

POST-PRIMARY SYPHILIS

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Post-primary syphilis may be distinguished according to clinical presentation and epidemiological features in: secondary, latent and late syphilis.

Secondary syphilis is the stage when generalized manifestations occur, prevalently on the skin and mucous membrane, after the chancre period. The clinical presentation results from propagation of spirochetes from a primary chancre.

The interval between the primary lesion and the secondary eruptions varies considerably. Secondary syphilis usually appears clinically 6 to 8 weeks after healing of the chancre, although in 15 percent of patients the primary lesion will still be present when the secondary symptoms begin. The secondary lesions subside within 2 to 6 weeks. In the pre-antibiotic era, up to 25 percent of untreated patients experienced one or more subsequent generalized or localized mucocutaneous relapses, particularly during the first year of infection, before entering the latent stage.

Constitutional symptoms

The patients with secondary syphilis may present with a flu like prodrome, although the majority of patients present only mucocutaneous manifestations. Constitutional symptoms include malaise, low-grade fever, appetite loss, headache and myalgia.

The headache, which is characteristically worst at night, may be the symptom which brings the patient to the doctor. It is often caused by early syphilitic meningitis with increased intracranial pressure and pleocytosis. Almost all secondary eruptions are accompanied by universal micropolyadenitis.

Cutaneous manifestations, termed syphilids, are seen in over 80 percent of secondary syphilis cases. They recur during the first 2 years of the disease unless adequate treatment is given. In the early stages of the disease the eruptions have a symmetric pattern; those occurring later infection) are pleomorphic, and more frequently asymmetrically distributed.

Over 95 percent of secondary syphilis eruptions have one of these four clinical presentations: macular, maculopapular, papular, and annular. Other less frequently encountered clinical presentations include nodular and pustular eruptions, nails changes and hair loss.

Macular syphilid

Macular syphilid represents the earliest cutaneous manifestation of the secondary stage. The lesions usually begin 7 to 10 weeks following infection and 3 to 6 weeks after the chancre.

The eruption, also known as "roseola syphilitica", consists of bilaterally symmetric, pink in light skin, coppery-red in black skin, round macules, about 1 to 2 cm in diameter, with indistinct edges.

The first spots are nearly always on the sides of the chest and the abdomen and may easily overlooked, especially if the examination takes place under artificial light. As the rash develops, the trunk and proximal extremities are progressively involved. The face is usually spared, but any area, including the palms and soles, can be involved. The macules do not scale or itch and, being in some patients sparse and evanescent, may pass unnoticed, particularly in subjects with deeply pigmented

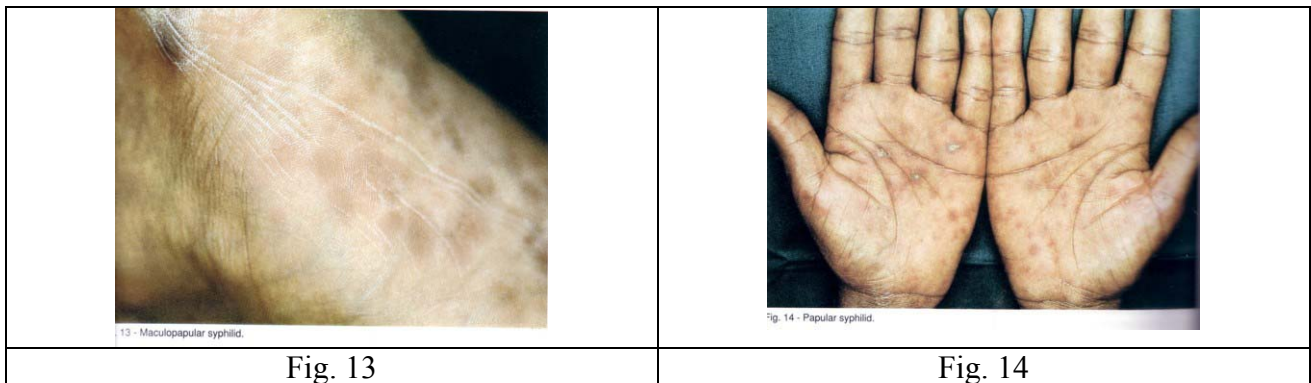
skin. In untreated cases macular eruptions may recur; these later eruptions often consist of a few larger lesions distributed irregularly and often confined to the limbs.

Papular syphilid

If this appears to be the first eruption, it usually means that the macular rash has passed undiagnosed. More usually, early papular rashes arise in an existing macular syphilide - maculopapular syphilide (fig. 13, below). As the secondary stage progresses, the lesions become frankly papular.

The papule is the basic lesion of secondary syphilis. Its particular form of presentation can vary widely depending on the nature and colour of the patient's skin, the site affected and the climate, hygiene and clothing.

The typical papule is rather firm and round or, in large papules, sometimes oval. The colour varies from reddish-brown in new lesions to brown in the older lesions. Early papules tend to be shiny, but gradually they become covered with a thin layer of scale (papulosquamous syphilides). A thin, white scaling ring on the surface of the lesion, known as Biette's collarette, is a helpful diagnostic sign, although it is not pathognomonic. Papular syphilides are widely distributed, frequently involve the palms (fig. 14, below) and soles, and may occur on the face and scalp.



On macerated skin surfaces eroded weeping papules with a tendency to hypertrophy often appear. On the genitals, they take the form of large exudating papules known as "condylomata lata" (fig. 15, below).

In men condylomata lata may occupy large parts of the glans, the coronal sulcus and the inner side of the prepuce. In women hypertrophy may be very pronounced and the lesions are commonly located around the vulva. Condylomata lata occur also around the anus.

In the later phases of secondary syphilis, papular eruptions are more frequently pleomorphic. Nummular lesions, 1-3 cm in diameter, covered by massive layers of scales resembling psoriasis, may appear. Papules can be arranged in annular or circinate configurations or appear as small conical or spinular elements. These micropapular and miliary eruptions tend to be arranged in larger or smaller groups over the body. The term "corymbose syphilide" is used when there is a large central papule surrounded by small satellite papules.

Pustular ulcerative syphilid

Purulent breakdown of lesions of a papular syphilide may create small pustules which rapidly dry up into crusts. Such a pustular rash occurs chiefly in debilitated or immunocompromized patients.

The widespread outbreak of these papulopustules evolving into ulcers characterizes the so called "malignant syphilis", also known as "lue maligna". With some exceptions, such as HIV-infected individuals, most of patients experiencing malignant syphilis probably have a selective, undefined impairment in the immunologic response to *T. pallidum*.

Pigmentary changes

When a roseola is fading, it sometimes leaves a pattern of depigmented spots superimposed on linear pigmented reticulated patches. Such a "leukoderma syphiliticum" is mostly located on the sides of the neck and was formerly known as the "necklace of Venus". In dark-skinned individuals intense loss of pigment within the affected areas may resemble vitiligo.

Nail changes

Nail changes of either the nail matrix, or the nail fold, is sometimes seen in the secondary stage. These changes have no specific characteristics.

Syphilitic alopecia

Patchy hair loss is characteristic of syphilis. The hair falls leaving small, scattered, irregularly thinned, "moth-eaten" patches of semi-baldness, never producing complete baldness (fig. 16, below). The disease can spread to the eyebrows and the beard.



Fig. 15 - "Condylomata lata" of secondary syphilis.

Fig. 15



Fig. 16 - Syphilitic alopecia.

Fig. 16

Mucus membrane lesions

On the mucous membranes secondary syphilis produces three manifestations: condilomata lata (previously described), mucous patches, and pharyngitis.

Mucous patches are macerated, grey, rounded and flat papules. The epithelium overlying the papules sloughs off, leaving non tender abraded areas on the tongue, palate, and inner aspects of the lips and cheeks. Ulceration is uncommon.

Pharyngitis of variable degrees may be identified in 25% of cases. Diffuse redness of the pharynx and tonsils may be very mild or severe with oedema and erosions.

Differential diagnosis

Syphilis is known as the "great imitator". The skin manifestations of secondary syphilis are so variable that this disease must be considered in the diagnosis of all dermatoses that are in any way "atypical".

With the macular rash, drug eruptions must first be considered. The history, itching and lack of adenopathy helps. Measles and rubella may cause difficulty but it is pityriasis rosea which is most often called into question. The presence of a herald patch and the collarette of scales distinguish this condition from macular syphilis.

With papular eruptions many diseases can cause difficulty in diagnosis. When the lesions are pruritic and lichenoid, the eruption may be difficult to distinguish from lichen planus and, when the scaling is thick, from psoriasis.

Exudative syphilitic papules on the face can be mistaken for impetigo and in the genital region for condylomata acuminata. The syphilitic condylomata lata, however, are broad-based in contrast to the papilliferous condylomata acuminata.

The micropapular varieties of syphilis can be confused with keratosis pilaris, lichen scrofulosorum and lichen planopilaris.

Eruption on the palms and soles can be strikingly similar to psoriasis and mycoses.

With oral lesions the question of aphthae has first to be considered. The painful nature of the lesions contrasts with syphilis and the aphthous lesions are markedly areolated.

Tonsillitis or tonsillary papules with multiple lymphadenopathy must be differentiated from infectious mononucleosis. The differential diagnosis is particularly difficult when infectious mononucleosis is accompanied by morbilliform rashes and biological false-positive tests for syphilis.

Systemic involvement in secondary syphilis

Secondary syphilis may produce complications in practically any organ. These include hepatitis, nephropathy, gastrointestinal involvement, arthritis, periostitis and iridocyclitis. The central nervous system may be invaded and abnormalities in the cerebrospinal fluid (CSF), such as raised cell count and increased protein content can be found in at least 15% cases.

LATENT STAGE

The latent stage corresponds to the asymptomatic stage following the secondary phase, which can be diagnosed solely by positive specific treponemal antibody test. Before the diagnosis of latent syphilis is accepted a thorough clinical examination should be made, including a CSF examination

and X-ray of the heart and aorta. Differentiation between latent syphilis and asymptomatic neurosyphilis is important because the latter has a more serious prognosis. This period is divided into early latent syphilis, within the first 2 years after infection, when the disease must be considered contagious and late latent syphilis where it is usually not. It has been estimated that about 30% of patients with untreated latent syphilis subsequently develop demonstrable signs of the disease. In the others where never develops clinically evident late syphilis, however, the occurrence of spontaneous cure is in doubt.

ASYMPTOMATIC NEUROSYPHILIS

Haematogenous dissemination of spirochetes to the central nervous system (CNS) occurs in early syphilis, although it may not be apparent for years.

The diagnosis of asymptomatic neurosyphilis is made in patients who no longer have manifestations of primary or secondary syphilis, who lack neurologic symptoms and signs, and who have certain CSF abnormalities (see "examination of CSF") due to *T. pallidum*. In patients with untreated asymptomatic neurosyphilis, the probability of progression to clinical neurosyphilis is about 20 percent in the first 10 years and is highest in those who show the greatest degree of pleocytosis or protein elevation. Patients with untreated latent syphilis and normal CSF probably have no future risk of subsequently developing neurosyphilis.

LATE (TERTIARY) SYPHILIS

The designation benign tertiary late syphilis includes any symptomatic manifestation, after the secondary and relapsing stages, that does not involve the cardiovascular or nervous systems. The more commonly involved organs are the skin, mucous membranes and bones, but the characteristic lesion, gumma, may appear in practical any organ.

LATE BENIGN SYPHILIS OF THE SKIN

Cutaneous manifestations may develop any time after the secondary stage resolves, with "precocious" lesions noted within the first 2 years and the late syphilides between 2 and 30 years.

Precocious tertiary syphilides were somewhat common in the pre-antibiotic era. Lesions usually occur during the first 4 years of infection. The skin manifestations have characteristics that border between secondary cutaneous lesions and consist of localized or generalized grouped papules with some degree of ulceration. On the skin tertiary syphilis normally produces two types of lesions: one superficial, the nodular syphilide, and the other deeper, the gummatous syphilide. Transitional forms also occur.

Nodular and noduloulcerative syphilide (tubercular syphilide)

The lesions begin as superficial, firm, pink to purple, papules or nodules that measure several millimetres to 2 cm in size. The lesions appear in a grouped configuration, rapidly extending peripherally in an irregular manner. Over weeks or months, central healing and advancing borders produce plaques with annular, arciform, serpiginous or polycyclic configurations that may reach over 30 cm. As the nodules grow, the skin appears red and eventually breaks down, resulting in ulcerations with raised borders and slightly purulent, crusted surfaces. The lesions of tubercular syphilide are asymptomatic and have a predilection for the extensor arms, back, and face. Even if untreated, the lesions heal over the years, leaving non-contractile, atrophic scars with increased or decreased pigmentation.

Gummas are painless pink to dusky red nodules of various sizes that are more common on the scalp, forehead, buttocks, and presternal, supraclavicular, or pretibial areas. The infiltration starts in the subcutis and subsequently involves the dermis, the epidermis and the underlying tissues. A gumma is nearly always painless. It has a characteristic tendency to necrosis, which begins in the middle where the tissue turns into a slimy and stringy mass, and which has given rise to the name "gumma". The gumma may be absorbed without ulceration of the skin but it always leaves a scar-like retraction. Ulceration may occur and is typically cylindrical, punched out, and covered with adherent yellowish-white slough. Large gummas may have several skin perforations and undergo necrotic changes that cause destruction of the intervening bridges of skin. Various geometric configurations are assumed (circles, ovals, etc.).

Mucous membrane lesions of late benign syphilis

The most commonly involved mucous membranes are those of the palate and of the nose. Ulcers in these areas may cause destruction of the bony and cartilaginous structures (saddle nose) or perforations that sometimes persist despite treatment. Gummas, nodules, and diffuse inflammation, with ulcers covered by a grey slough may appear in the tonsils, pharynx and tongue.

Differential diagnosis

On the face lupus vulgaris, epithelioma, sycosis barbae, infiltrated types of rosacea and lupus erythematosus frequently cause diagnostic difficulties.

On the trunk and limbs tertiary syphilides may resemble circinate psoriasis or mycosis fungoides. On the legs gummas can be confused with varicose ulcers, Bazin's disease and necrobiosis lipoidica. The changes in the tongue should not be confused with carcinoma; in these cases a biopsy must always be taken.

LATE SYPHILIS IN OTHER ORGANS

Almost any visceral organ may be affected in the late tertiary syphilis. The more commonly involved organs, other than skin and mucous membranes, are bones and joints. Skeletal changes occur commonly and are classified as gummatous osteitis, periostitis, and sclerosing osteitis. The chief symptoms are nocturnal pain and swelling, and the most common sign is tenderness.

Joint manifestations of late syphilis include arthralgias, synovitis, and arthritis and are caused by adjacent periostitis or gummatous infiltration from adjacent bone and skin lesions.

CARDIOVASCULAR SYPHILIS

Cardiovascular syphilis is essentially a disease of the aorta. Presumably, during the early stages of syphilis, treponemes invade the aortic wall, where they can remain dormant indefinitely. Predilection of *T. pallidum* for the ascending aorta is probably explained by the large number of lymphatics and vasa vasorum in this portion of the vessel. Infiltration of the vasa vasorum in the intima layer by lymphocytes and plasma cells produces an obliterative endarteritis, which over the years, weakens the wall of the aorta. This results in necrosis of the muscular and elastic tissues of this layer and consequential scarring.

Overt clinical cardiovascular disease occurs around 15 to 30 years following initial infection. Most frequently, aortitis remains asymptomatic and is usually found inadvertently at postmortem examination. The diagnosis is suspected when linear calcifications of the anterolateral aortic wall are present in chest radiographs.

In other cases, aortitis progresses to aortic aneurysm, coronary ostial stenosis and aortic valvular disease.

NEUROSYPHILIS

Despite the protean nervous system manifestations caused by syphilis, the major clinical categories of symptomatic neurosyphilis include meningovascular and parenchymatous syphilis (general paresis and tabe dorsalis). Meningovascular syphilis most commonly presents as a stroke syndrome. Other symptoms are headaches, vertigo, insomnia and psychological abnormalities. General paresis reflect widespread parenchymal damage and include a wide variety of CNS disturbances. Tabe dorsalis presents symptoms and signs of demyelination of the posterior columns, dorsal roots, and dorsal root ganglia. The Argyll-Robertson pupil, seen in both tabe dorsalis and paresis, is a small, irregular pupil which reacts to accommodation but not to light.

CONGENITAL SYPHILIS

Intrauterine infection with *T. pallidum* may occur at any stage of pregnancy. Untreated maternal infection may result in foetal loss, prematurity, neonatal death or nonfatal congenital syphilis.

The manifestations of congenital syphilis can be divided into (1) early manifestations, which appear within the first 2 years of life, often between 2 and 10 weeks of age, that are infectious, and resemble severe secondary syphilis in the adult; (2) late manifestations, which appear after 2 years and are non-infectious; and (3) the residual stigmata of congenital syphilis. The earliest sign of congenital syphilis is usually rhinitis soon followed by other mucocutaneous lesions that include bullae (syphilitic pemphigus), papulosquamous lesions, mucous patches and condylomata lata.

The most common early manifestations are osteochondritis and osteitis, particularly involving the metaphyses of long bones. Hepatosplenomegaly, lymphadenopathy, anaemia, jaundice, thrombocytopenia, and leukocytosis are also common.

Late congenital syphilis is defined as congenital syphilis which remains untreated after 2 years of age. In perhaps 60 percent of cases, the infection remains sub-clinical, while the clinical spectrum in the remainder resembles the acquired late syphilis in the adult. The clinical manifestations include cardiovascular syphilis, interstitial keratitis, neurosyphilis and gummatous periostitis.

Stigmata of congenital syphilis include Hutchinson's teeth, the centrally notched, widely spaced, peg-shaped upper central incisors, and "mulberry" molars, sixth-year molars which have poorly developed cusps, numbering more than the usual four. The abnormal facies of congenital syphilis, which includes frontal bossing, saddle-nose and poorly developed maxilla, may also be seen.

LABORATORY EXAMINATIONS

Dark-field examination technique

Dark-field examination is essential in evaluating cutaneous lesions, such as the chancre of primary syphilis, or condylomata lata of secondary syphilis. The surface of the suspected ulcerated lesion should be cleaned with saline and gauze and then gently abraded further with dry gauze, without

production of bleeding. A drop of the transudate is picked up on the surface of a glass slide, covered with a cover-slip and examined immediately for *T. pallidum* with a dark-field or phase contrast microscope by an experienced individual.

Serologic tests for syphilis

Syphilis produces two types of antibodies, the non specific "reaginic" antibody and the specific antitreponemal antibody, which are measured by the non nontreponemal and treponemal tests, respectively. Both tests are reactive in persons with any treponemal infection, including yaws, pinta, and endemic syphilis.

The nontreponemal antibodies produced in syphilis are directed against a lipodal antigen that results from the interaction of *T. pallidum* with host tissues. The most widely nontreponemal antibody test for syphilis is the Venereal Diseases Research Laboratory (VDRL) slide test. Normally the reaction becomes positive 5-8 weeks after infection (2-4 weeks after the appearance of the chancre). If insufficient penicillin treatment is given in the incubation phase, for instance in case of concomitant for gonorrhoea, the reaction may be delayed for several months. VDRL can be performed not only qualitative, but also quantitatively. The reagin titer reflects the activity of the disease: a four-fold or greater rise in titer may be seen during the evolution of primary syphilis: a persistent fall in titer following treatment of early syphilis provides essential evidence of an adequate response to therapy.

Because the antigen used in the non-treponemal tests is found in other tissues, it may be reactive in persons without treponemal infection, although rarely in titers exceeding 1:8. False-positive reagin tests are classified as acute if they become negative within 6 months and may occur during a variety of acute infections, such as viral diseases, mycoplasma pneumonia, and malaria, and following certain immunizations. Chronic reactions, which persist 6 months or longer, occur in intravenous drug addiction, autoimmune diseases, and aging. In patients with a false-positive reagin test, syphilis is excluded by obtaining a nonreactive treponemal test.

Treponemal tests

There are three standard treponemal tests: the fluorescent treponemal antibody absorption (FTA-ABS) test, the *T. pallidum* hemagglutination assay (TPHA) and the *T. pallidum* immobilization (TPI) test.

The FTA-ABS shows reactivity with IgM and IgG antibodies directed against *T. pallidum*. A quantitative evaluation has very little value in routine testing. Advantage of the FTA-ABS test include detection of recent infection, 1 or 2 weeks before other assays, and high specificity and sensitivity. In addition, determination of IgM might be useful for estimating the activity in late syphilis. However, performance of the test requires highly trained personnel. It is time-consuming, and reading the results is tiresome. Thus, FTA-ABS should be applied as a method for confirmation when reactivity is detected in other assays.

The TPHA renders the most reliable results in syphilis serology among the presently available tests. Its sensitivity and specificity is superior to the VDRL and to the FTA-ABS, except in primary syphilis. However, the reagents are rather expensive, and internal quality control and proficiency testing are very important, due to lack of standardization.

The TPI, in which immobilization of alive *T. pallidum* is induced by immune serum plus complement, is the most specific treponemal test (almost 100%), but technically demanding and,

therefore, not available in the majority of laboratories in developing countries. TPI becomes positive later than the other serological tests.

In summary, for practical purposes, VDRL should be used (1) for testing large numbers of sera for screening or diagnostic purposes and (2) to assess the clinical activity of syphilis and the response to therapy, whereas the other assays (TPHA, FTA-ABS and TPI), should be performed (3) for confirmation of the diagnosis of syphilis in patients with positive VDRL.

EXAMINATION OF CEREBROSPINAL FLUID (CSF)

The examination of the CSF is mandatory in the presence of clinical evidence of neurosyphilis or in any case of untreated syphilis of more than 2 years' duration. By contrast examination of the CSF in early secondary syphilis, that has been adequately treated, is unnecessary.

CFS is considered abnormal in the presence of pleocytosis (more than 3-5 lymphocytes per ml), elevation of protein content (total protein over 40 mg per cent), and positivity to serological tests for syphilis.

TREATMENT GUIDELINES

Penicillin is the drug of choice for all stages of syphilis. In penicillin allergic patients, other antibiotics, such as tetracyclines, erythromycin, and cephalosporins can be prescribed. However, because penicillin is the only effective therapy in neurosyphilis, congenital syphilis, or syphilis during pregnancy, allergy skin testing and eventual desensitisation is recommended in those patients reporting a history of penicillin allergy.

Recurrence rates for a given regimen increase as infection progresses. Thus, a longer duration of therapy is required in the later stages of the disease.

Two-twelve hours after administration of drugs with strong treponemicidal effect (e.g. penicillin), a febrile reaction often accompanied by an aggravation of the syphilitic symptoms may occur (Jarish-Herxheimer reaction). The reaction occurs more frequently when early secondary syphilis is treated. Corticosteroid given simultaneously with penicillin is indicated to reduce the risk for this reaction. The treatment regimens recommended for syphilis are described below.

Early syphilis (Primary, secondary, and latent syphilis of less than one year's duration).

Benzathine penicillin, in a single dose of 2.4 million units intramuscularly (i.m.), cures over 95 percent of cases of primary syphilis. In secondary syphilis a second dose of 2.4 million units 1 week after the initial dose is recommended. Because of the accelerated progression to neurosyphilis associated with HIV infection, early syphilis in HIV-positive individuals should be treated with penicillin G administered intravenously (i.v.) as in neurosyphilis.

Latent syphilis of indeterminate or more than one year's duration, cardiovascular, and late benign syphilis (gumma).

Benzathine penicillin, 2.4 million units i.m. once a week for 3 successive weeks (7.2 million units total) is the treatment of choice of latent and late benign syphilis. However, because up to 25 percent of patients with gummas will also have cardiovascular syphilis or neurosyphilis, careful examination of the patient and CSF examination is recommended for determination of optimal therapy. In particular, CSF examination is clearly indicated in certain situations: presence of

neurologic signs or symptoms, treatment failure, non penicillin therapy planned, serum nontreponemal antibody titer greater than 1:32. If CSF examination demonstrates abnormal findings, or there are signs of cardiovascular involvement, patients should be treated with the same regimen as neurosyphilis. Quantitative nontreponemal serologic tests should be repeated at 6 and 12 months after treatment. If titers increase fourfold or if an initially high titer fails to decrease, the patient should be reevaluated for neurosyphilis and re-treated appropriately.

Neurosyphilis

Treatment with benzathine penicillin is not recommended in neurosyphilis because it does not produce detectable drug concentration in CSF. Intravenously administration of penicillin G in doses of 12 million units per day for 10 days or longer ensures treponemicidal concentrations of penicillin in CSF. If CSF pleocytosis is present before treatment, CSF examination should be repeated every 6 months until the cell count is normal. If it has not decreased at 6 months, or it is not normal by 2 years, re-treatment should be strongly considered.

Pregnancy

Routine serologic testing in early pregnancy is considered cost effective in virtually all populations, even in areas of low prenatal prevalence of syphilis.

Where the prevalence of syphilis is high, and in high-risk patients, syphilis serology should be repeated in the third trimester and at delivery.

Pregnant women with seropositive results should be considered infected unless treatment can be verified and sequential serology antibody titers convincingly demonstrate an appropriate response. Treatment with penicillin is strongly recommended in pregnancy. The only potential serious side effect is the Jarish-Herxheimer reaction, which may precipitate labour (placental shock).

Infected pregnant women with penicillin allergy should be desensitised and treated. Erythromycin is prescribed only when penicillin desensitisation is impossible.

Newborn infants of mothers with positive VDRL or FTA-ABS tests may themselves have reactive tests, whether or not they have become infected, because of transplacental transfer of maternal IgG antibody. Thus, monthly quantitative VDRL should be performed on seropositive infants even if they were born to women who were treated adequately with penicillin during therapy. In addition, as IgM do not pass the placenta, the FTA-IgM test might be helpful to distinguish between actively produced antibody and passively transferred antibody.

In the absence of infection, nontreponemal antibody titers should be decreasing by 3 months of age and have disappeared by 6 months of age. Accordingly, treponemal antibodies should not persist beyond the first year of life. Unless this is the case, the infant should be treated for congenital syphilis, with penicillin, 50000 units/kg twice a day for 10-14 days.

It is essential to evaluate carefully infants born to seropositive mothers who remained untreated or received penicillin treatment less than 1 month before delivery or at any time during pregnancy with a non-penicillin regimen. Also, the offspring of mothers who did not have the expected decrease in serologic titers after treatment need to be carefully observed. The neonate's evaluation should include a thorough physical examination, antibody titration, CFS analysis, long-bone x-rays and chest x-ray. These infants should be treated if they have any evidence of active disease by the above examinations. Even with a normal evaluation, infants should be treated if their mothers have untreated syphilis or evidence of relapse or re-infection after therapy.

Treated infants should be followed with nontreponemal antibody titers, which should disappear by 6 month of age. Treponemal tests, however, may remain positive despite effective therapy.

PREVENTION

The prevention of syphilis depends upon use of condoms, and detection and treatment of infectious cases. The doctor treating early syphilis assumes a great responsibility towards all persons who have had contact with an infectious patient. Persons sexually exposed to a patient with infectious syphilis should be evaluated clinically and serologically. It may be advisable to treat prophylactically persons who were exposed to infectious syphilis within the previous 6 weeks with a single dose of benzathine penicillin 2.4 millions units i.m., if serologic test results are not immediately available or compliance appears uncertain (epidemiologic treatment).

Patients who have other sexually transmitted diseases should have a serologic test for syphilis. Alternatively, treatment with the same regimen as in primary syphilis should be considered if compliance with testing cannot be guaranteed.

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