causes an obliterative endarteritis. In this stage, the spirochete can be isolated from the surface of the ulceration or the overlying exudate of the chancre. Whether treated or not, healing occurs within 3-12 weeks, with considerable residual fibrosis.

Secondary syphilis develops about 4-10 weeks after the appearance of the primary lesion. During this stage, the spirochetes multiply and spread throughout the body. Secondary syphilis lesions are quite variable in their manifestations. Systemic manifestations include malaise, fever, myalgias, arthralgias, lymphadenopathy, and rash.

Widespread mucocutaneous lesions are observed over the entire body and may involve the palms, soles, and oral mucosae. Most often, the lesions are macular, discrete, reddish brown, and 5 mm or smaller in diameter; however, they can be pustular, annular, or scaling. All such lesions contain treponemes. Of these, wet mucous patches are the most contagious. Histologically, the inflammatory reaction is similar to but less intense than that of the primary chancre.

- ❖ Latent syphilis is a stage at which the features of secondary syphilis have resolved, though patients remain seroreactive. Some patients experience recurrence of the infectious skin lesions of secondary syphilis during this period. About one third of untreated latent syphilis patients go on to develop tertiary syphilis, whereas the rest remain asymptomatic.
- ❖ Currently, tertiary syphilis disease is rare. When it does occur, it mainly affects the cardiovascular system (80-85%) and the CNS (5-10%), developing over months to years and involving slow inflammatory damage to tissues. The 3 general categories of tertiary syphilis are gummatous syphilis (also called late benign), cardiovascular syphilis, and neurosyphilis.
- ❖ Gummatous syphilis is characterized by granulomatous lesions, called gummas, which are characterized by a center of necrotic tissue with a rubbery texture. Gummas principally form in the liver, bones, and testes but may affect any organ. Histological examination shows palisaded macrophages and fibroblasts, as well as plasma cells surrounding the margins. Gummas may break down and form ulcers, eventually becoming fibrotic. Treponemes are rarely visualized or recovered from these lesions.

- * Cardiovascular syphilis occurs at least 10 years after primary infection. The most common manifestation is aneurysm formation in the ascending aorta, caused by chronic inflammatory destruction of the vasa vasorum, the penetrating vessels that nourish the walls of large arteries. Aortic valve insufficiency may result.
- * Neurosyphilis has several forms. If the spirochete invades the CNS, syphilitic meningitis results. Syphilitic meningitis is an early manifestation, usually occurring within 6 months of the primary infection. CSF shows high protein, low glucose, high lymphocyte count, and positive syphilis serology.
- * Meningovascular syphilis occurs as a result of damage to the blood vessels of the meninges, brain, and spinal cord, leading to infarctions causing a wide spectrum of neurologic impairments.

Congenital syphilis

- * Congenital syphilis, discussed briefly here, is a veritable potpourri of antiquated medical terminology. The treponemes readily cross the placental barrier and infect the fetus, causing a high rate of spontaneous abortion and stillbirth. Within the first 2 years of life, symptoms are similar to severe adult secondary syphilis with widespread condylomata lata and rash. “Snuffles” describes the mucopurulent rhinitis caused by involvement of the nasal mucosae.
- * Later manifestations of congenital syphilis include bone and teeth deformities, such as “saddle nose” (due to destruction of the nasal septum), “saber shins” (due to inflammation and bowing of the tibia), “Clutton’s joints” (due to inflammation of the knee joints), “Hutchinson’s teeth” (in which the upper incisors are widely spaced and notched), and “mulberry molars” (in which the molars have too many cusps).
- * Tabes dorsalis and general paresis may develop as in adults, with 8th cranial nerve deafness and optic nerve atrophy as well as a variety of other ophthalmologic involvement leading to blindness being additional features.

- * Etiology

- * The cause of syphilis is infection with the spirochete *T pallidum*. *T pallidum* is solely a human pathogen and does not naturally occur in other species. *T pallidum* has, however, been cloned in *Escherichia coli* and has been used experimentally in rabbits.
- * Transmission of *T pallidum* occurs via penetration of the spirochetes through mucosal membranes and abrasions on epithelial surfaces. It is primarily spread through sexual contact but can be spread by exposure to blood products and transferred in utero. *T pallidum* is a labile organism that cannot survive drying or exposure to disinfectants; thus, fomite transmission (eg, from toilet seats) is virtually impossible.
- * Risk factors of syphilis include the following:
 - * Unprotected sex, promiscuous sex, and intravenous drug use are the major risk factors.
 - * Health care workers are at occupational risk.

- * Primary syphilis

- * Primary syphilis occurs within 3 weeks of contact with an infected individual. It manifests mainly on the glans penis in males and on the vulva or cervix in females. Ten percent of syphilitic lesions are found on the anus, fingers, oropharynx, tongue, nipples, fingers, or other extragenital sites. Regional nontender lymphadenopathy follows invasion.

- * Lesions (chancres) are usually solitary, raised, firm, red papules that can be several centimeters in diameter. The chancre erodes to create an ulcerative crater within the papule, with slightly elevated edges around the central ulcer. It usually heals within 4-8 weeks, with or without therapy.

- * Syphilitic chancre
- * Although genital chancres are frequently solitary, they may be multiple in some patients. Sometimes they appear as “kissing” lesions on opposing skin surfaces—for example, the labia.

- * Secondary syphilis

- * Secondary syphilis manifests in various ways. It usually presents with a cutaneous eruption within 2-10 weeks after the primary chancre and is most florid 3-4 months after infection. The eruption may be subtle; 25% of patients may be unaware of skin changes. A localized or diffuse mucocutaneous rash (generally nonpruritic and bilaterally symmetrical) with generalized nontender lymphadenopathy is typical. Patchy alopecia and condylomata lata may also be observed.
- * Mild constitutional symptoms of malaise, headache, anorexia, nausea, aching pains in the bones, and fatigue often are present, as well as fever and neck stiffness. A small number of patients develop acute syphilitic meningitis and present with headache, neck stiffness, facial numbness or weakness, and deafness.
- * Other less-common manifestations include GI involvement, hepatitis, nephropathy, proctitis, arthritis, and optic neuritis.
- * Latent syphilis
- * Latency may last from a few years to as many as 25 years before the destructive lesions of tertiary syphilis manifest. Affected patients may recall symptoms of primary and secondary syphilis. They are asymptomatic during the latent phase, and the disease is detected only by serologic tests.
- * Latent syphilis is divided into early latent and late latent. The distinction is important because treatment for each is different. The early latent period is the first year after the resolution of primary or secondary syphilis. Asymptomatic patients who have a newly active serologic test after having a serologically negative test result within 1 year are also considered to be in the early latent period. Late latency syphilis is not infectious; however, women in this stage can spread the disease in utero.
- * A small percentage of infants infected in utero may have a latent form of infection that becomes apparent during childhood and, in some cases, during adult life. The earliest symptom that occurs prior to age 2 years is rhinitis (snuffles), soon followed by cutaneous lesions. After age 2 years, parents may note problems with the child's hearing and language development and with vision. Facial and dental abnormalities may be noted.

- * Tertiary syphilis
- * Tertiary (late) syphilis is slowly progressive and may affect any organ. The disease is generally not thought to be infectious at this stage. Manifestations may include the following:
 - * Altered mental status
 - * Focal neurologic findings, including sensorineural hearing and vision loss
 - * Dementia
 - * Symptoms related to the cardiovascular system or the central nervous system (CNS)
 - * The lesions of benign tertiary syphilis usually develop within 3-10 years of infection. The typical lesion is a gumma, and patient complaints usually are secondary to bone pain, which is described as a deep boring pain characteristically worse at night. Trauma may predispose a specific site to gumma involvement.
- * CNS involvement may occur, with presenting symptoms representative of the area affected (ie, brain involvement [headache, dizziness, mood disturbance, neck stiffness, blurred vision] and spinal cord involvement [bulbar symptoms, weakness and wasting of shoulder girdle and arm muscles, incontinence, impotence]).
- * Some patients may present up to 20 years after infection with behavioral changes and other signs of dementia, which is indicative of neurosyphilis.

- * Physical Examination
- * Conduct the physical examination with the manifestations of primary, secondary, and tertiary syphilis in mind. The lesions and exanthem of primary and secondary syphilis are infectious; thus, gloves and other relevant personal protective equipment must be worn.
- * Primary syphilis
- * The patient is typically afebrile. Symmetric rash is typical; however, the presence of overlying superinfection, scratching, or scaling may make the presentation atypical.
- * The chancre of primary syphilis usually begins as a single, painless papule that rapidly becomes eroded and indurated, with a surrounding red areola. The edge and base of the ulcer have a cartilaginous (buttonlike) consistency on palpation. Although classic chancres are not painful, they can become so if superinfected with bacteria. Atypical primary lesions are common and may manifest as a papular lesion without subsequent ulceration or induration.
- * The primary lesion usually is associated with regional lymphadenopathy that may be unilateral or bilateral. Inguinal adenitis is usually discrete, firm, mobile, and painless, without overlying skin changes.
- * Chancres usually are located on the penis in heterosexual men, but in homosexual men, they may be found in the anal canal, mouth, or external genitalia. Common primary sites in women include the cervix and labia. Extragenital chancres occur most commonly above the neck, typically affecting the lips or oral cavity.
- * The lesion is highly infectious; when abraded, it exudes a clear serum containing numerous *T pallidum* organisms.
- * The healing primary chancre may remain present in 15-25% of patient

- * Secondary syphilis
- * Secondary syphilis may present in many different ways but usually includes a localized or diffuse mucocutaneous rash and generalized nontender lymphadenopathy. The exanthem may be macular, papular, pustular, or mixed.
- * Initial lesions are bilaterally symmetric, pale red to pink (in light-skinned persons) or pigmented (in dark-skinned persons), discrete, round, nonpruritic macules that measure 5-10 mm in diameter and are distributed on the trunk and proximal extremities. After several days or weeks, red papular lesions 3-10 mm in diameter appear. These lesions often become necrotic and are distributed widely with frequent involvement of the palms and soles.
- * Tiny papular follicular syphilids involving hair follicles may result in patchy alopecia. In addition to the classic moth-eaten alopecia, a diffuse alopecia also has been reported.
- * Reddish-brown papular lesions on the penis or anogenital area can coalesce into large elevated plaques up to 2-3 cm in diameter, known as condylomata lata. Lesions usually progress from red, painful, and vesicular to “gun metal grey” as the rash resolves. Condylomata lata are highly infectious. They are sometimes confused with condylomata acuminata or venereal warts.
- * Condylomata lata
- * From 10-15% of patients with secondary syphilis develop superficial mucosal erosions, usually painless, on the palate, pharynx, larynx, glans penis, vulva, or in the anal canal and rectum. These mucous patches are circular silver-gray erosions with a red areola. The erosions harbor treponemes and can transmit disease.
- * Ocular abnormalities, such as iritis, are a rare clinical finding, although anterior uveitis has been reported in 5-10% of patients with secondary syphilis. Less common findings include periostitis, arthralgias, meningitis, nephritis, hepatitis, proctitis, and ulcerative colitis. Go to Interstitial Keratitis for complete information on this topic.
- * Thirty percent of patients experience recurring symptoms after the primary or secondary stage of syphilis. Lesions are less numerous but are still infectious.

- * Tertiary syphilis
- * Symptomatic tertiary syphilis is the result of a chronic, progressive inflammatory process that eventually produces clinical symptoms years to decades after the initial infection. The liver and skeleton are commonly affected. Fever, jaundice, anemia, and nighttime skeletal pain are characteristic.
- * Gummatous syphilis is characterized by coalescent granulomatous lesions, called gummas, that usually affect skin, bone, and mucous membranes but may involve any organ system, often causing local destruction of the affected organ system. Cutaneous gummas are indurated, nodular, papulosquamous or ulcerative lesions that form characteristic circles or arcs with peripheral hyperpigmentation. They may mimic other granulomatous ulcerative lesions and may be histologically indistinguishable from them.
- * Although gummas may be identified on the skin, in the mouth, and in the upper respiratory tract, they appear most commonly on the leg just below the knee. Gummas may be multiple or diffuse but usually are solitary lesions that range from less than 1 cm to several centimeters in diameter. They are generally asymmetric and grouped together.
- * Cardiovascular syphilis usually involves the aorta, though other large arteries may be affected as well. Invading treponemes cause scarring of the tunica media. Over many years, the inflammatory scarring weakens the aortic wall, leading to aneurysm formation, which causes incompetence of the aortic valve and narrowing of the coronary ostia.
- * The most common clinical finding on cardiovascular examination is a diastolic murmur with a tambour quality, secondary to aortic dilation with valvular insufficiency.
- * Neurosyphilis is caused by invasion of *T pallidum* into the CNS. It manifests as an insidious but progressive loss of mental and physical functions and is accompanied by mood alterations.
- * Neurosyphilis may be either asymptomatic or symptomatic. In asymptomatic neurosyphilis, no signs or symptoms are present, but CSF abnormalities are demonstrable, including possible pleocytosis, elevated protein, decreased glucose, or a reactive CSF Venereal Disease Research Laboratory (VDRL) test.
- * Symptomatic neurosyphilis produces various clinical syndromes that develop in approximately 5% of patients with syphilis who remain untreated. It may manifest in the following three forms:

- * Diagnostic Approach Considerations

- * T pallidum cannot be cultivated in vitro and is too small to be seen under the light microscope. Serologic testing is considered the standard method of detection for all stages of syphilis. (Note, however, that serologic tests cannot be used to differentiate the different species of the treponeme family—for example, yaws.)
- * In suspected acquired syphilis, first perform nontreponemal serology screening using the Venereal Disease Research Laboratory (VDRL), rapid plasma reagin (RPR), or the recently developed ICE Syphilis recombinant antigen test.
- * Sensitivity of the VDRL and RPR tests are estimated to be 78-86% for detecting primary syphilis, 100% for detecting secondary syphilis, and 95-98% for detecting tertiary syphilis. Specificity ranges from 85-99% and may be reduced in individuals who have coexisting conditions (ie, collagen vascular disease, pregnancy, intravenous drug use, advanced malignancy, tuberculosis, malaria, viral and rickettsial diseases).
- * VDRL test results turn positive 1-2 weeks after chancre formation. Nontreponemal tests usually become nonreactive with time after treatment. However, in some patients, nontreponemal antibodies can persist, sometimes for the life of the patient.
- * Because of the possibility of false-positive results, confirmation for any positive or equivocal nontreponemal test result should follow with a treponemal test, such as the fluorescent treponemal antibody-absorption (FTA-ABS), quantitative VDRL/RPR, microhemagglutination assay T pallidum (MHA-TP), T pallidum hemagglutination (TPHA), and T pallidum particle agglutination (TPPA) tests. Treponemal enzyme immunoassay (EIA) for immunoglobulin G (IgG) and immunoglobulin M (IgM) may be performed.
- * FTA-ABS is commonly used as a confirmatory test following positive VDRL or RPR test findings. FTA-ABS has a sensitivity of 84% for detecting primary syphilis infection and almost 100% sensitivity for detecting syphilis infection in other stages. Its specificity is 96%.

*Treatment Approach Considerations

- *Penicillin is the treatment of choice for treating syphilis. According to the Centers for Disease Control and Prevention (CDC) (see current CDC recommendations), patients with known penicillin allergies should undergo penicillin allergy skin testing and penicillin desensitization, if necessary. The 2010 CDC STD treatment guidelines recommend desensitization in penicillin-allergic pregnant women, followed by treatment with penicillin.
- *Clinical and serologic conversions are the endpoints of medical treatment for syphilis. Follow-up Venereal Disease Research Laboratory (VDRL) test levels should be obtained to document treatment efficacy.

*Discussion questions

- *1. Differential diagnosis with the viral exanthema of child age.
- *2. Etiological, pathogenetic and epidemiological features
 - *3. Principle of classification
 - *4. Differential diagnosis
- *5. The main approaches to the general and local treatment



Questions?