# Syphilis – Theory and Practice in Latvia

**A. Rubins, MD, S. Rubins, I. Jakobsone, L. Chigarevska**
Department of Dermato-Venereology at the Medical Academy of Latvia, Kr. Valdemara Street 76-75, LV-1013 Riga, Latvia. Fax: 00371-736 1615. arubins@apollo.lv

Syphilis, a chronic somatic sexually transmitted disease causing non-specific inflammation in the primary and secondary stages and specific lesions in the tertiary stage, is an ancient disease. There are three contradictory theories explaining its origin: the American theory, the Eurasian theory and the African theory. Adherents of the American theory believe that South American Indians suffered from syphilis and that Columbus' sailors were infected by them on the island of Haiti. After returning to Spain in 1493, one part of Columbus' crew serving as mercenaries in the army of King Charles VIII of France took part in the siege of Naples. It was in Naples that the first known syphilis epidemic in Europe broke out. Soldiers and merchants were to blame for the spread of syphilis to the whole of Western and Eastern Europe while it was through Portuguese seafarers under Vasco de Gama that the disease reached India and from there the Far East.

Supporters of the Eurasian theory hold that syphilis on this continent has been known since prehistoric times. The works by Hippocrates, Sushruta, Avicenna and other scientists and physicians of the ancient world bear evidence of this when they describe a disease similar to syphilis and its treatment, using mercury. Damage to human bones in a manner characteristic of syphilis has been detected in archaeological excavations in the Transbaikal region, Japan, Italy, Egypt and other areas.

The place of origin of the pathogenic agent of syphilis, as well as that of man (according to a number of scientists), is most likely to be Africa, where one can still find such diseases as framboesia (yaws), bejel and pinta. Their causative agents, which are almost identical to those of syphilis, are difficult to discern by diagnostic methods in the laboratory. Trade, migration of the population, the crusades, slave traffic from Africa and several other factors have contributed to the spread of the disease throughout the world.

The word "syphilis" was first used in 1530 by the Italian physician and poet G. Fracastoro in the poem written in Latin "Syphilis or the French Disease", describing how the gods punish the herdsman Syphilis by inflicting this disease. Another name for the disease is lues (Latin lues, plague, pestilence).

## Aetiology and pathogenesis

Syphilis is caused by the pale treponeme (Treponema pallidum) discovered by German scientists Fritz Richard Schandinn and Erich Hoffmann in 1905. This is a coiled micro-organism. Its length equals 6–14 μ and its cross-section 0.25–0.30 μ, whereas the number of coils varies from 8 to 12. The treponeme is characteristic of four kinds of movement: rotation, contraction, oscillation, undulation. Treponema pallidum does not take up aniline stains and has thus been given the name of pale treponeme. Under the electron microscope one can discern the surface of the pale treponeme as enveloped in a mucoid covering, under which lies the outer coat of the microbe, consisting of three layers. Beneath this outer coat one finds a cytoplasmic membrane possessing both superficial and deep fibrils that ensure motility of the micro-organism. Treponemes multiply by dividing crosswise (the cycle lasts for 30 hours). In a special culture medium of + 25°C the pale treponeme retains is motility for 3–6 days. In blood or serum at a temperature of + 4°C the microbe may survive for 24 hours. This should be taken into account in cases of direct blood infusion. Treponemes easily perish in a dry medium, in ultraviolet rays and at temperature above 42°C. Instantaneous destruction of treponemes occurs at contact with arsenic, mercury and bismuth preparations. In a moist medium treponemes may preserve their vital capacity for 15 hours, in frozen tissue for up to several weeks. The treponeme gains entrance into the organism through damaged skin or mucous membrane. There is an incubation period averaging from 3

to 4 weeks after treponemes infection. At this time the treponeme begin to multiply and act as an antigen. They circulate in the blood in small amounts for a short time. At the site of treponeme entrance the hard chancre (ulcus durum, syphiloma primarium, and sclerosis primaria) develops and the first stage of syphilis begins. Some 7–10 days after the appearance of the hard chancre an attending bubo forms, usually as an inguinal lymph node. Antibody synthesis is not yet intensive (negative Wassermann reaction) and this primary period of syphilis is called syphilis primaria seronegativa. Treponemes gradually tend to damage the whole lymphatic system and polyscleradenitis develops. It is not until 3–4 weeks after the appearance of the chancre or 6–7 weeks after infection that the antibody titre in blood increases and Wassermann reaction can be ascertained. This period is called syphilis primaria seropositive. (This division into seronegative and seropositive primary syphilis was used in the days when Wassermann reaction was performed. Recently more sensitive reaction tests have been developed and introduced, e.g. treponemal enzyme immunoassay (EIA) and fluorescent treponemal antibody absorption test (FTA-abs test), which show positive findings 1–3 weeks following infection. Thus, it is not currently advised to use Wassermann reaction and the above-mentioned division into periods is no longer of interest.) In the further course of the disease treponemes penetrate the lymphatic system barrier and via ductus thoraticus reach the blood system. Short-term treponemal sepsis occurs, followed by generalisation of the infection in the organism. In this phase so-called prodromal symptoms may be observed in some patients: rise in temperature, nausea, pain in bones, muscles, joints.

At the site of treponeme entry, due to their hematogenic dissemination, eruptions appear in skin and mucous membranes. This occurs 7–10 days following prodromal symptoms. The disease progresses to the secondary or generalised stage of syphilis, secondary fresh syphilis (syphilis secundaria recens). The first eruptions to appear in secondary syphilis are roseolae, papules, flat condylomata; alopecia develops. Along with an increase in the antigen (treponeme) count antibody titres increase as well, reaching their highest limit at this period (1:160; 1:320; 1:640; 1:2560). Antibodies bind and suppress treponeme increase, eruption fades and syphilis secundaria latens begins. At this phase of latent syphilis, positive serological reactions constitute the only evidence of syphilitic infection in the organism. Antibody titres have decreased to a medium level (1:80). Because of this decrease treponemes begin to multiply most intensively at the sites where they are still preserved. Eruption starts once again, being linked with treponeme reactivation as hematogenic dissemination no longer takes place. This period of secondary syphilis is called syphilis secundaria recidiva. It is replaced by the latent period followed again by a relapse and this change goes on for several years.

Table I. *Morbidity from syphilis in Latvia (1991-2001)*

| Year | Intensive index (per 100000 population) | Cases of congenital syphilis (absolute proportion) |
|---|---|---|
| 2001 | 24.5 | 5 |
| 2000 | 42.1 | 8 |
| 1999 | 63.2 | 6 |
| 1998 | 105.6 | 15 |
| 1997 | 121.4 | 22 |
| 1996 | 124.9 | 25 |
| 1995 | 91.9 | 15 |
| 1994 | 59.8 | 2 |
| 1993 | 31.8 | 0 |
| 1992 | 10.3 | 1 |
| 1991 | 8.1 | 1 |

Syphilis II recens differs from syphilis II recidiva through the following symptoms: Patients suffering from fresh syphilis still have a primary syphiloma. Of all polyscleradermic lymph nodes the attending bubo is the largest. These patients have more eruptions and they are smaller than is the case in secondary relapse syphilis. The later the relapse the fewer eruptions to occur, grouped only in definite areas (the skin of the genitals, mucous membranes and the circum anum region are the sites most commonly affected; soles and palms may be involved). In secondary fresh syphilis, eruptions are symmetrically and regularly disseminated in the body skin and in flexures of extremities; during a relapse phase they are more frequently observed in extensor areas. Alopecia and leucodermma are more

Table II. *Distribution of syphilis according to diagnoses in Latvia (1996-2001).*

| Year | Proportion | Lues I | Lues II recens | Lues II recidiva | Lues latens praecox | Lues latens tarda | Neuro-lues | Lues latens ignorata |
|---|---|---|---|---|---|---|---|---|
| 1996 | 3124 | 729 | 478 | 1134 | 750 | 7 | 1 | - |
| 1997 | 3008 | 621 | 364 | 1135 | 863 | 1 | 1 | 1 |
| 1998 | 2597 | 416 | 282 | 985 | 978 | 11 | - | - |
| 1999 | 1541 | 183 | 109 | 415 | 805 | 16 | 3 | 1 |
| 2001 | 1021 | 89 | 42 | 193 | 662 | 25 | 2 | - |
| 2001 | 594 | 63 | 25 | 93 | 376 | 19 | 6 | 7 |

often present in relapse syphilis patients.

Tertiary syphilis starts as late as in 3–4 years after infection. At that time inflammation at the site of treponeme localisation gets more specific; infection granuloma develops. Tertiary syphilis has characteristic eruptions: tubercles in the dermis or gummas in the hypodermis. In tertiary syphilis there are few treponemes (no evidence in bacteriological tests). The reaction of the organism, however, is dramatic. Tissue destruction occurs and ulcers form and leave scars. Active tertiary syphilis lasts from six months to 1–2 years. Then the latent tertiary period sets in, during which remainders of the active tertiary period are observable as scars and atrophy. For patients of tertiary syphilis, serological reactions may be of low titres or even negative. Untreated syphilis may cause damage to internal organs and the nervous system. The most common localisation of visceral syphilis is in the cardiovascular system (particularly in the ascending aorta-specific mesoarthritis, aneurysm of the aorta and rupture of the aneurysm with rapid lethal outcome), in the liver, lungs, stomach and other organs, also in bones and joints.

Early neurosyphilis may manifest itself as a vascular lesion. Later, gummas may develop.

Late degenerative damage of grave consequences to the nervous system are tabes dorsalis and progressive paralysis, conditions to be handled by neurologists and psychiatrists. Under unfavourable conditions (lack of effect from antibiotics, lack of substances needed for metabolism), treponema pallidum may form cysts and L-shapes that persist in the tissues of macro-organisms. With the disappearance of noxious factors revival of these protective forms is possible.

Treponema pallidum is partly an anaerobic bacterium with an intricate protein, polysaccharide and lipoid antigen structure that does not grow in artificial cultures. This makes investigation very difficult.

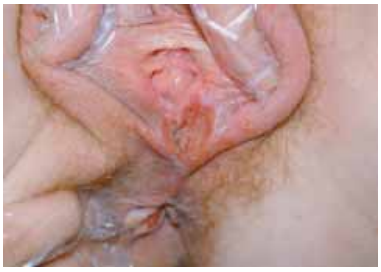
## Epidemiology

The disease is acquired from the source of infection, a person suffering from syphilis. Syphilis is classified as acquired and congenital. The method of infection may differ in any of the cases. Infection may be transmitted through the patient's

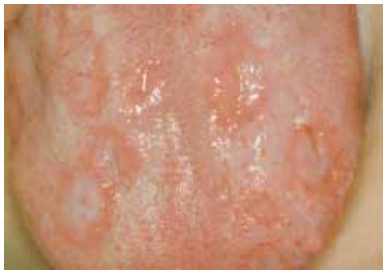
a) eruption with an erosive and ulcerous surface;
b) secretion (saliva, sperm, mother's milk);
c) blood, lymph.

*Ways of infection*

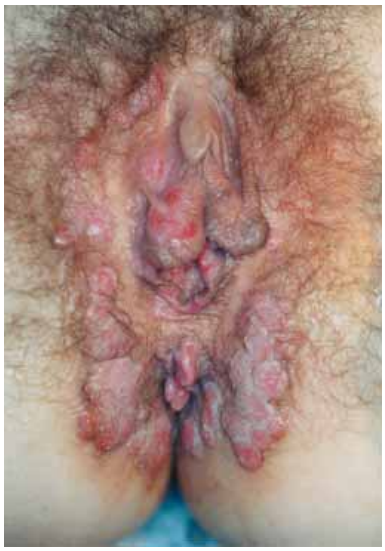
Infection through skin and mucous membranes (acquired syphilis). According to the prevailing opinion infection is not likely to be acquired through intact skin and mucous membranes. The pale treponeme gains entrance into the human organism only if at least a microscopic lesion of skin and the mucosa is present. Infection is by direct or indirect contact with the affected person. Direct infection with syphilis occurs through direct bodily contact, most frequently during sexual intercourse. Infection can also take place without any sexual contact, e.g. through kissing and the like. Direct bodily contact is the way in which infection occurs in most cases. Indirectly, in the non-sexual way, the disease may also be communicated through contact with articles used by a syphilitic: dishes, instruments etc. This is the so-called "syphilis through everyday contact." Although possible in unsanitary conditions, this kind of infection is



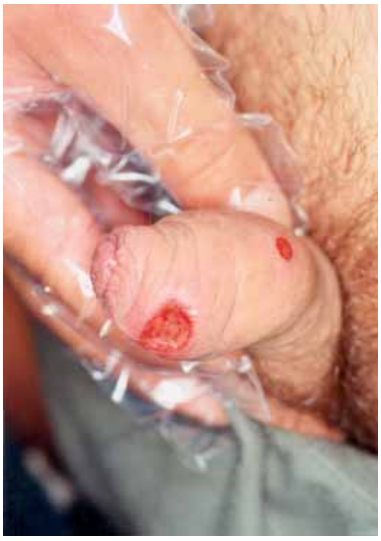
Ulcus durum preputii



Papulae erosivae ad linguam



Condyloma lata



Duo ulcera dura

Corona veneris

Alopecia syphilitica

Roseolae

rarely observed at present. Syphilis through everyday contact was widespread in Bosnia-Herzegovina after World War II and in other areas.

Infection due to blood transfusion (acquired syphilis). Infection by means of blood transfusion is chiefly possible in case of direct blood transfusion, resulting in transfusion syphilis. This kind of infection is rare because:

1) direct blood transfusion is currently seldom done;
2) the donor's blood is tested for syphilis;
3) the pale treponeme perishes through conservation of the blood and preserving it for at least five days.

*Infection of the foetus by the mother (congenital syphilis)*

In this case infection takes place during pregnancy as the pale treponeme from the syphilitic expectant woman gets into the foetus via the placenta. About 40% of infected offspring die during pregnancy (late spontaneous abortion, stillborn child) or in the neonatal period from birth to the 28th day of life.

*Immunity*

Natural (inborn) immunity to syphilis has not been observed in humans. Permanent immunity is not conferred by having had syphilis and repeated infection and disease (reinfection) is possible. In the ill person's organism non-sterile immunity to the infection develops. It starts on the 10–14th day after appearance of the hard chancre. While the treponeme is still in the patient's organisms he or she is practically immune and reinfection does not occur. Immunity persists as long as the pale treponeme continues to exist, but disappears after a complete cure from syphilis. In cases where the syphilitic patient gets additionally infected this provokes the appearance of syphilis. Thus on contact with a syphilis case in a conta-

*Table III.* Scheme of the course of acquired syphilis

| Diagnosis | Duration of the period | Symptoms | Diagnostic methods |
|---|---|---|---|
| Incubation period | 3– 4 weeks | - | IFR/IFA |
| Primary syphilis | 6– 7 weeks | 1. Primary syphiloma (erosion, ulcer, fissure)<br>2. Regional lymphadenitis<br>3. Polyscleradenitis | A. bacterioscopic<br>B. SED (VDRL)/RPR<br>C. TPHA<br>D. IFR/IFA |
| Secondary fresh syphilis | 1.5– 2 months | 1,2,3<br>secondary syphilids:<br>4. Roseola<br>5. Papules<br>6. flat condylomata<br>7. diffuse hair loss<br>8. pustule ± | A, B, C, D<br>E. TPI (Treponema pallidum immobilisation)<br>F. Examination of cerebrospinal liquor |
| Early latent syphilis | 1.5– 2 months | - | A, B, C, D, E, F, G |
| Secondary relapse syphilis | 1.5– 2 months | 4, 5, 6, 7, 8<br>9. leukoderma | A, B, C, D, E, F, G |
| Late latent syphilis | 6 months– 2 years | - | B, C, D, E, F, G |
| Secondary relapse syphilis (repeated x times) | 1.5– 2 months | Secondary syphilids (tendency to group):<br>4, 5, 6, 7, 8, 9 | A, B, C, D, E, F, G |
| Late latent syphilis | X years | - | D, E, G, G |
| Tertiary syphilis | X years | 1. Tubercles<br>2. Gumma | B, C, D, E, F<br>G. Histologic examination |

gious form a person suffering from secondary latent syphilis gets still more treponemes and the eruption of secondary syphilis appears. Penetrating into human organisms treponemes give rise to response reaction from the organism's immune system: formation of various antibodies to treponeme antigens. The following antibodies exist: immunofluorescines, immobilisins, reagins. A number of laboratory diagnostic tests are based on their presence in the patient's serum. In the organism the pale treponeme provokes the formation of a substance (reagin) similar to treponeme antibodies that results in positive findings in complement (KSR, Wassermann reaction) and flocculation tests in which lipid suspensions obtained from normal tissues of mammals, e.g. cor bovinum muscle (cardiolipin antigen) are used as an antigen.

In the affected person's organism specific antibodies to Treponema pallidum antigens start developing as immunoglobulins according to their structure. IgG, IgM and to some extent IgA are of diagnostic value in syphilis. The antibodies do not form simultaneously. At various stages of syphilis some of the globulin fractions prevail in the patient's plasma. At the onset of syphilis large molecular IgA and IgM antibodies (immunofluorescines) are the first to appear, while antibodies to protein antigens develop later (reagins, precipitins). The last to form are immobilisins, chiefly IgG class antibodies.

*Incubation period*

In young healthy individuals the incubation period usually falls between 21–24 days. In cases of

Table IV. *Advised therapy for acquired syphilis*

| | I | II | III | IV | |
|---|---|---|---|---|---|
| 1. Benzathini benzylpenicillinum (Retarpen). 2.4 mill. units i/m at 2 injection sites once weekly | 2 injections | 3 injections | 5 injections | For continuation of therapy 3 injections | - |
| 2. Procainpenicillinum (Benzylpenicillinum--novocainum). 600 000 units i/m once daily | 12 days | 18 days | 21 days | - | |
| 3. Benzylpenicillinum 1 millon units i/m once a day | 10– 14 days | 10– 14 days | 10– 14 days, therapy is continued with preparation No 1– 3 injections | 10– 14 days, therapy is continued with preparation No 1– 3 injections | Advisable for neurosy-philis patients, 12– 24 million units i/v daily, as 2– 4 million units every 4 hours for 14– 21 days |
| 4. Benzylpenicillinum 400 000 units i/m every 3 hours | 14 days | 28 days | 28 days | For continuation therapy 28 days | Advisable for pregnant women |
| 5. Doxycyclinum 0.1 twice daily | 15 days | 30 days | 30 days | For continuation of therapy 30 days | In case of intolerance to penicillin |
| 6. Eryhtromycinum 0.5 4 times daily | 15 days | 15 days | 30 days | 30 days for continuation of therapy | In case intolerance to penicillin |

The duration of therapy and methods used in various stages of syphilis are different. For treatment we advise the following division into groups:

Group I. Syphilis primaria seronegativa, syphilis primaria seropositiva;

Group II. Syphilis secundaria recens, syphilis secundaria recidiva, syphilis latens praecox (duration of the disease up to 2 years);

Group III. Syphilis secundaria recidiva, syphilis latens tarda (duration of the disease more than 2 years);

Group IV. Neurosyphilis, syphilis cardiovascularia, syphilis tertiaria.

massive infection the incubation period may be as short as 14 days. For patients with immunodepression (alcoholics, drug addicts, persons having a chronic infection etc.) and for those who have used antibacterial preparations for other diseases at this time the incubation period may persist for several months.

*Periods of acquired syphilis and their characterisation*

Primary syphilis (syphilis primaria), which starts after the incubation period with the formation of a primary syphiloma, persists for 6–7 weeks. During the first week regional lymphadenitis develops, with polysceladenitis occurring at the end of the period. In the first three weeks of this phase Wassermann reaction is negative and this is called the seronegative period. The following 3–4 weeks comprise the seropositive period. Clinically this period differs from the previous one only by a positive Wassermann reaction. In Latvia, this reaction is no longer applied, due to its non-specific character, and the division into two periods is not of current interest.

Secondary fresh syphilis (syphilis secundaria recens) sets in following treponeme dissemination. Secondary syphilids appear and the primary syphiloma gradually regresses. At this period the number of treponemes is the highest, the highest antibody titre is present, as well as the largest amount of eruption. This is a most contagious period lasting for 1,5–2 months.

*Early latent syphilis [syphilis (secundaria) latens praecox]*

With the disappearance of secondary syphilids the latent period of syphilis sets in and syphilis can be diagnosed only serologically. Following secondary fresh syphilis the stage of early latent syphilis lasts for 1,5–2 months. However, after each following relapse, the latent periods last increasingly longer and may persist for years. The period is considered to be early latent syphilis if it sets in two years after infection.

*Secondary relapse syphilis (syphilis secundaria recidiva)*

Secondary syphilids occur at the sites of treponeme reactivation, a

stage lasting for 1.5–2.5 months. Interchanging with latent syphilis periods of varying extension, secondary relapse syphilis may recur several times. It is often said that the "older" the syphilis, the "poorer" it is, meaning there are less eruptions. In cases of late relapse syphilis there may be very few secondary syphilids that are difficult to discern for both patient and physician.

*Late latent syphilis [syphilis (secundaria) latens tarda]*

This is of at least a two-year duration. Contrary to early latent syphilis serological reactions are of low titres. Sexual partners of recent years are not likely to contract the disease and a non-specific pathology of internal organs and the nervous system is possible.

*Tertiary syphilis (syphilis tertiaria)*

In tertiary syphilis (syphilis tertiaria) there are few treponemes in the organism whereas the humoral immune system has become exhausted and cellular immunity predominates in the organism's defence reactions. The onset of this stage is highly individual – from 3–20 and more years depending on the state of the immune system.

*Primary syphilomas (Syphilis primaria)*

*Clinical picture*. The classical forms are *hard chancre (ulcus durum)* or erosion at the site of treponeme entry. In its classical appearance the primary syphiloma is round, oval or appears as a fissure with even margins and a smooth, flat, dish-like surface (diameter 0.5–1 cm). At its base a densely elastic plate-like infiltrate forms. As a rule the genitals are affected although it may occur extragenically as well. The most common form of non-typical primary syphiloma is *indurative edema (oedema indurativum)* that may combine with a typical primary syphiloma. *Amigdalitic chancre* occurs by way of orogenital infection and simulates common tonsillitis in being only unilateral and with erosion or ulcer on the tonsil. *Chancre panaritium* is rare and may be chiefly due to professional infection acquired by the physician. This primary syphiloma bears resemblance to common panaritium.

*Regional lymphadenitis (scleradenitis regionaris)* develops in a week's time following primary syphiloma. Lymph nodes are densely elastic and non-confluent. In the overlying skin changes are not evident.

*Differential diagnosis*

- Traumatic erosion.
- Herpes progenitalis.
- Ulcus molle.
- Pyodermia chancriformis.
- Scabies on genitals.
- Carcinoma.
- Balanopostites.

*Secondary syphilids (syphilis secundaria)*

*Clinical picture.* Maculous syphilids. Roseola (roseola corporis) is the first symptom of secondary syphilis giving evidence of treponemal dissemination. The roseola is usually localised on lateral surfaces of the body as a pale pink patch the size of a nail without sharply demarcated borders. It does not desquamate.

*Differential diagnosis*

- Toxicodermia.
- Pityriasis rosea Gibert.
- Cutis marmorata.
- Roseola typhosa.
- Maculae caeruleae.

*Depigmented patches (leucoderma*) of various size and localised on the posterior and lateral surfaces of the neck are a characteristic symptom of relapse syphilis rarely seen as early as the sixth month after infection. In most cases leucoderma gives proof of early neurosyphilis (most commonly of asymptomatic meningitis).

*Differential diagnosis*

- Pityriasis versicolour.
- Leucoderma secundarium.
- Vitiligo.

*Papulous syphilids (papulae lenticulares).* The preferred localisation sites are the genitals, the region of the anal orifice, oral mucosa, palms, soles, and areas where the skin gets irritated (body creases). Papules are of a copper red coloration, flat, and do not become confluent. There may be desquamation on their surface *(papulae psoriasiformes)* whereas on scratching the scales separate and in the periphery of the papule a de-

tached wall of the epidermis Biett collarette becomes evident. At sites of irritation to the papules (mucosa, skin creases) erosions *(papulae erosivae)* develop on their surface. These erosive papules may become hypertrophic and form flat condylomas *(condylomata lata)*. Typical sites affected are the genitals, the region of the anal orifice, and skin creases. In the relapse phase syphilis papules group and progress to the skin of the forehead at the hairline *(corona veneris)*.

*Differential diagnosis*

- Psoriasis vulgaris.
- Parapsoriasis guttata.
- Lichen ruber planus.
- Mycosis pedum.
- Haemorrhoides.

In the phase of secondary syphilis the oral mucosa presents an erythematous appearance. Erythema of the mucosa of the fauces (angina erythematosa) is a characteristic sign with sharply demarcated borders and a cyanotic coloration. There are no subjective complaints. Oral syphilitic papules are most frequently present in the mucosa of the fauces, on the lips, tongue and palate (diameter 0.5–1 cm). Erosions easily form on their surfaces with a characteristic pale fibrosal tunic in the centre. Erosive papules are often observed in oral mucosa.

*Differential diagnosis*

- Angina catarrhalis.
- Lichen ruber planus.
- Stomatitis.

During the period of secondary syphilis, focal, rarely diffuse hair loss (alopecia areolaris et diffusa) is observed in the hairy part of the head. At the sites of hair loss hair sacs are preserved, signs of inflammation are not evident and in 1–1.5 months hair starts growing again.

*Differential diagnosis*

- Alopecia areata.
- Trichophytia adultorum chronica.
- Alopecia seborrhoica.

Papulous syphilids develop in patients with immune depression. Syphilitic impetigo *(impetigo syphilitica)* may develop as well as syphilitic ecthyma *(ecthyma syphiliticum)* syphilitic acne *(acne syphilitica)* and some other conditions simulating various forms of pyodermia. Syphilitic pustules are sterile and a papulous infiltrate is found at their base.

*Differential diagnosis*

- Impetigo streptogenes.
- Ecthyma vulgare.
- Acne vulgare.

In the past decade morbidity from syphilis in Latvia has increased dramatically, reaching the highest level in 1996 when 124.9 cases per 100,000 inhabitants were registered, or 3,124 cases (the population of Latvia is 2.6 million), including 25 cases of congenital syphilis (see Table I.) More than æ of the patients were diagnosed as having syphilis in the secondary stage (see Table II) [1, 2].

In the management of syphilis in Latvia doctors follow the guidelines developed in this country [1] that are very similar to the European guidelines for the management of syphilis [3, 4], with some insignificant differences. In Latvia, we follow the division of syphilis in stages of primary, secondary, and tertiary as opposed to such phases as early or late. Thus, the doses for a course are larger in some cases, aimed at preventing relapses. For about 70% of adult patients in Latvia prolonged procainpenicillinum or benzylpenicillinum is used. In cases of intolerance to penicillin, doxycycline or erythromycin is used [1, 3, 5] (see Table IV).

## References


1. Rubins A., Gutmane R., Rubins S., Chigarevska L., Treija I., Syphilis in: Sexually Transmitted Diseases, LDF 2001, Riga, p. 8–37.
2. Rubins A., Rubins S., Jakobsone I., Syphilis and gonorrhoea in the Baltic countries, J. Sexually Trans. Infection., June 2000, Vol 76, Nr.3 p. 214.
3. Goh B.T., Van Voorst Vader P.C., European guideline for the management of syphilis, International Journal of STD & AIDS, 2001; 12 (suppl.): 14–26.
4. Van Voorst Vader P.C., Syphilis management and treatment, Dermatol Clin., 1998; 16: 699–711.
5. Akovbyan V.A., Kubanova A.A., Akovbyan G.V. et al., Benzylpenicillin benzathine (Extencillin) in the treatment of syphilis: five years' experience [in Russia], Vestnik Dermatologii I Venerologii, 1998, no. 4: 61–64.