- الاستاذ الدكتور وسام سهيل نجم
- كلية الطب جامعة تكريت

Sexually Transmitted Diseases (STDS)

Sexually Transmitted disease presentation:

- Genital ulcers or sores
- Urethra discharge
- Vagina discharge
- Lower abdominal pain
- Inguinal bubo
- Scrotum swelling
- Rectal or pharyngeal inflammation
- papules

STI versus STD----

- STI – Infections acquired through sexual intercourse (may be symptomatic or asymptomatic)
- STD – Symptomatic disease acquired through sexual intercourse
- STI is most commonly used because it applies to both symptomatic and asymptomatic infections

Types and their pathogenic causes

Disease	Cause
Bacterial	
Gonorrhea	Neisseria gonorrhoeae
Vaginitis	Gardnerella vaginalis, Anaerobes
Chancroid	Haemophilus ducreyi
Granuloma inguinale (Donovanosis)	Calymmatobacterium granulomatosis

Types and their pathogenic causes

Disease	Cause
Spirochaetes	
Syphilis	Treponema pallidum
Chlamydia	
Non-specific urethritis	Chlamydia trachomatis type D - K
Lymphogranuloma venereum	Chlamydia trachomatos type L 1,2,3.

Types and their pathogenic causes

Disease	Cause
Mycoplasma	
Pelvic inflammatory disease	Mycoplasma hominis
Non-specific urethritis	Ureaplasma urealyticum

Types and their pathogenic causes

Disease	Cause
Protozoa	
Trichomoniasis	Trichomonas vaginalis
Dysentery*	Entamoeba histolytica
Diarrhoea*	Giardia lamblia
Fungi Vaginal thrush	Candida albicans

Types and their pathogenic causes

Disease	Cause
Ectoparasites	
Pubic lice	Phthirius pubis
Genital scabies	Sarcoptes scabiei
Viruses	
AIDS	HIV
Genital herpes	Herpes simplex, type 2 (and 1)
Warts	Papilloma viruses types 6,11,16 & 18)
Hepatitis*	Hepatitis B

Syphilis

Syphilis, also known as lues, is a contagious, sexually transmitted disease caused by the spirochete Treponema pallidum subspecies pallidum. The only known host is the human.

BIOLOGY AND PATHOPHYSIOLOGY

- Treponema pallidum subspecies pallidum is a motile, spiral-shaped bacterium for which humans are the only natural host
- ranges in size from 5 to16 µm in length and 0.2 to 0.3 µm in diameter.
- It has corkscrew motility.
- Microscopically the bacterium is indistinguishable from other pathogenic treponemes that cause nonvenereal diseases, including bejel, yaws, and pinta.
- T. pallidum does not survive more than a few hours to days outside its host and cannot be cultured in vitro for long periods

BIOLOGY AND PATHOPHYSIOLOGY

- Following inoculation, T. pallidum attaches to host cells, including epithelial, fibroblast-like, and endothelial cells, likely by binding to fibronectin, laminin, or other components of host serum, cell membranes, and the extracellular matrix.
- It can invade rapidly into the bloodstream—within minutes of inoculation—and can cross many barriers in the body, such as the blood–brain, placenta, and infect many tissues and organs.

BIOLOGY AND PATHOPHYSIOLOGY

- That dissemination leads ultimately to manifestations of syphilis distant from the site of the chancre(s) and in a developing fetus.
- T. pallidum lacks virulence factors common to many other bacteria, including lipopolysaccharide endotoxin
- It does, however, produce a rapid immune response, mediated by membrane lipoproteins, that begins shortly after infection.
- Infection at all stages leads to infiltration by lymphocytes, macrophages, and plasma cells. CD4+ T cells predominate in chancres, and CD8+ T cells predominate in lesions of secondary syphilis

BIOLOGY AND PATHOPHYSIOLOGY

- Infection leads also to elaboration of Th1 cytokines, including IL-2 and IFN-γ, although downregulation (reduction in a cellular response) of the Th1 response during secondary syphilis, coincident with the peaking (reach a highest point) of antibody titers, might contribute to the organism's ability to evade the host immune response.
- The humoral immune response begins with production of IgM antibodies approximately 2 weeks after exposure, followed 2 weeks after that by IgG antibodies. IgM in addition to IgG continues to be produced during infection and can lead to immune-complex formation. Antibody titers peak (the highest) during bacterial dissemination, in secondary syphilis.

BIOLOGY AND PATHOPHYSIOLOGY

- The immune response is sufficient to prevent syphilis reinfection in persons who have untreated syphilis In other words, in what is called ‘Colles’ law or “chancre immunity,” persons with untreated syphilis will not experience another episode of primary syphilis as long they remain untreated.
- However, the immune response is insufficient to eradicate T. pallidum from the host
- The immune response is also not adequate to prevent reinfection after a person is cured of syphilis,
- Compared with persons with syphilis for the first time, for example, reinfected persons are less likely to have manifestations of primary or secondary syphilis and more likely to be diagnosed with latent syphilis.

BIOLOGY AND PATHOPHYSIOLOGY

- The immune response is also likely responsible for the tissue damage caused in syphilis. Damage to axons located near the site of a chancre might explain why that lesion, although ulcerative, is typically painless.
- Interest in a vaccine for syphilis continue, with focus on using outer membrane protein antigens to elicit an immunoprotective response

CLINICAL COURSE-**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) (1 year from contact)

↓

Late latent (more than 1 year)	↓
Remission (⅔)	Tertiary (⅓) Late benign (16%) Cardiovascular (10%) Neurosyphilis (5–10%)

PRIMARY SYPHILIS

- As defined by The Centers for Disease Control and Prevention (CDC), primary syphilis is a stage of syphilis characterized by one or more chancres, in the presence of laboratory evidence from tissues or serum
- At the inoculation site, a chancre develops after an incubation period that ranges from 10 to 90 days (average,3 weeks).
- The typical chancre, also called a Hunterian chancre or “ulcus durum” (hard ulcer), ranges in diameter from a few millimeters to 2 cm and is sharply demarcated with regular, raised borders that are indurated, giving the lesion a cartilaginous feel.
- The base is usually clean, and the chancre is classically not painful. Up to 35% of chancres, however, are reported painful, and multiple chancres have been reported in 32%–47% of cases

PRIMARY SYPHILIS

The absence of any of the typical features of a chancre does not rule out syphilis

Variations in clinical presentation can result from

- the number of spirochetes,
- the patient's immune status,
- concurrent antibiotic therapy,
- impetiginization.

Patients might not be aware of chancres, especially if painless and located in areas that are not visible, such as the anus, vagina, cervix, or oral cavity.

PRIMARY SYPHILIS

- Common genital locations for a chancre in men include the glans, the coronal sulcus, and the foreskin. Retraction of the foreskin when a chancre is present on the underside causes the foreskin to flip suddenly, a sign known as the dory flop, after the movement of a dory, a small wooden fishing boat, which flips suddenly when overturned.
- The dory flop sign can help distinguish chancres from other nonindurated causes of genital ulcer disease, such as herpes simplex virus infection and chancroid, that present without the induration that leads to the sudden flip of the foreskin

PRIMARY SYPHILIS

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,
- balanitis.

PRIMARY SYPHILIS

- Common genital locations in women, in decreasing order, include the cervix, labia majora, labia minora, fourchette, and urethra.
- Chancres in women can be more edematous than indurated. Edema indurativum is a unilateral labial swelling with rubbery consistency and intact surface, indication of a deep-seated chancre.

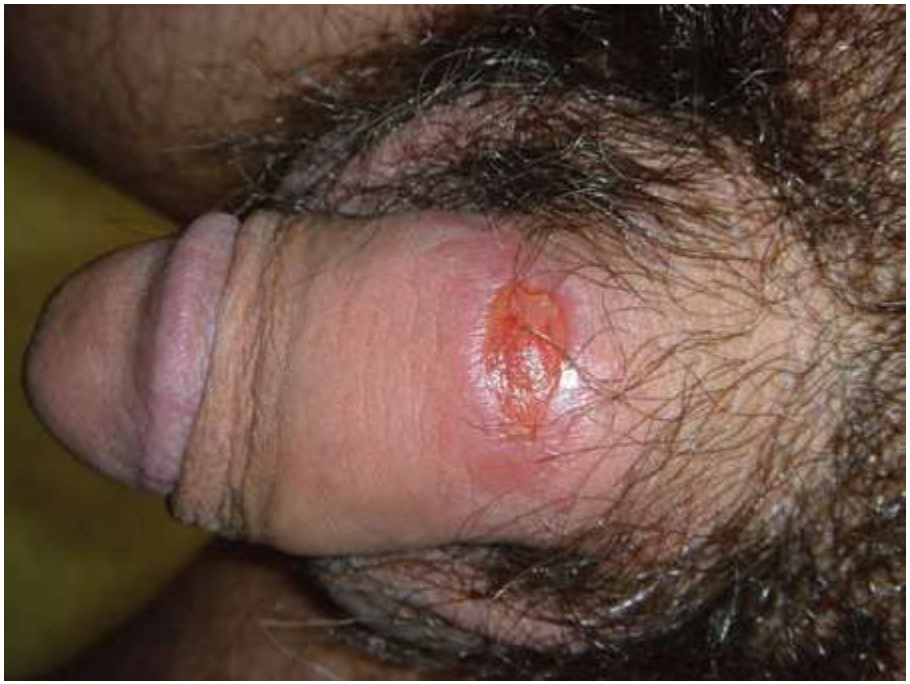
PRIMARY SYPHILIS

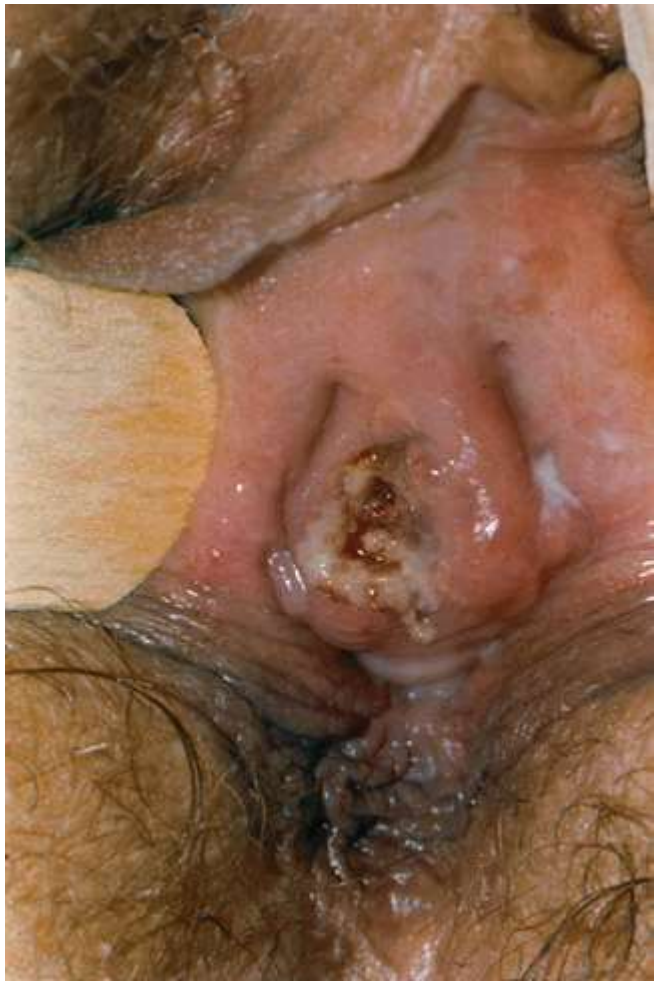
- Extragenital chancres in many areas of the body have been reported. Oral, perianal or anal areas (that can be difficult to detect on routine physical examination)
- The chancre heals in 3–6 weeks without treatment and1–2 weeks with treatment
- Scarring typically does not occur, although thin atrophic scars may occur. Coinfection with herpes simplex virus or Haemophilus ducreyi, the causative organism of chancroid, can be present in rare cases.

PRIMARY SYPHILIS

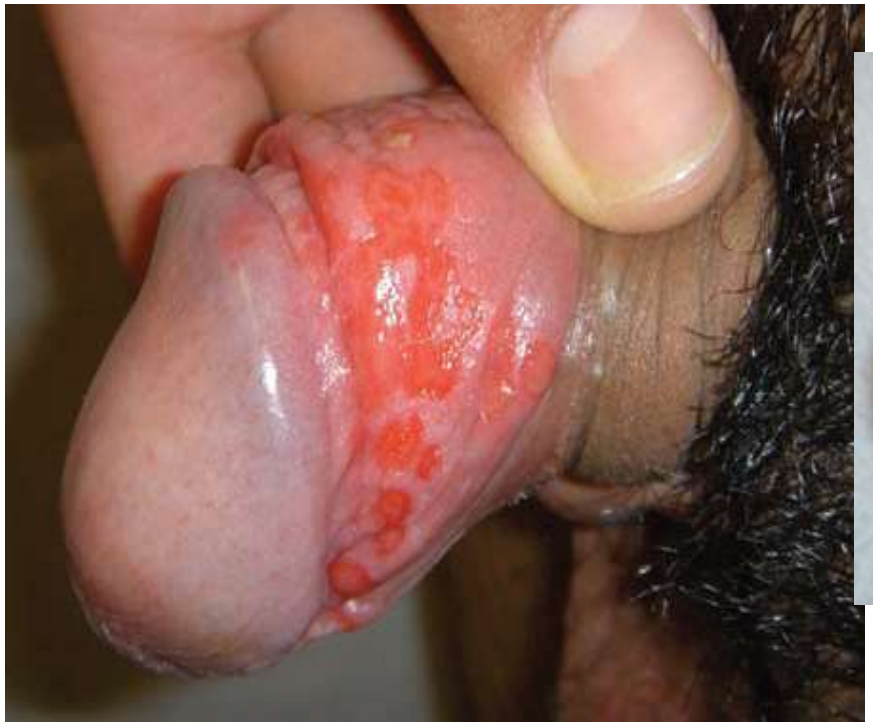
- Relapses of primary syphilis, called *monorecidive syphilis or chancre redux*, arise in the setting of untreated or inadequately treated syphilis and are rare.
- In 60%–70% of cases of primary syphilis, painless regional lymphadenopathy arises 7–10 days after the chancre appears, especially when the chancre's location is genital. Unilateral lymphadenopathy is more common early in the course of disease, with bilateral involvement later in the course.

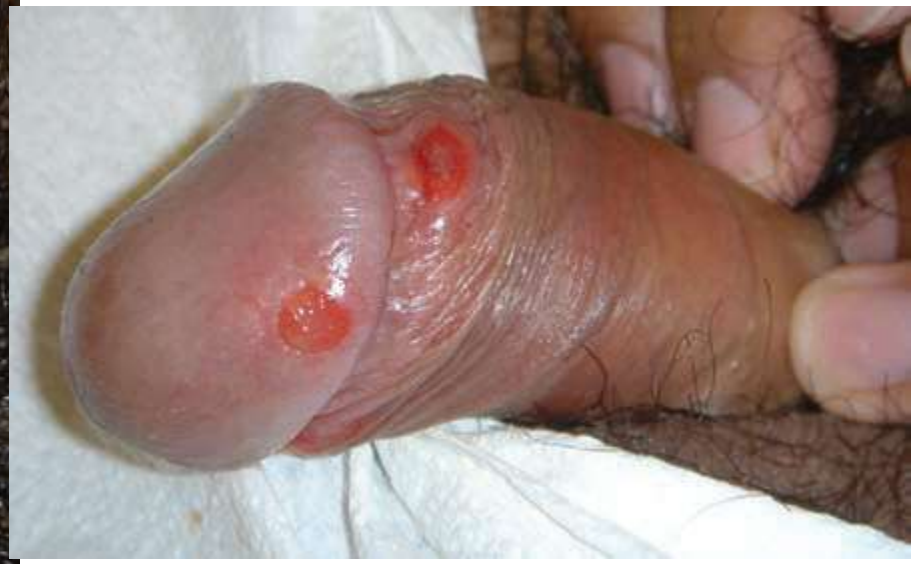
Chancre on the penile shaft, demonstrating a clean base and elevated borders on the shaft of the penis.
Chancre in a female. Necrotic ulcer at the orifice of the urethra.



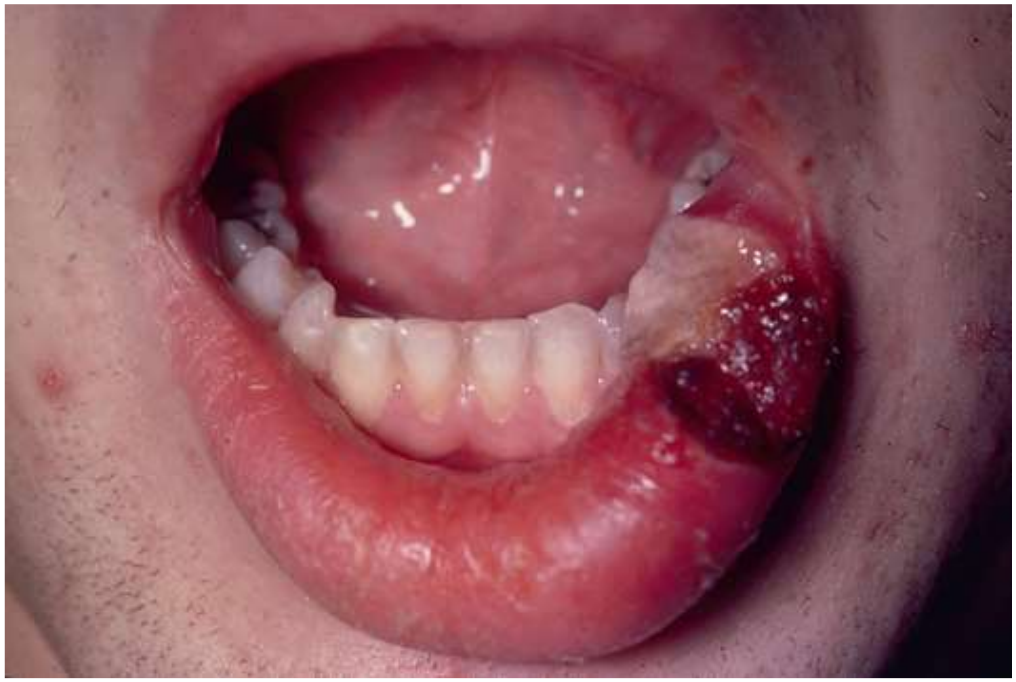


Multiple chancres

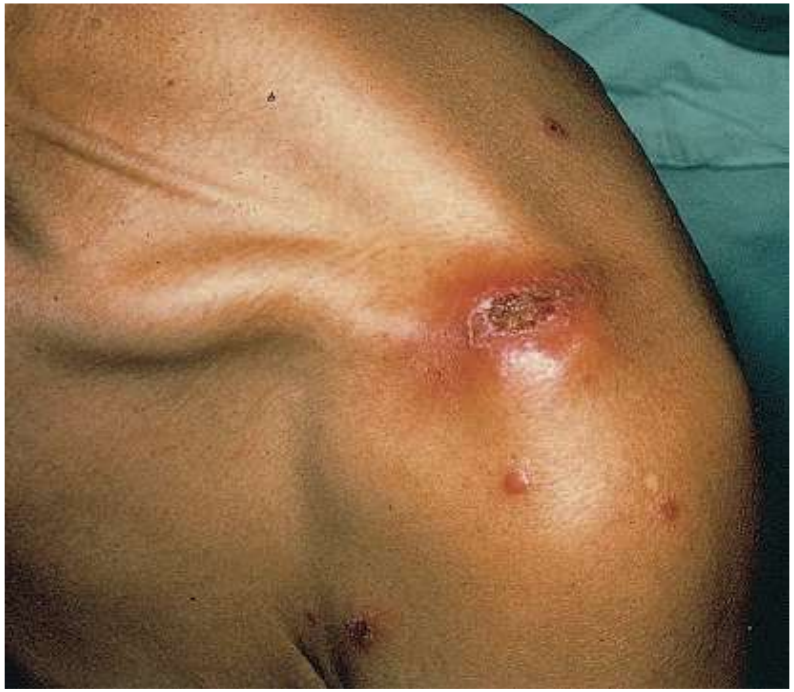




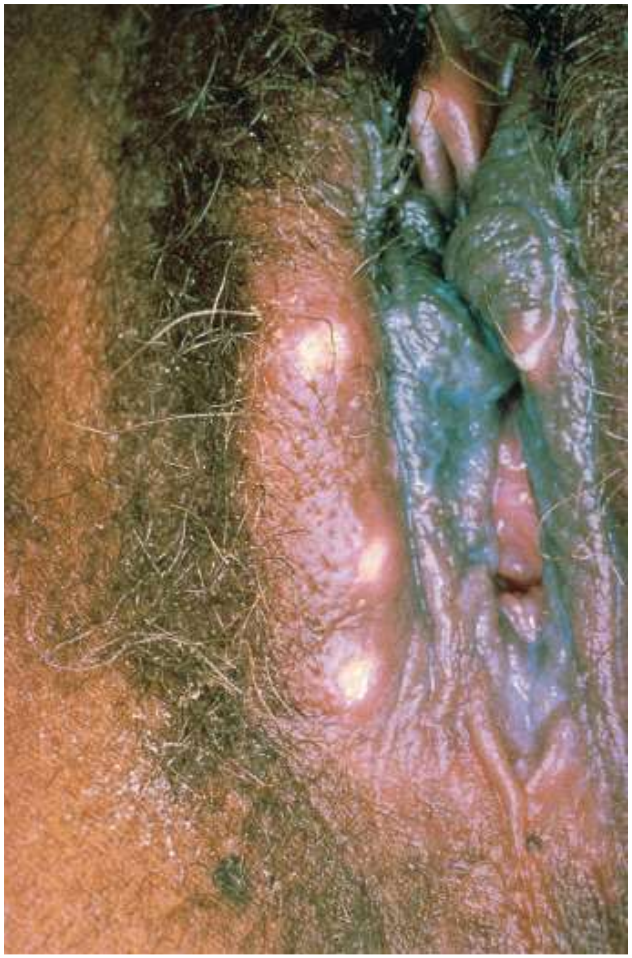
Ulcer of the lip, chancre of primary syphilis.



Primary syphilis, chancre on shoulder with secondary lesions present.



Multiple syphilitic chancres in a woman.



SECONDARY SYPHILIS

- As defined by CDC, secondary syphilis is a stage of syphilis characterized by localized or diffuse mucocutaneous lesions, often with generalized lymphadenopathy, in the presence of laboratory evidence from tissues or serum. The chancre may still be present.
- Lesions of secondary syphilis, classically called “syphilids” or, when affecting the skin, “syphiloderms,” typically erupt 3–12 weeks after the chancre appears (up to 6 months after exposure).
- Rash is present in nearly all cases of secondary syphilis. Erythematous macules (roseola syphilitica) or maculopapules are commonly present symmetrically on the trunk and extremities in 40%–70% of cases, with papular, papulosquamous, or lichenoid presentations less common.

SECONDARY SYPHILIS

- A white scaly ring on the surface of papulosquamous lesions, called Biette's collarette, is characteristic but not pathognomonic for syphilis.
- The face is typically spared in these generalized syphilids, although seborrheic dermatitis-like lesions around the hairline, termed the Crown of Venus or corona veneris, can form a crown-like pattern.
- Lesions are not usually pruritic, although pruritus was reported in up to 40% of patients in one study.
- Erythematous to copper-colored round papules, well demarcated and sometimes with an annular scale, are present on the palms and soles in nearly 75% of cases.
- Plantar lesions can be mistaken for calluses (clavi syphilitici).

SECONDARY SYPHILIS- Other manifestations:

- 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.
- Annular papules and plaques can be present around the mouth and nose, referred to as “nickels and dimes”.
- Papules and plaques, sometimes annular and papulosquamous, can also be present on the penis and scrotum
- Mucous patches are white-to-yellow erosions on the tongue. Confluence of mucous patches on the tongue has been termed plaques *fauches en prairie*. Mucous patches can be present elsewhere in the oral cavity, or at the corners of the mouth, where they appear as “split papules,” with an erosion traversing the center. Mucous patches are teeming with spirochetes and, hence, highly infectious.

SECONDARY SYPHILIS- Other manifestations:

- Also highly infectious are condyloma lata, 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 patients
- However, any moist intertriginous area of the body can have condyloma lata, including the axillae, web spaces between toes, and the folds under breasts or an abdominal panniculus.
- Mucous patches and condyloma lata have been reported in 8% and 17% of patients with secondary syphilis, respectively.

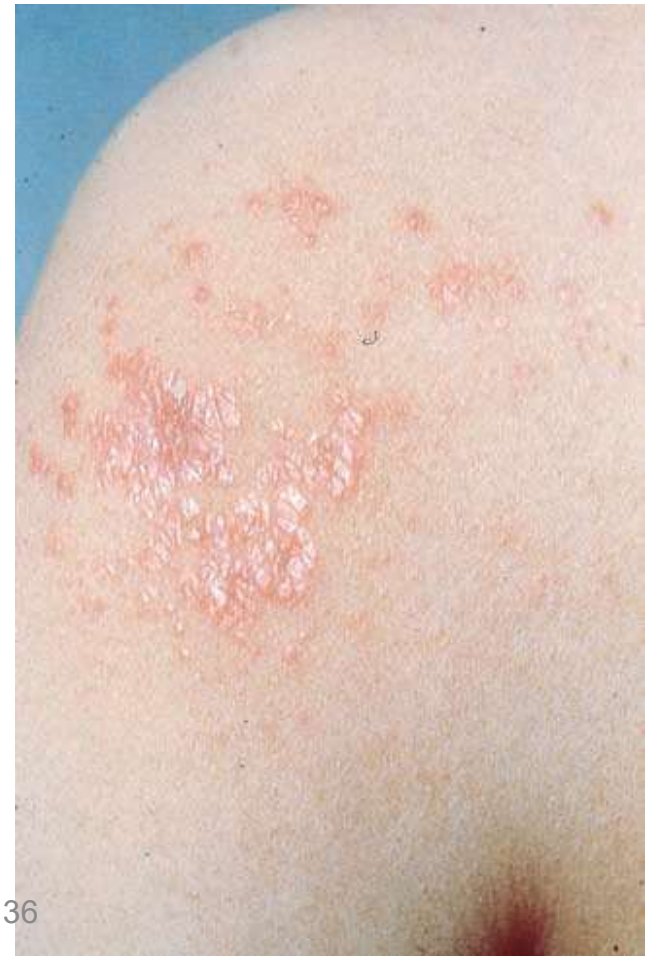
SECONDARY SYPHILIS- Other manifestations:

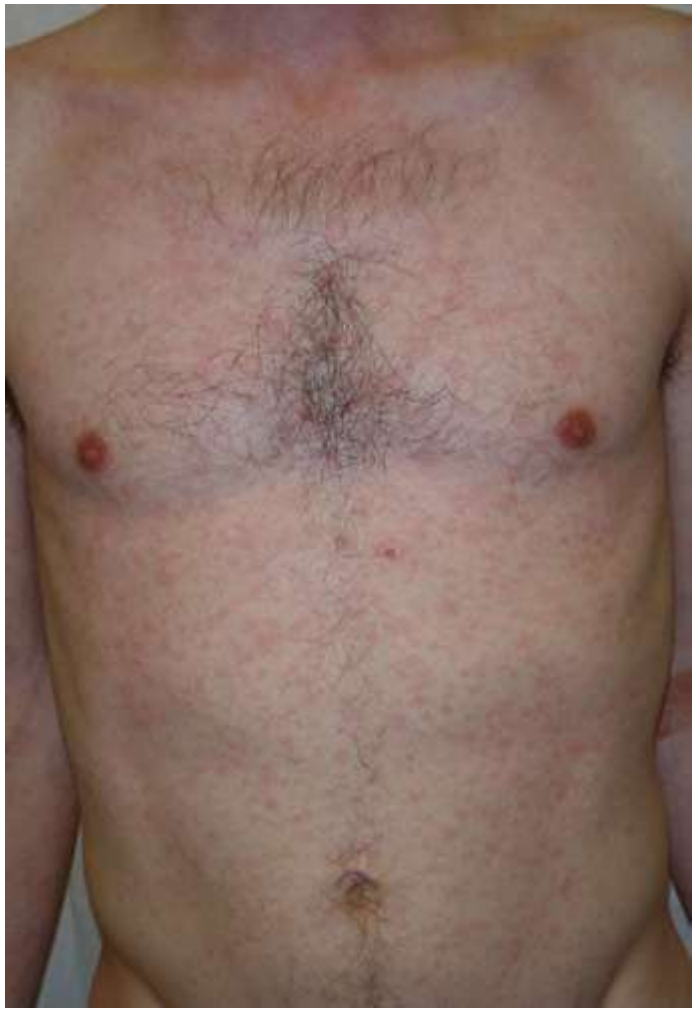
- Malignant lues is a rare manifestation that presents as crusted or scaly papules and plaques that can ulcerate or become necrotic, with an oyster shell-like surface.
- With the exception of mucous patches and condyloma lata, cutaneous manifestations of secondary syphilis do not contain a substantial number of treponemes and, therefore, are not typically infectious.

SECONDARY SYPHILIS:

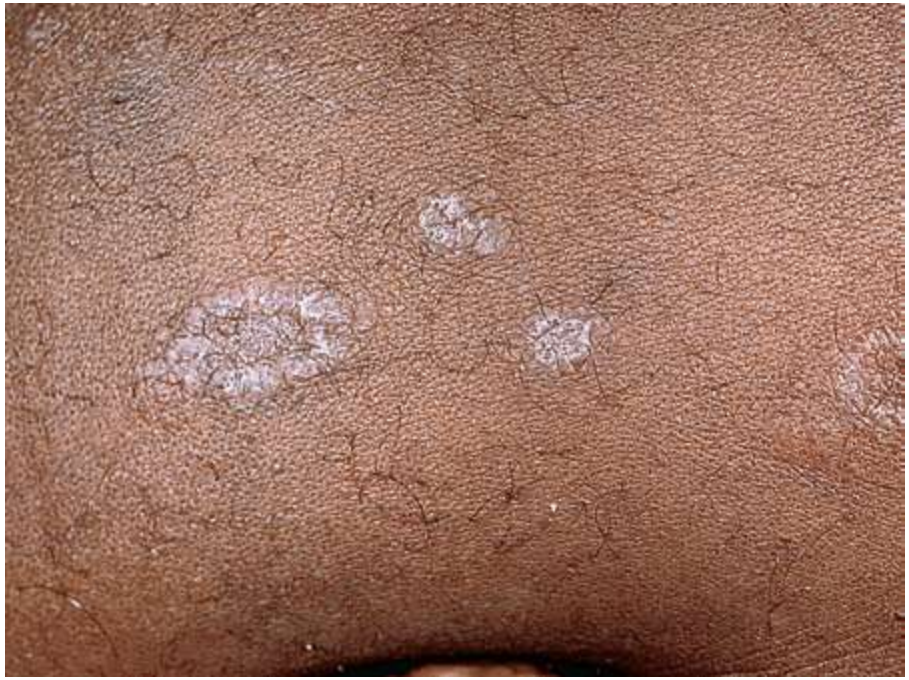
- Without treatment, the secondary stage typically recedes in 4–12 weeks. Scarring typically does not occur although pigmentary changes (leukoderma colli syphiliticum or, if on the neck, “necklace of Venus”) can result from inhibition of melanogenesis. In addition to neurosyphilis, discussed later, patients with secondary syphilis can experience systemic symptoms .

Lichenoid syphilitic eruption resembling lichen planus. Macular syphilis with a more florid presentation of nonscaling, ill-defined macules and patches on the trunk.

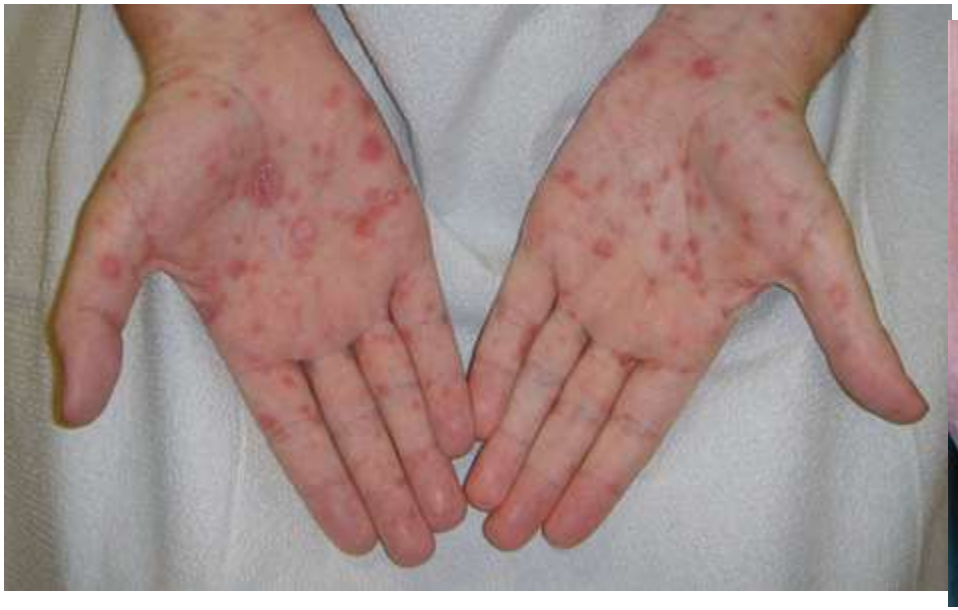


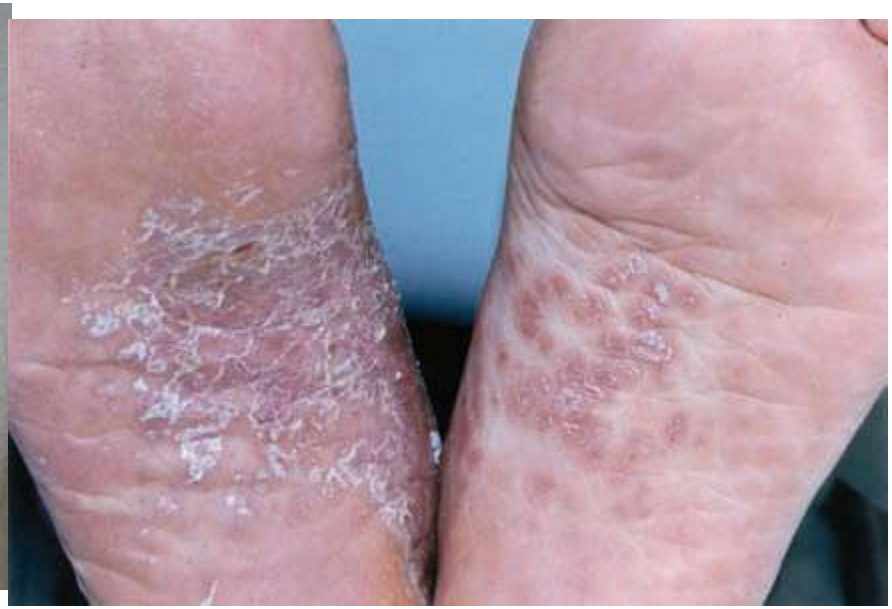


Papulosquamous syphilitic eruption with erythematous, well-demarcated, flattened plaques covered with scales (Biette's collarette). Moth-eaten alopecia of secondary syphilis, which is more common than diffuse alopecia

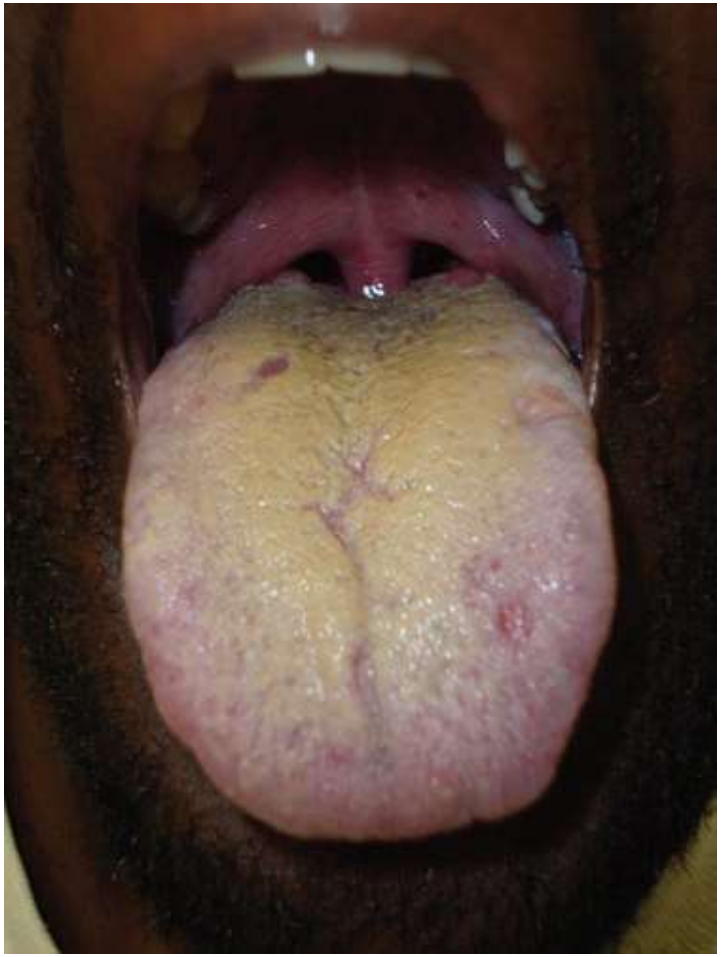


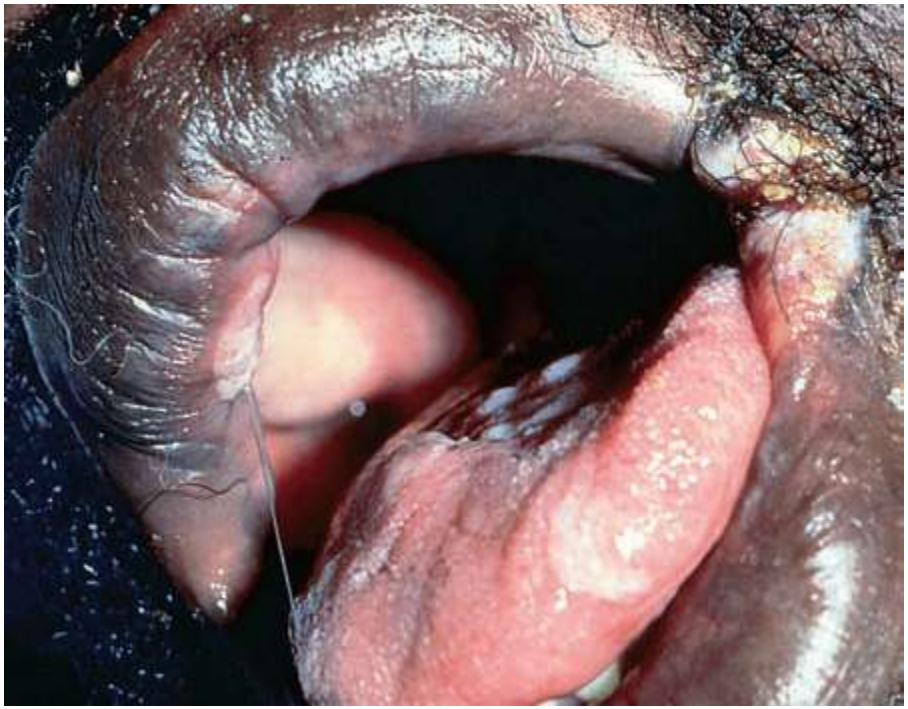
Palmoplantar lesions may be macular or papular, discrete or diffuse, and nonscaling, slightly scaly, or hyperkeratotic ("syphilitic corn").



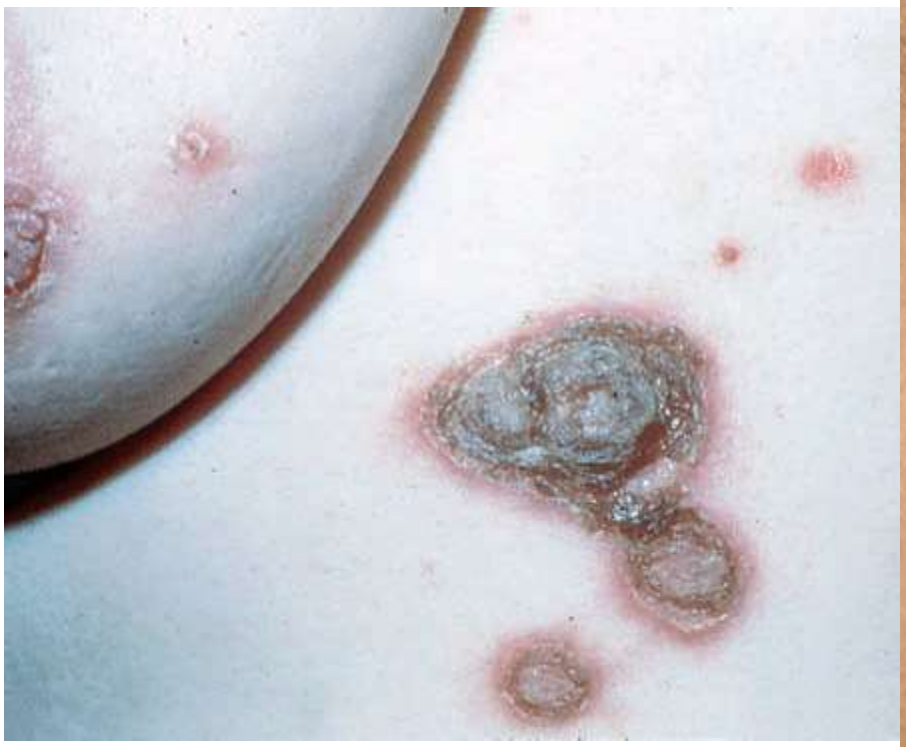


Mucous patches of the tongue in secondary syphilis. Split papule, a type of mucous patch of secondary syphilis that can be present at the angle of the mouth, with a characteristic erosion traversing its center.

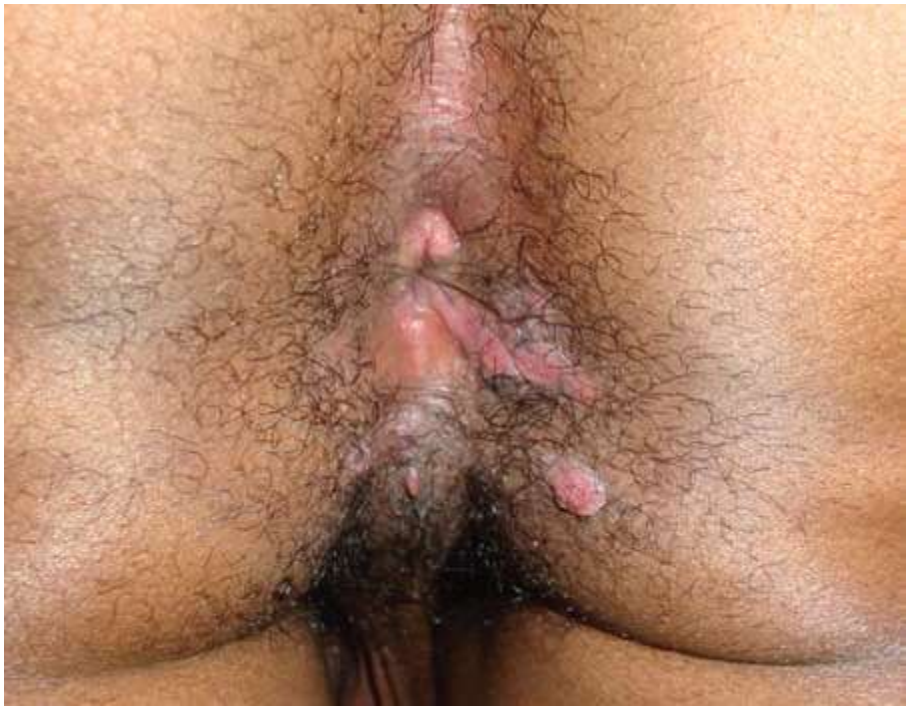


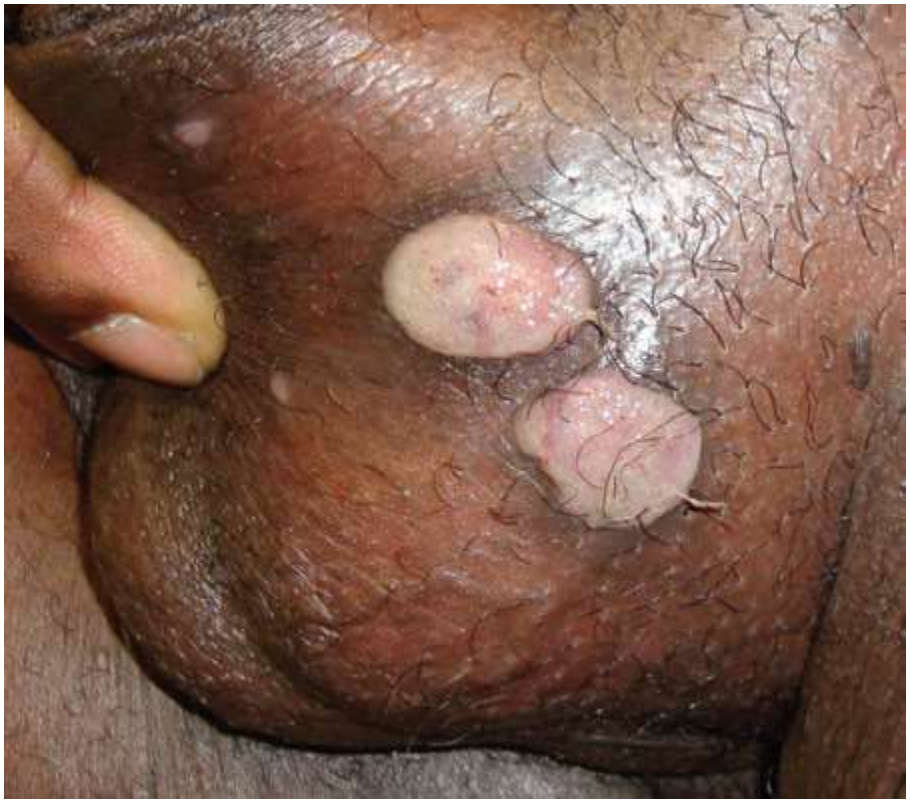


Sharply marginated, necrotic ulcers of secondary syphilis covered by thick, dirty crusts (like oyster shells), which are characteristic of malignant syphilis (lues maligna). Papules of secondary syphilis on the penis.

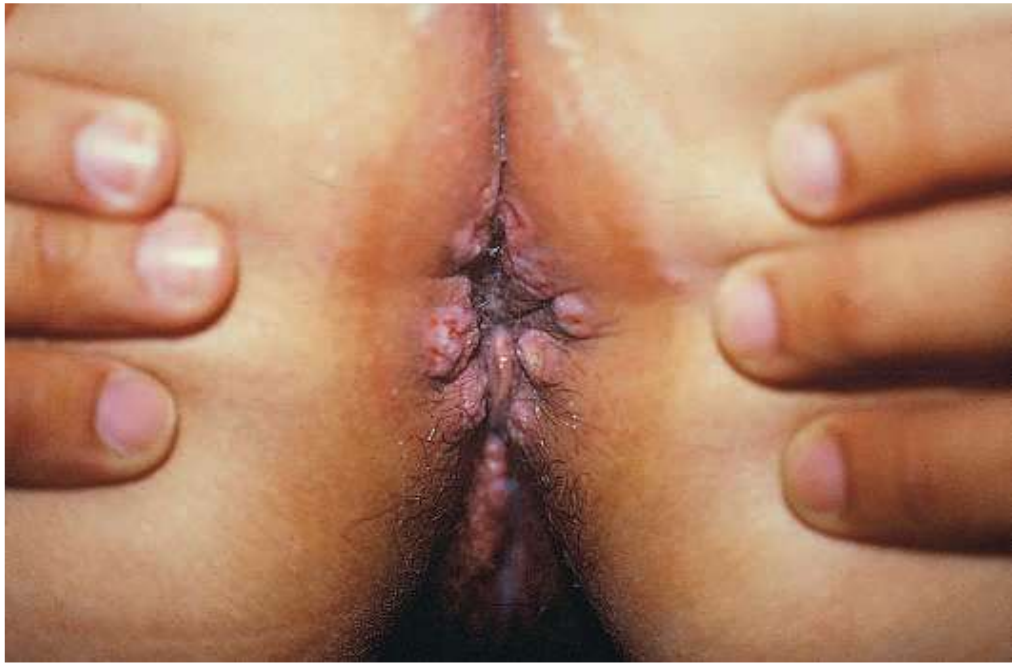


Condyloma lata, presenting as papules and plaques in the perianal area. Condyloma lata, presenting as moist, flat topped plaques on the scrotum.

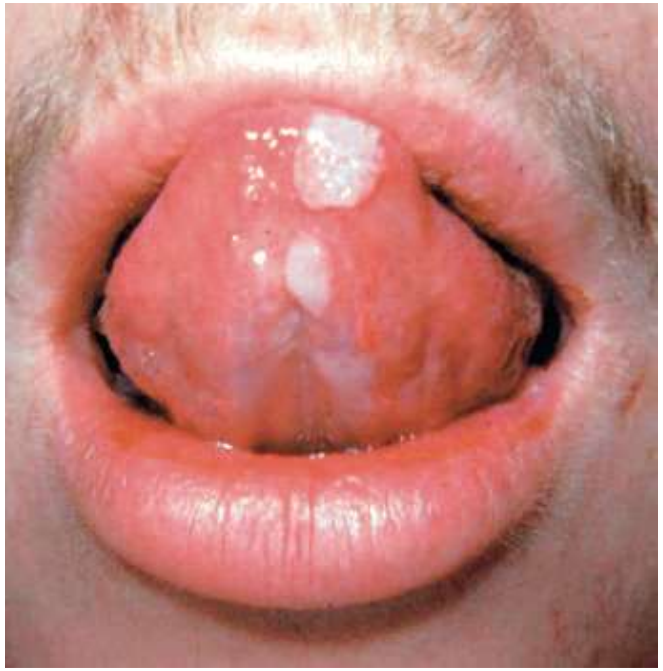


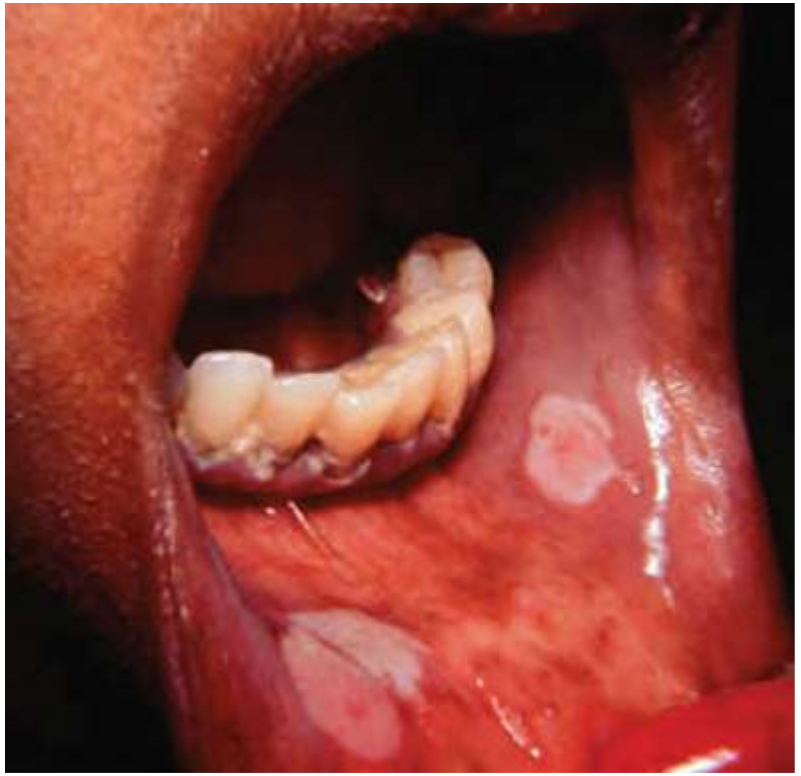


Condylomata lata

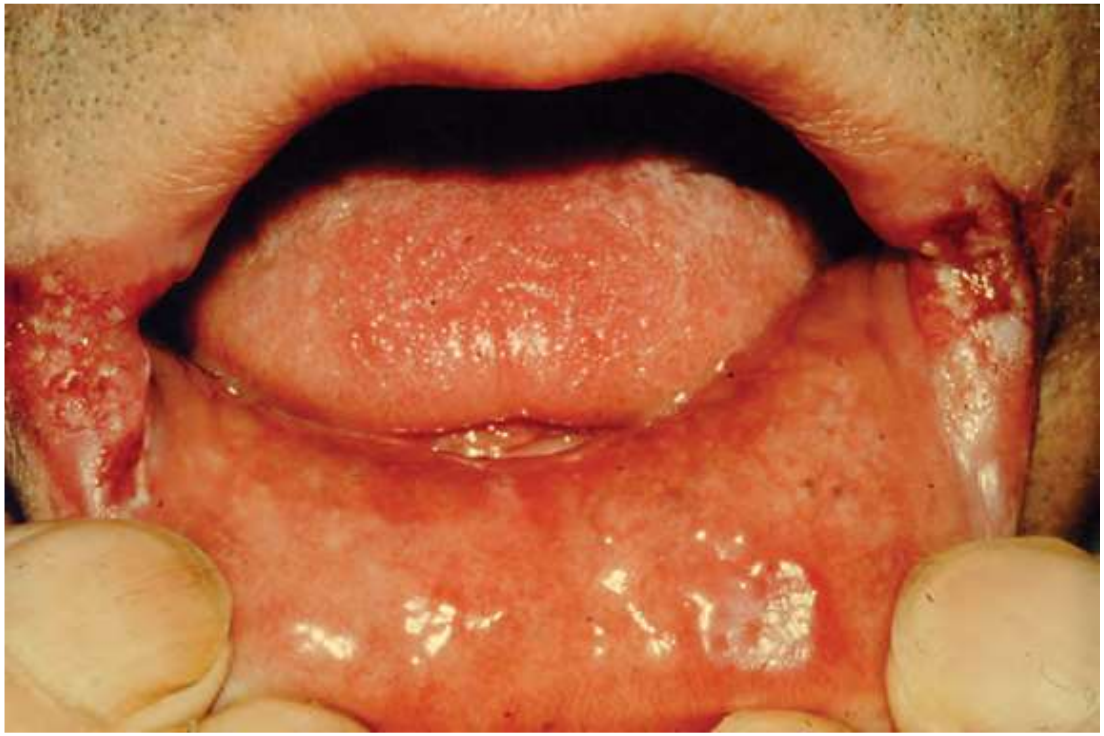


Mucous patches of secondary syphilis.

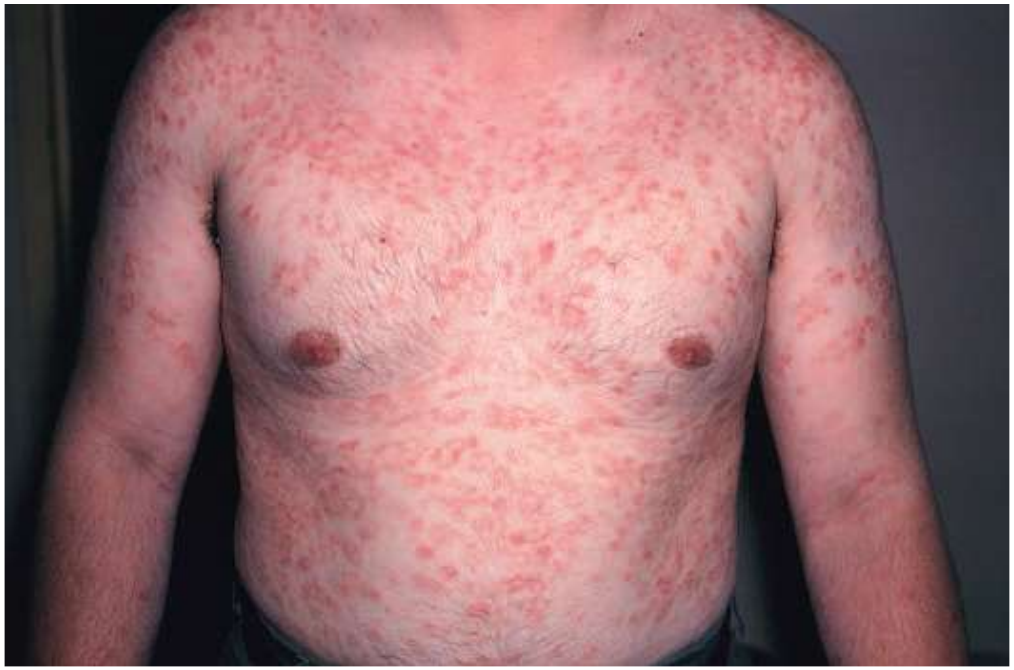




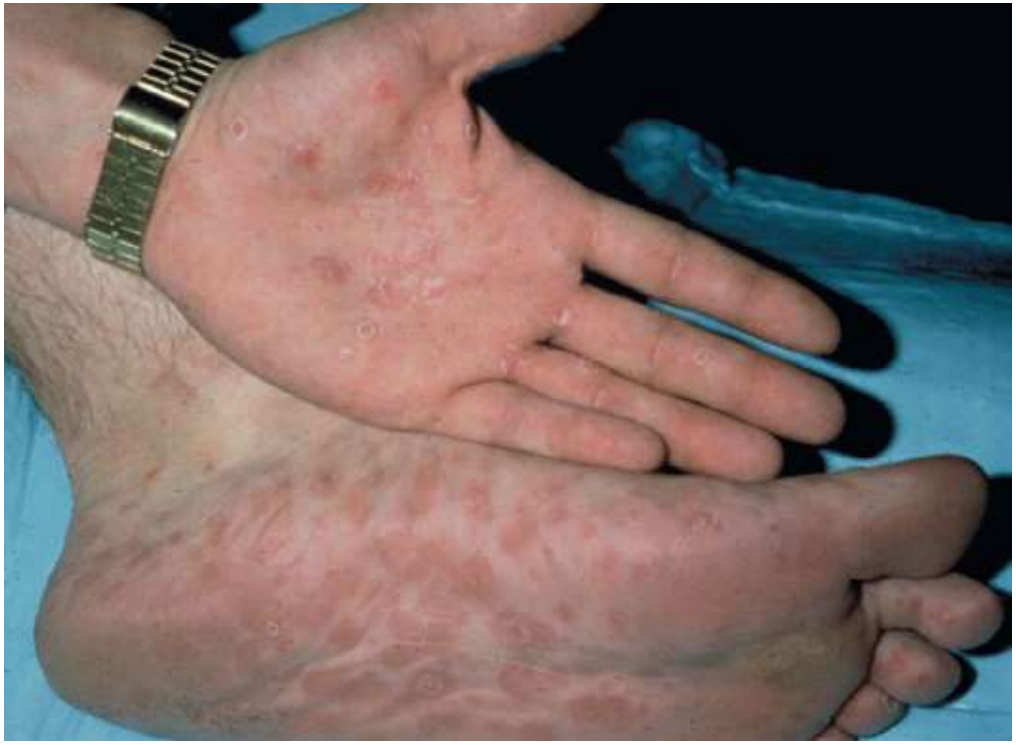
Split papules at the angle of the mouth



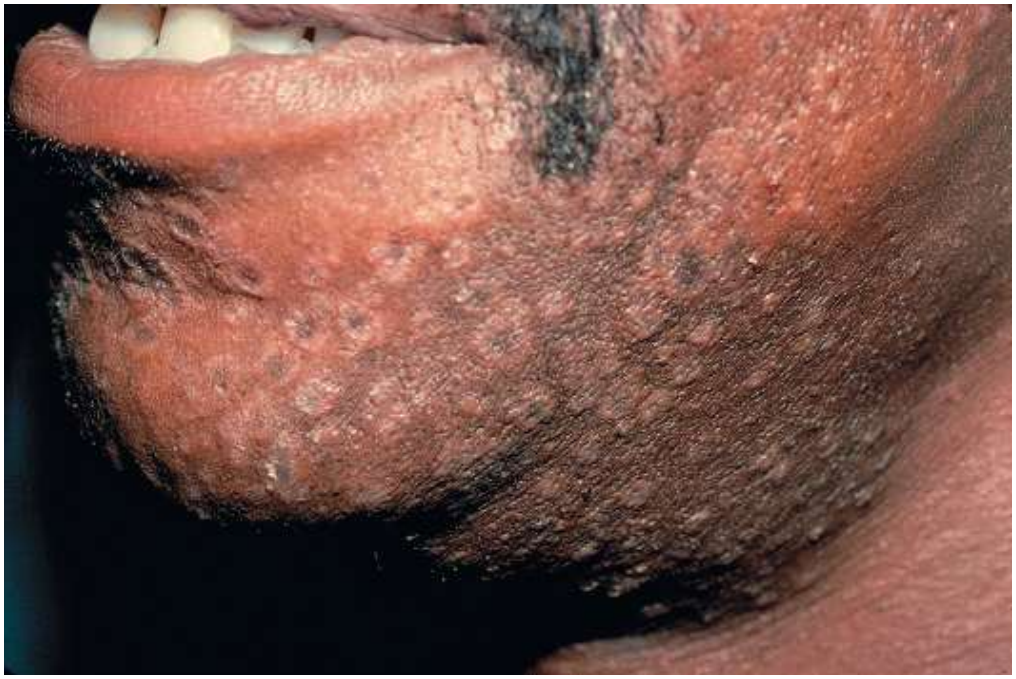
Secondary syphilis, lichenoid lesions



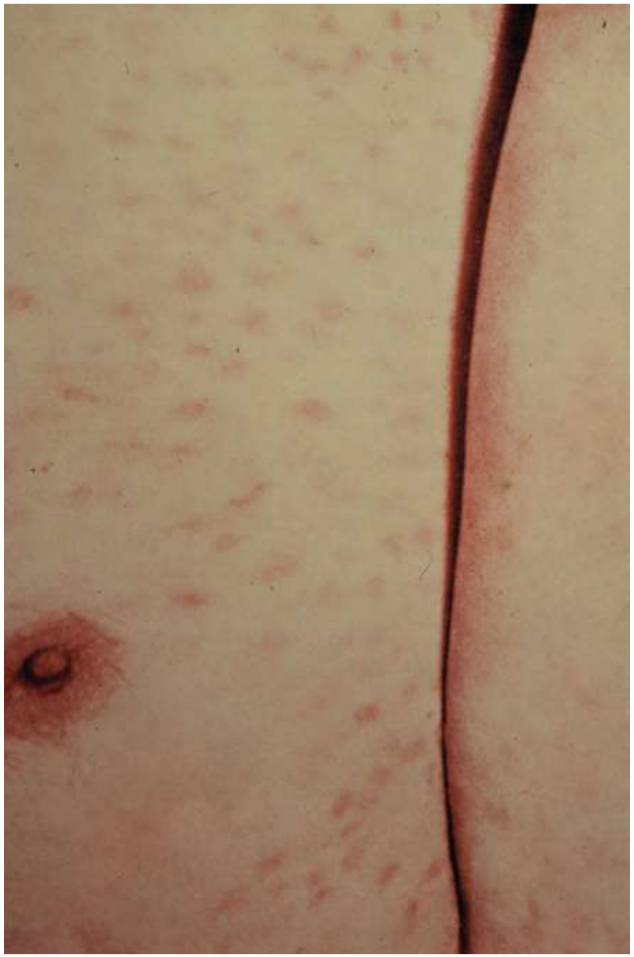
Secondary syphilis; red, flat-topped papules of the palms and soles.

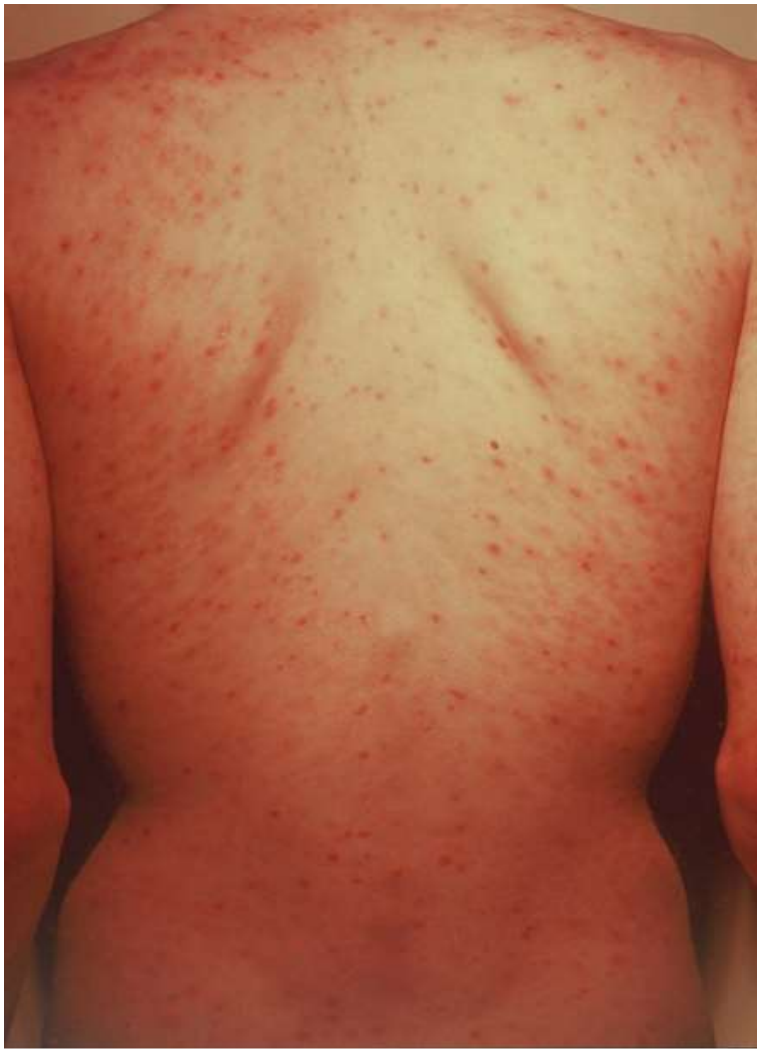


Annular secondary syphilis.

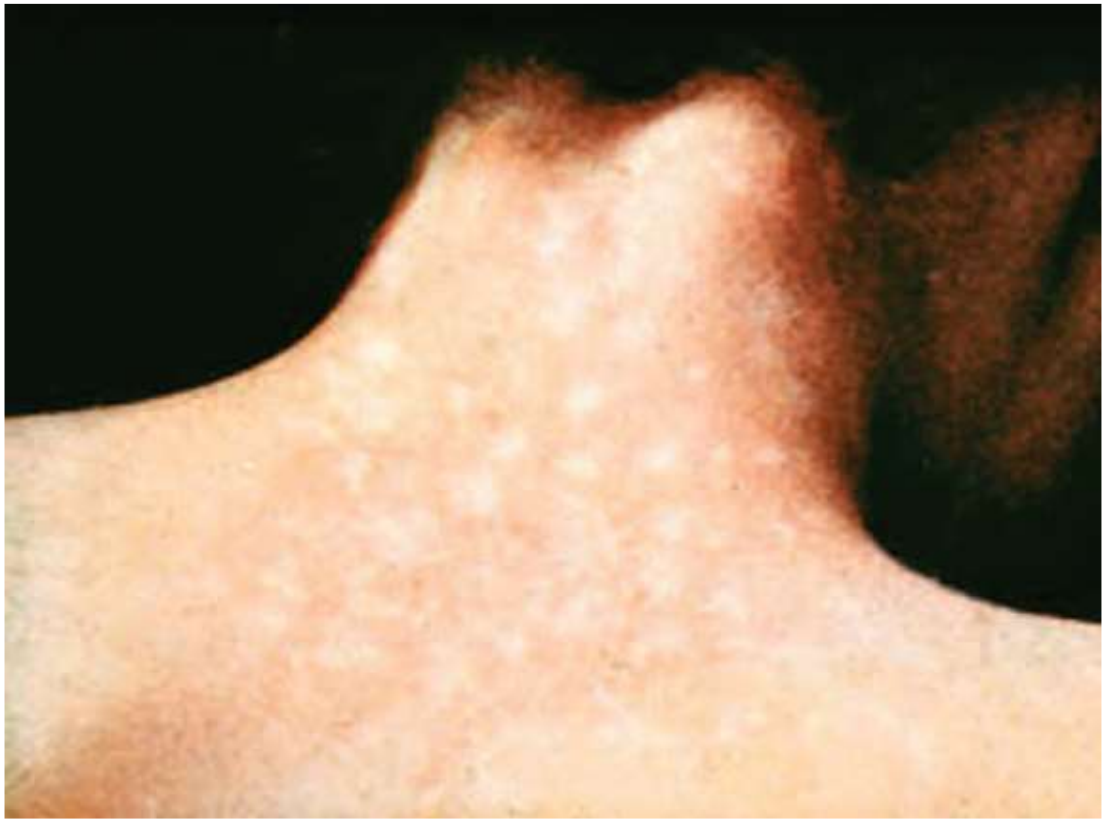


Secondary syphilis. (a) Extensive truncal maculopapular rash. (b) Macular rash with lesions following the skin lines of cleavage

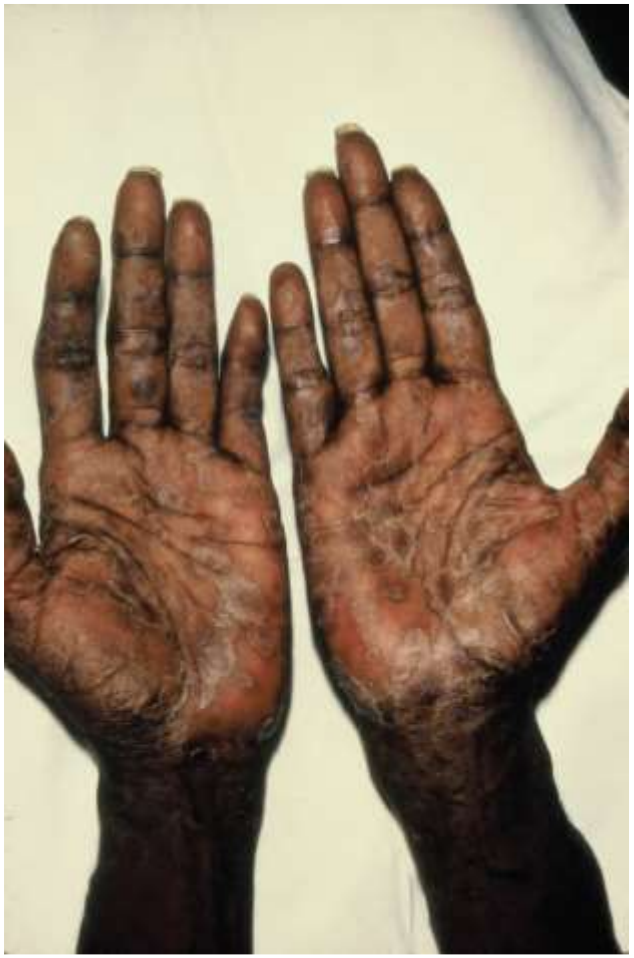




Syphilitic leukoderma showing depigmentation at sites of healed secondary lesions on the neck and upper back.



Secondary syphilis showing psoriasiform lesions of the palms.



LATENT SYPHILIS

- The secondary stage is followed by an asymptomatic stage with no clinical findings, with **seroreactivity** by definition the only evidence of infection
- Latency may remain infinite, be interrupted by a relapse of secondary syphilis, or progress to the tertiary stage.
- The Centers for Disease Control and Prevention (CDC) divides latent syphilis into three subcategories, ***early latent, late latent, and latent syphilis of unknown duration***
- 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**.

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. symptoms of primary or secondary syphilis;

3. A sex partner documented to have primary, secondary, or early latent syphilis;

4. Reactive nontreponemal and treponemal tests from a person whose only possible exposure occurred within the previous 12 months.

LATENT SYPHILIS

- ***Latent syphilis of unknown duration*** is a subcategory of latent syphilis that is diagnosed in patients aged 13–35 years who have a nontreponemal titer ≥32and in whom early latent syphilis cannot be diagnosed according to the criteria previously mentioned.
- ***Late latent syphilis***, the final subcategory of latent syphilis, is diagnosed in a patient with latent syphilis who cannot be diagnosed with one of the other two subcategories.

TERTIARY SYPHILIS

- Although not a formal stage of syphilis, as defined by CDC observation case definitions, **“tertiary syphilis "is a commonly used term clinically.** A CDC case definition does exist for disease manifestations clinically considered “tertiary syphilis.” That case definition is for “syphilis, late, with clinical manifestations other than neurosyphilis (late benign syphilis and cardiovascular syphilis),” which is characterized by inflammatory lesions of the cardiovascular system, skin, bone, and rarely, other structures, in the presence of laboratory evidence from tissues or sera consistent with syphilis.

TERTIARY SYPHILIS

- approximately one-third of patients with untreated latent syphilis progressed to tertiary syphilis, typically after 15–40 years, while the other two-thirds remain in latency.
- **Late benign syphilis refers to signs and symptoms of syphilis that occur after secondary syphilis that do not involve the cardiovascular or nervous systems.** Lesions of late benign syphilis are caused by delayed type hypersensitivity response to the small number of treponemes present in the involved tissue or organ.
- The hallmark of late benign syphilis is the **gumma, a granulomatous lesion with central necrosis, which most commonly affect the skin or mucous membranes (80% of gummas).**

Gummas

- Gummas are nontender pink to dusky-red nodules or plaques that vary in size from millimeters to many centimeters in diameter.
- They favor sites of previous trauma and may arise anywhere in the body but are more common on the scalp, forehead, buttocks, and presternal, supraclavicular, or pretibial areas.
- As the central gumma heals, new lesions may develop on the periphery forming scallop borders.
- In contrast to noduloulcerative lesions, gummas are deeper and more destructive.
- Superficial gummas heal with atrophic scars, whereas deeper lesions leave thickened, pitted, ridged scars.
- The lesions are rarely contagious, but infection following contact with gummas has been reported.

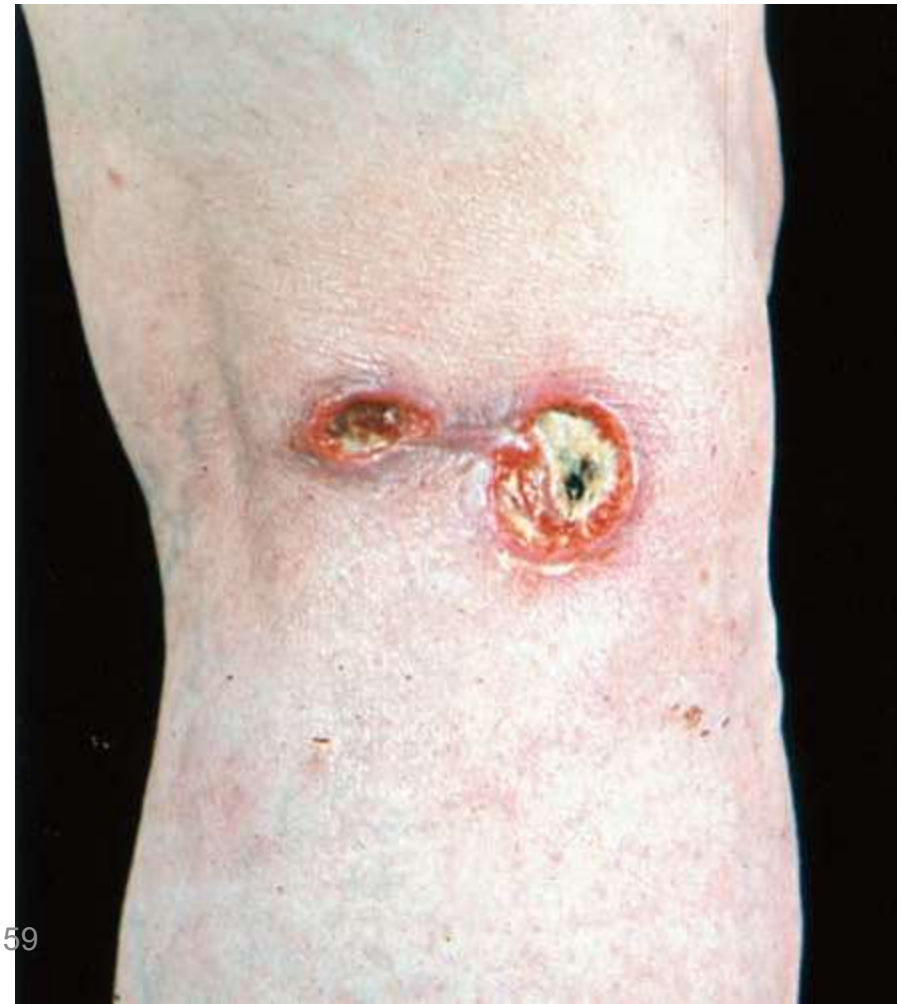
Gummas

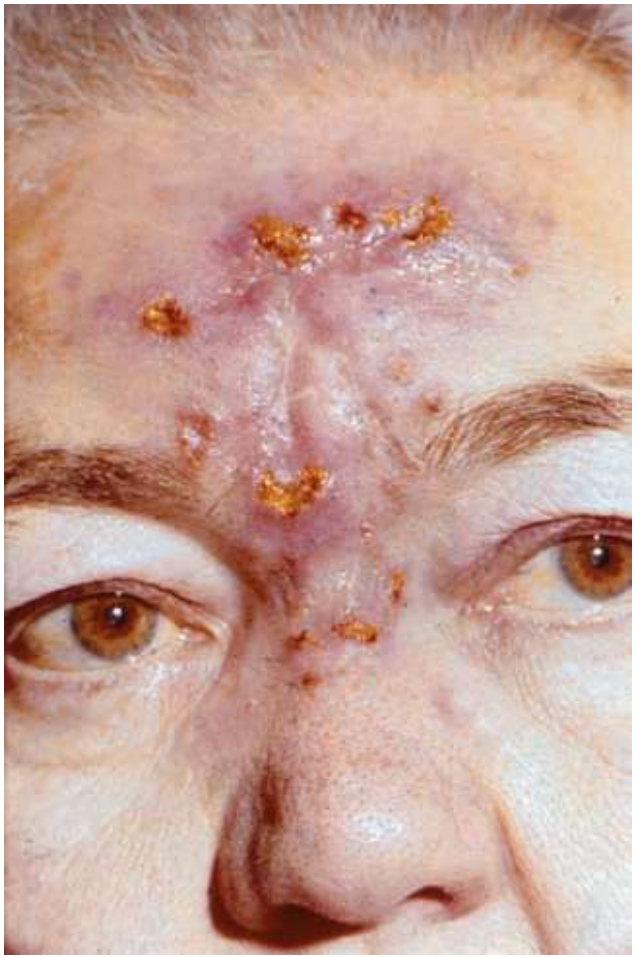
- Pseudochancre redux refers to a solitary gumma of the penis.
- Gummas involving the mucous membranes typically affect the palate, nasal mucosa, tongue, tonsils, and pharynx. The lesions ulcerate and can be disfiguring, as when they cause a saddle-nose deformity
- Besides the skin and mucous membranes, gummas can affect practically any organ
- Gummas do not heal without antibiotic therapy, and leaving scars.
- Other manifestations of late benign syphilis affecting the skin include granulomatous and noduloulcerative lesions and psoriasiform plaques

Nodular and noduloulcerative

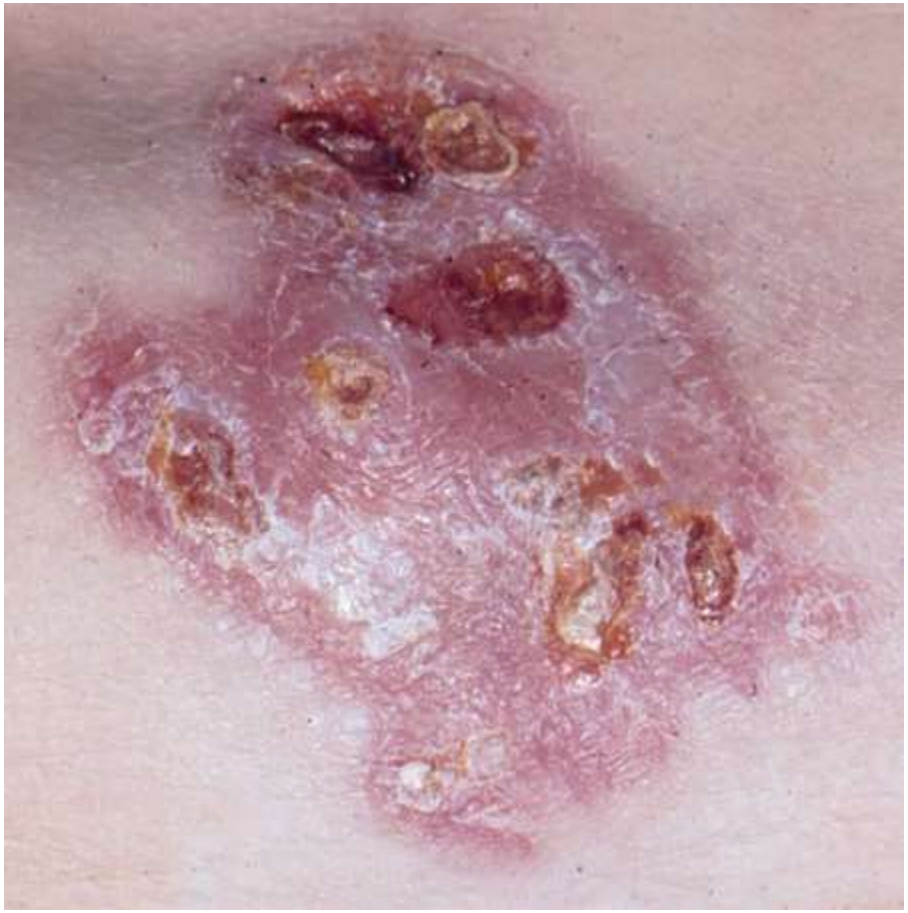
- Nodular and noduloulcerative lesions are superficial firm, painless, dull-red, shiny, flat nodules that range in size from several millimeters to 2 cm. They appear in a grouped configuration, can coalesce into large plaques or ulcerate and can resemble granuloma annulare. Psoriasiform plaques are most commonly seen on the arms, back, and face.

Two deep, punched-out ulcers in the popliteal fossa covered with an adherent yellow slough at the base (This is the classical appearance of nodular gummas). Disfiguring gumma of the face with scattered ulcerations in a 60-year-old woman with late benign syphilis.

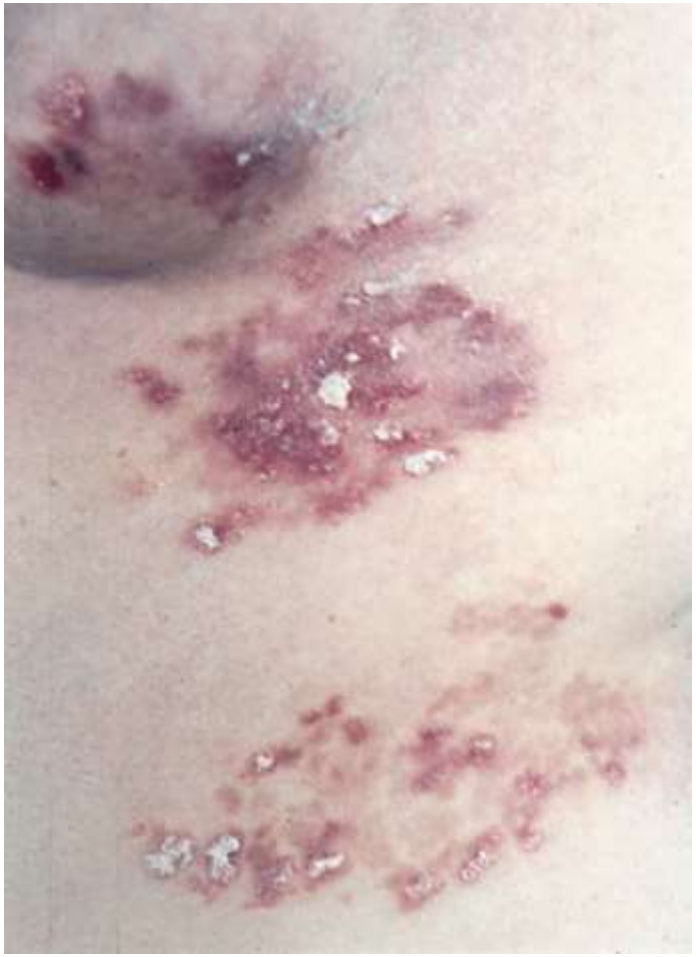




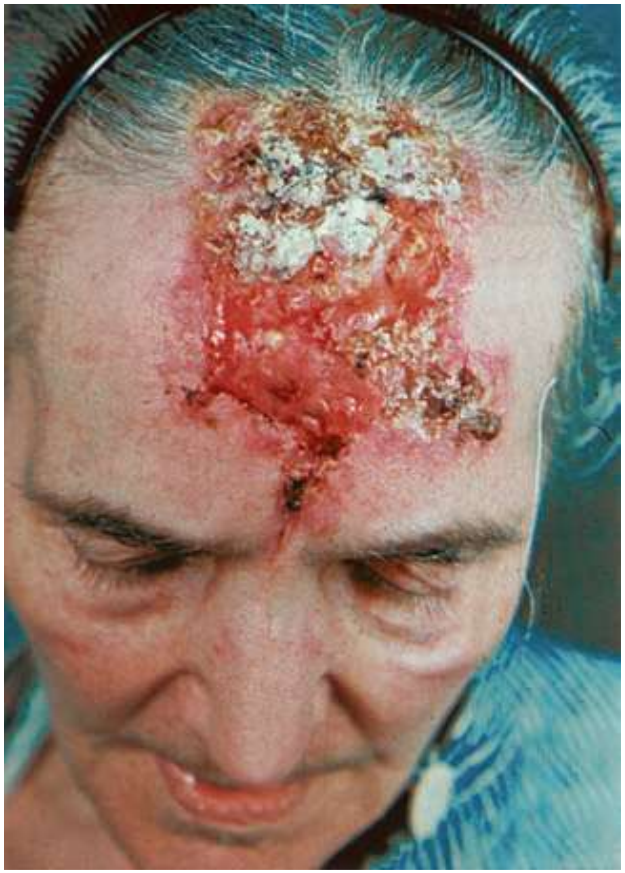
A noduloulcerative tertiary syphilitic lesion is a sharply defined and irregular shaped of a dull red color, firm consistency, and superficial ulcerations.



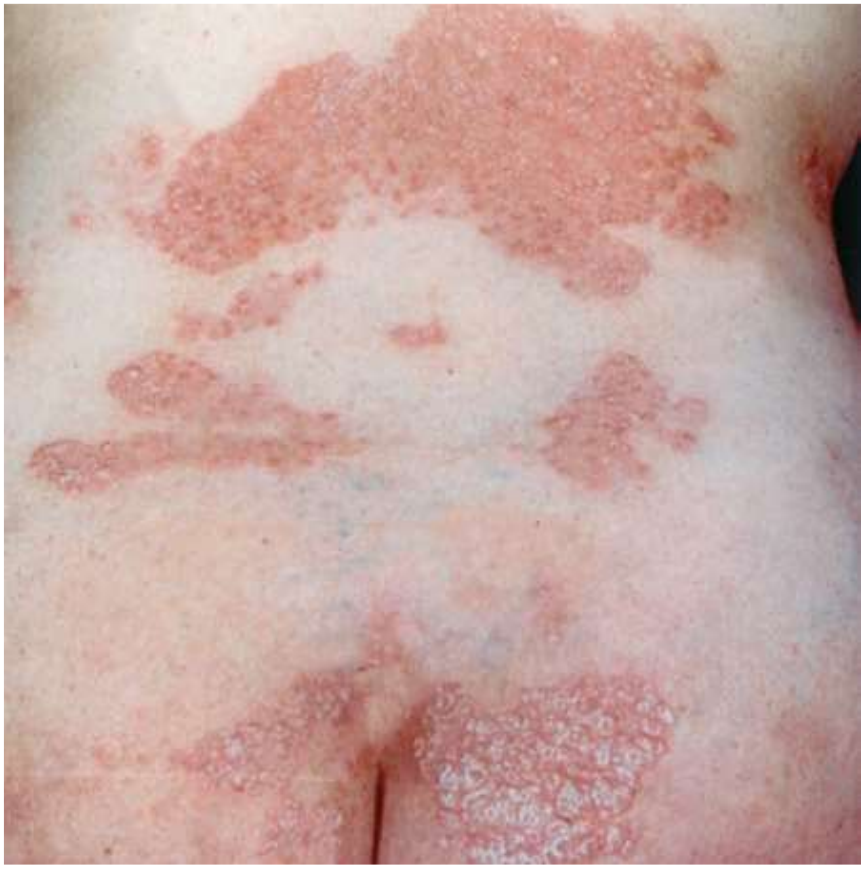
Crusted and scaly noduloulcerative tertiary syphilis plaques with characteristic serpiginous borders and scarring.



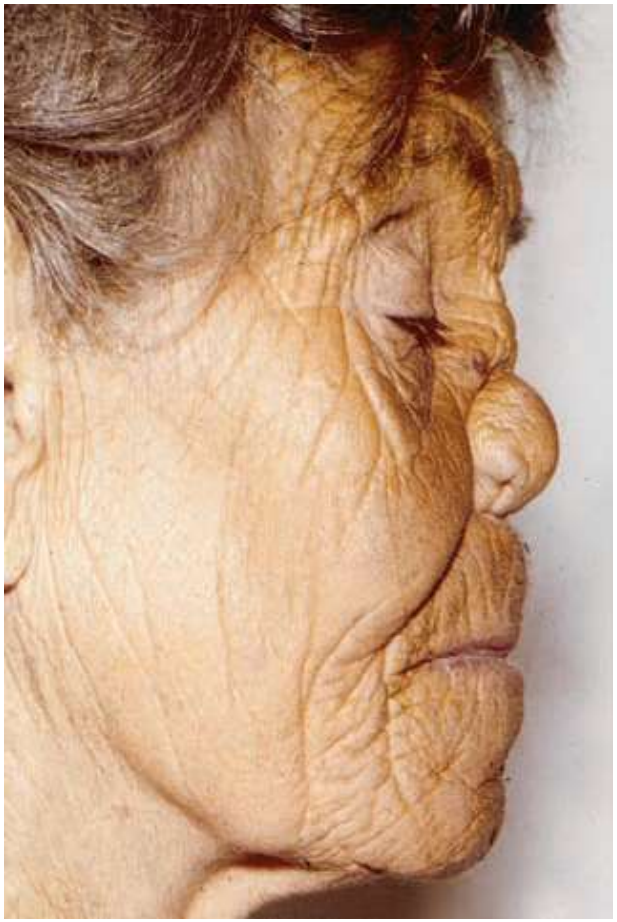
Aggressive gumma of the forehead, mimic advanced, destructive basal cell carcinoma.

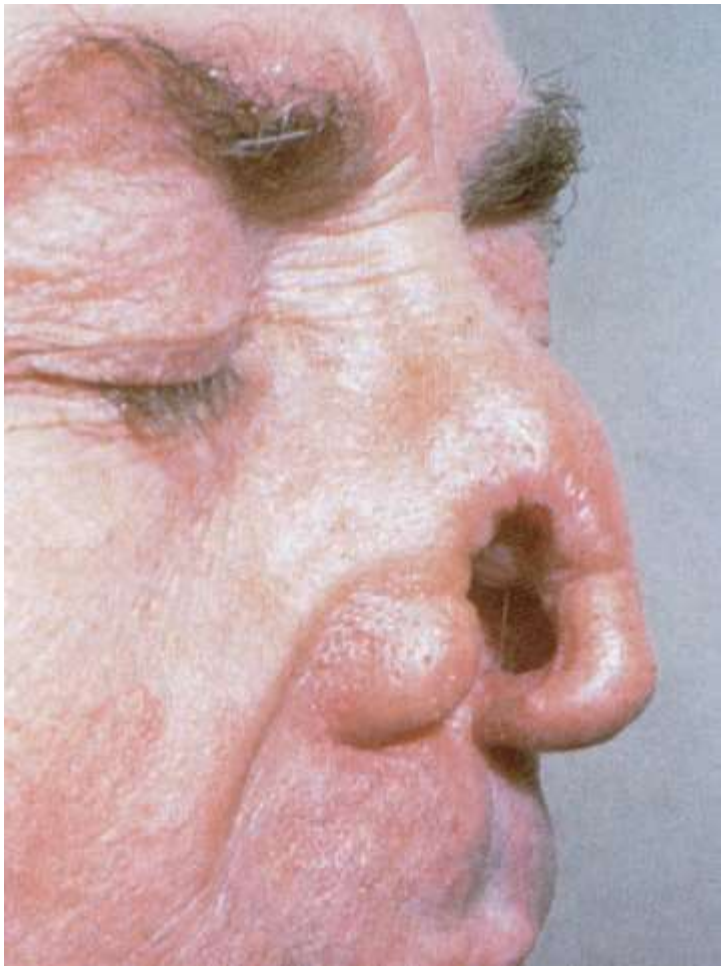


Plaque of tertiary syphilis, covered with scales, and may be indistinguishable from psoriasis.

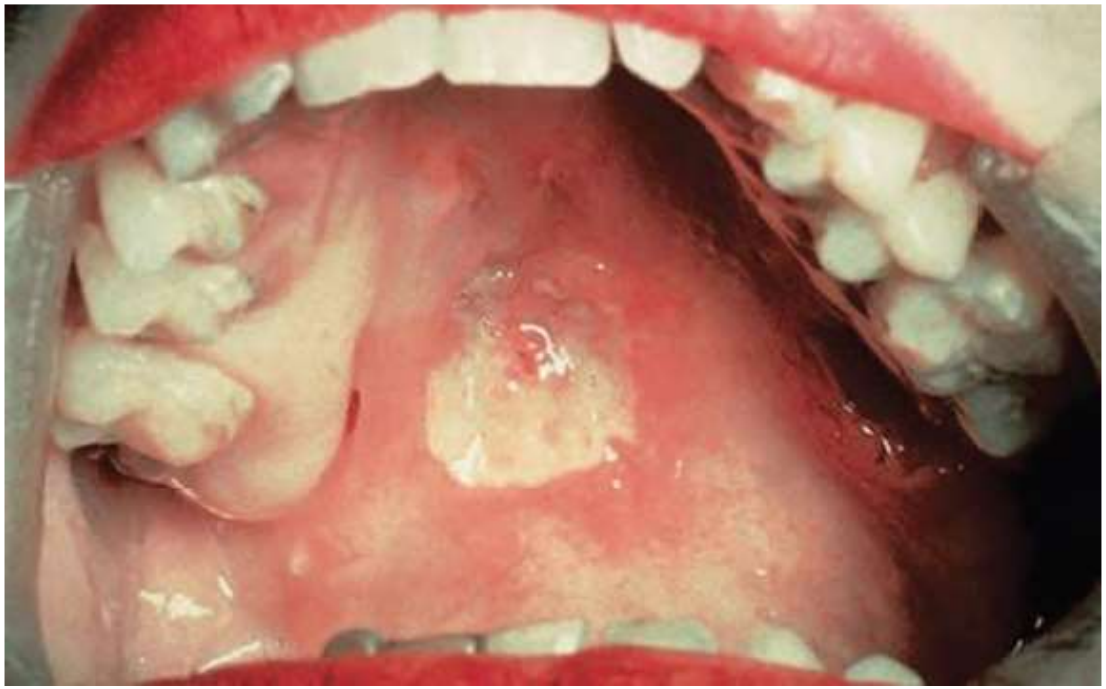


Destruction of the nasal cartilage and bone by a gumma leads to a saddle nose and to the perforation of the nasal cartilage and skin and thus to mutilation .

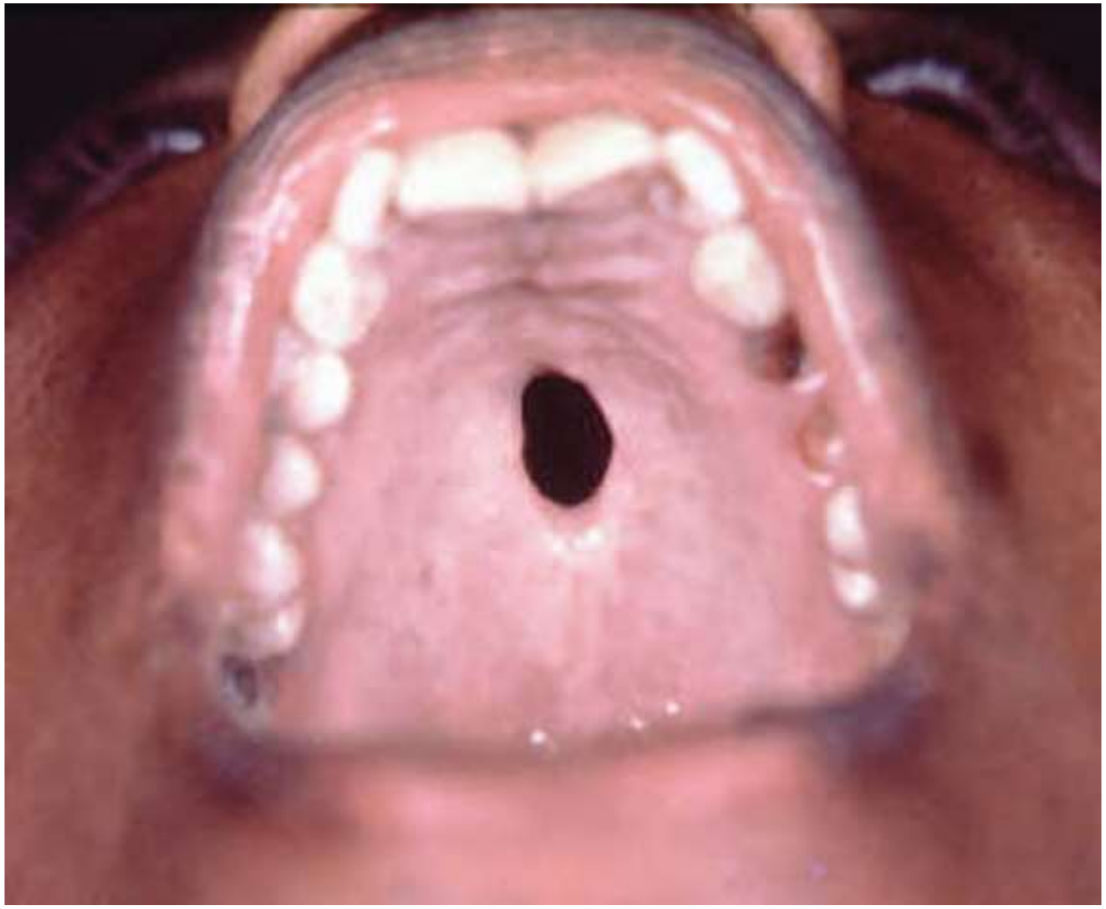




Early gumma of the hard palate.



Perforated gumma of the hard palate.



NEUROSYPHILIS

- Neurosyphilis—it is infection of the central nervous system (CNS) by T. pallidum—is commonly considered to be a manifestation of “tertiary syphilis, "although neurosypyhilis can in fact occur during any stage of infection.
- “Neuroinvasion,” in which T. pallidum disseminates to cerebrospinal fluid and meninges, occurs very early in syphilis. Neuroinvasion can be transient (the body clearing the infection) or more sustained, in which case it is called asymptomatic neurosyphilis, defined by CSF abnormalities.

NEUROSYPHILIS

The Centers for Disease Control and Prevention (CDC) case definitions for neurosypyhilis are divided into:

- **Confirmed** (any stage of infection and a reactive CSF-VDRL)
- **Probable** (any stage of infection, a nonreactive CSF-VDRL, **elevated protein or white blood count** without other known causes , and clinical symptoms or signs of neurosyphilis without other known causes).

Early symptomatic neurosyphilis typically manifests as:

- meningitis, resulting in *meningismus* (meningeal irritation with symptoms suggesting meningitis), fever, or cranial nerve abnormalities (especially cranial nerves II, III, IV, VI, VII, and VIII), or meningo-vasculitis, resulting in meningitis with stroke
- Uveitis is the most common manifestation of early neurosyphilis, presenting as eye pain, redness, and photophobia
- hearing loss is the most common manifestation of syphilis

late neurosyphilis

- The two syndromes commonly associated with *late neurosyphilis* are general paresis of the insane, also known as dementia paralytica, and tabes dorsalis

According to CDC recommendations, indications for CSF examination in persons with syphilis include

- neurologic, ophthalmic, or otologic signs or symptoms;
- evidence of active tertiary syphilis
- treatment failure;
- HIV infection itself is not an indication for CSF examination.

CONGENITAL SYPHILIS

- Congenital syphilis refers to syphilis caused by infection in utero with T. pallidum. CDC defines:

a confirmed case

- of congenital syphilis as **signs of disease** in an infant or child **with *specific laboratory*** *evidence* of infection with T. pallidum.

A probable case is defined

- ❖ as a condition affecting an infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant
- ❖ or an infant or child who has a reactive treponemal test for syphilis and evidence of
- congenital syphilis on physical examination or radiograph of long bones,
- a reactive CSF-VDRL, an elevated CSF cell count or protein (without other known cause), or a reactive fluorescent treponemal antibody absorption assay(FTA-ABS) test or IgM enzyme-linked immunosorbent assay.

CONGENITAL SYPHILIS

- Transplacental fetal infection can occur at any time during pregnancy and at any stage.
- Probability of transmission of infection depends on the stage of infection in an untreated mother, ranging from 70%–100% in primary syphilis, 40% for early latent syphilis and 10% for late latent syphilis.
- Because infection is spread hematogenously, a chancre is not present on the fetus or infant.
- In 30%–40% of cases, congenital syphilis results in stillbirth.
- Of infants who survive, two-thirds are asymptomatic at delivery and only later develop symptoms.
- Clinical findings in symptomatic infants are similar to congenital infections caused by cytomegalovirus, toxoplasmosis, herpes simplex virus, and other infections.

early congenital syphilis

- defined as syphilis in a child aged <2 years, with fever, rash, hepatosplenomegaly, and persistent rhinitis (“snuffles”).
- Hydrops fetalis (edema), lymphadenopathy, neurosyphilis, leukocytosis, thrombocytopenia, periostitis and osteochondritis may also be present. pain associated with osteochondritic lesions causing the infant to refuse to move the affected anatomic area (“pseudoparalysis of Parrot”).
- If present at delivery, the rash is usually bullous (“syphilitic pemphigus”) and very infectious. Rash that presents at two weeks or more after birth, similar to lesions of secondary syphilis most commonly affecting the hands and feet.
- Other cutaneous lesions present can include condyloma lata, mucous patches, fissures around the lips, nares, or anus, and petechia from thrombocytopenia. The skin is often dry and wrinkled and, in newborns with fair skin, may have a café-au-lait hue

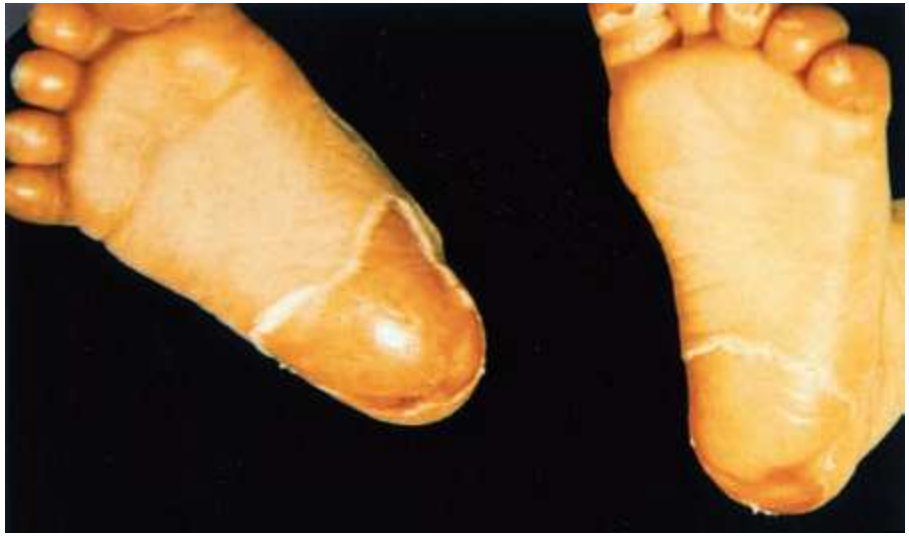
Late congenital syphilis

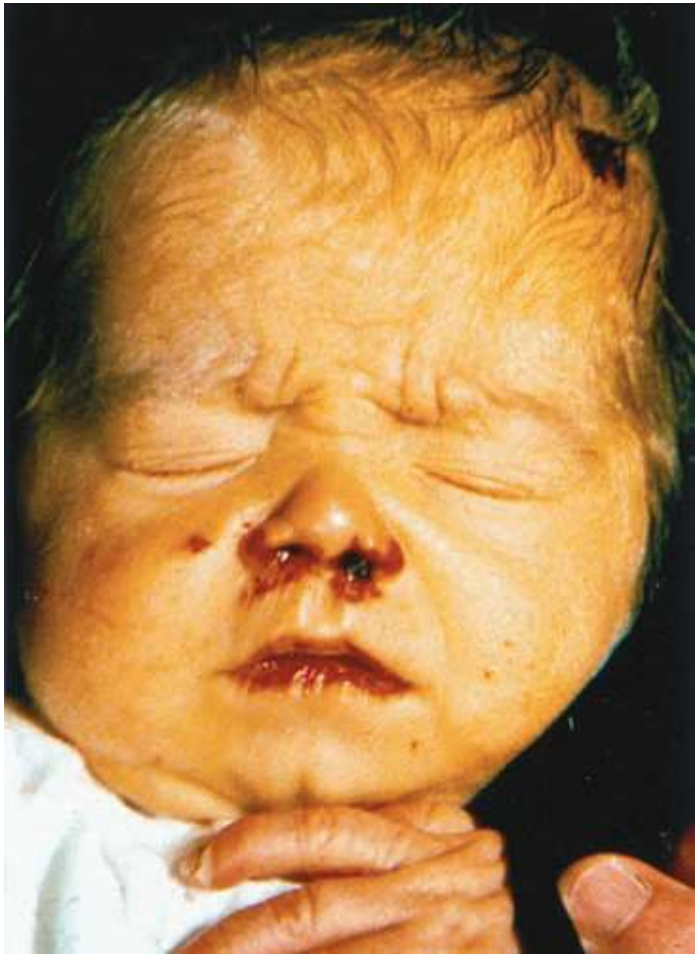
- *Late congenital syphilis* is defined as disease occurring in a child at least 2 years old that typically manifests over the first two decades of life. Those manifestations include
- scars (“rhagades”) resulting from cutaneous fissures;
- saddle-nose deformity, resulting from destruction of nasal cartilage from snuffles;
- frontal bossing (Olympian brow), thickening of the sternoclavicular portion of the clavicle (Higoumenakis sign), anterior bowing of the midtibia (saber shins), and scaphoid scapula, all resulting from chronic periostitis

Late congenital syphilis

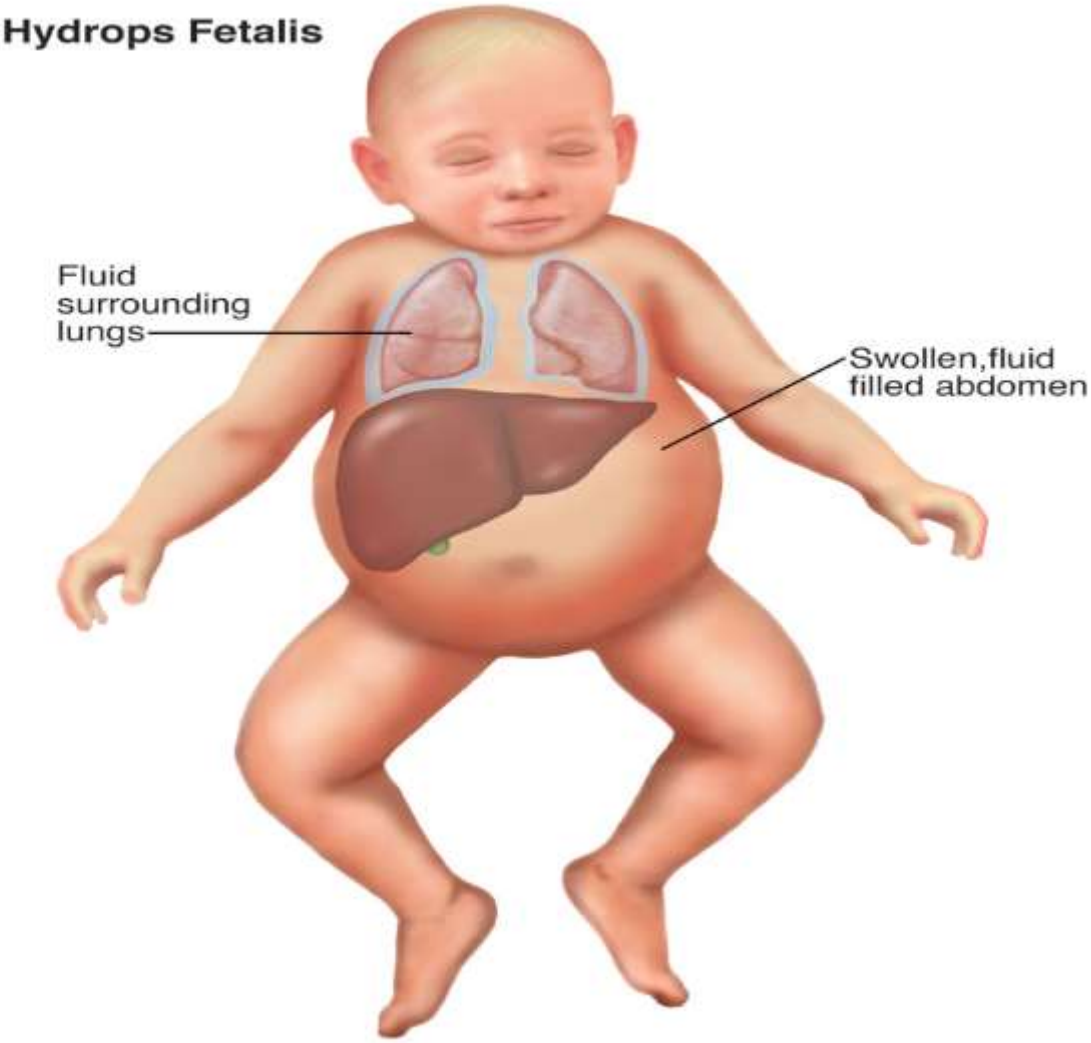
- peg-shaped notched central incisors (Hutchinson teeth) and mulberry molars, resulting from syphilis vasculitis in developing tooth buds.
- Other manifestations include eighth nerve deafness and eye abnormalities, including interstitial keratitis, glaucoma, or corneal scarring.
- Hutchinson's triad refers to Hutchinson teeth, interstitial keratitis, and eighth nerve deafness.

The skin is dry and wrinkled, with a yellowish-brownish hue. There is hemorrhagic rhinitis. Bullous eruptions on the soles. Bullae have ruptured and now present as erosions ("syphilitic pemphigus").



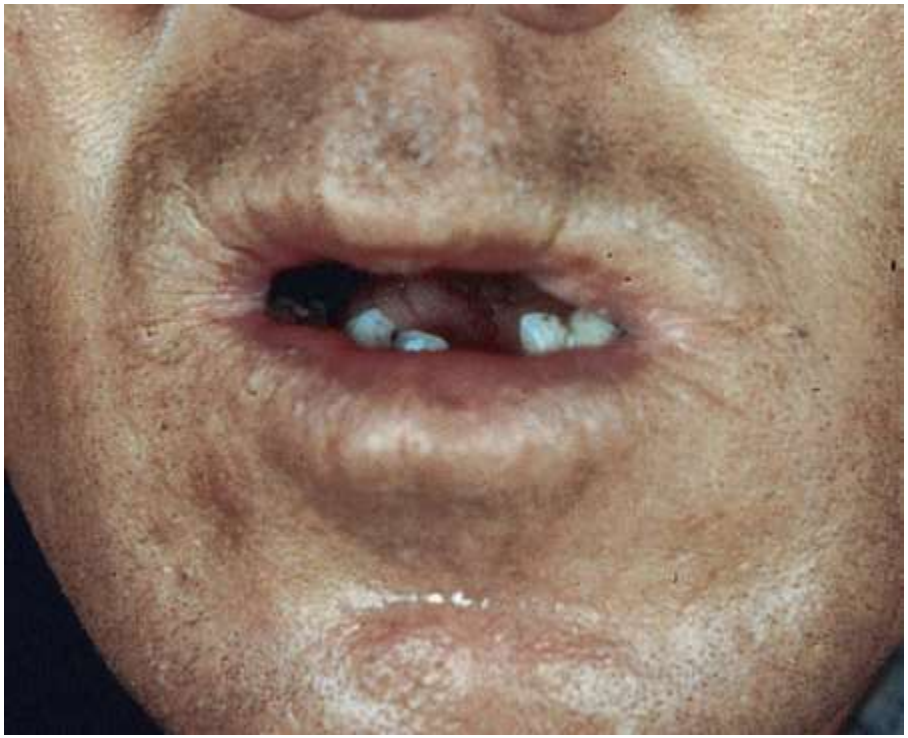


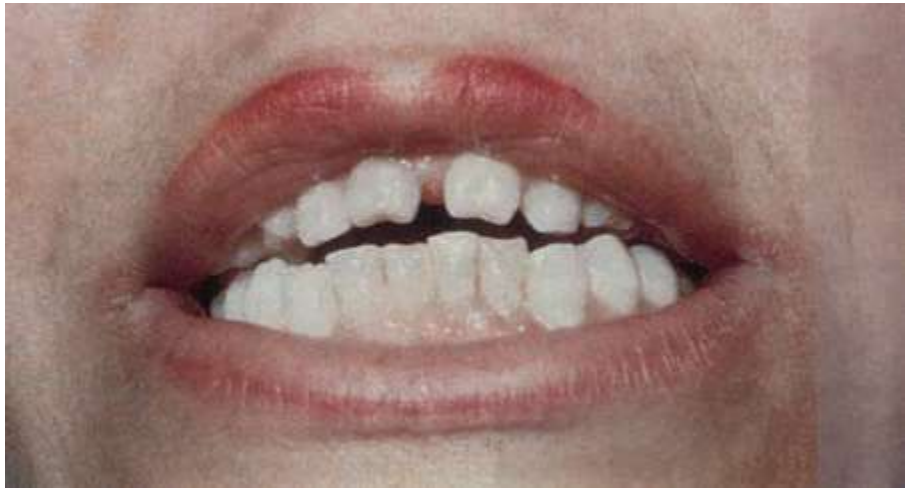
Hydrops fetalis (edema),

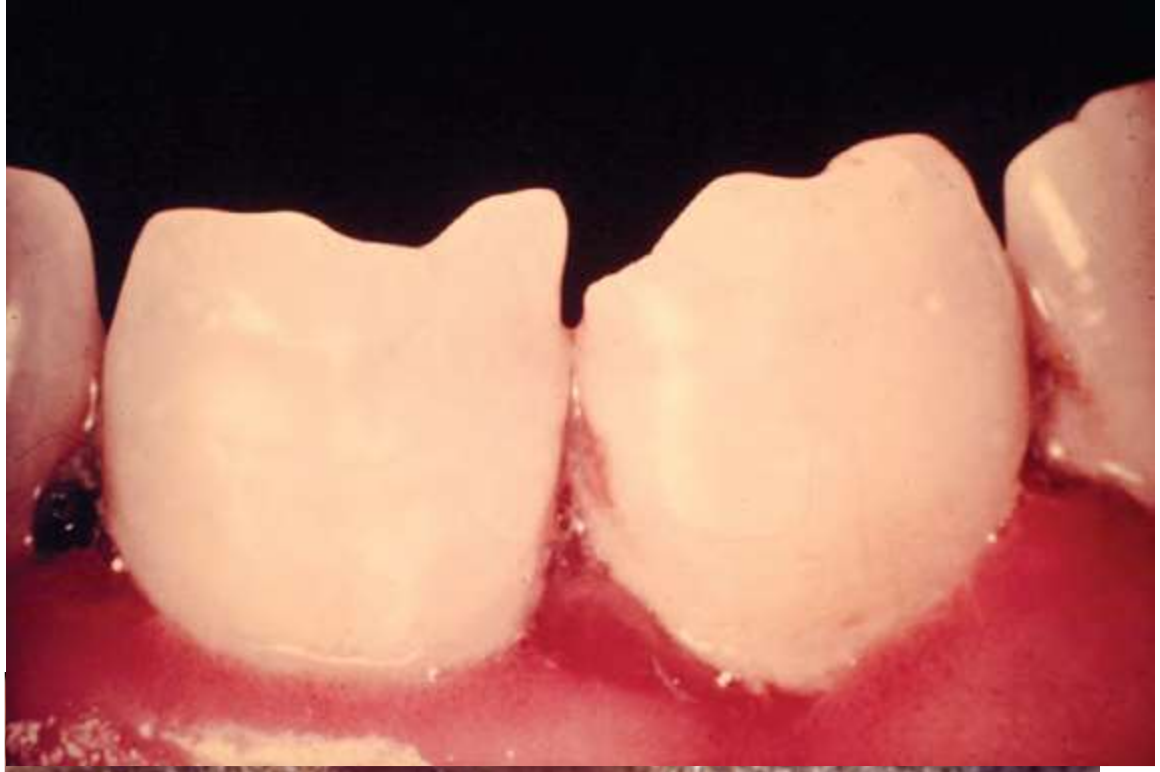


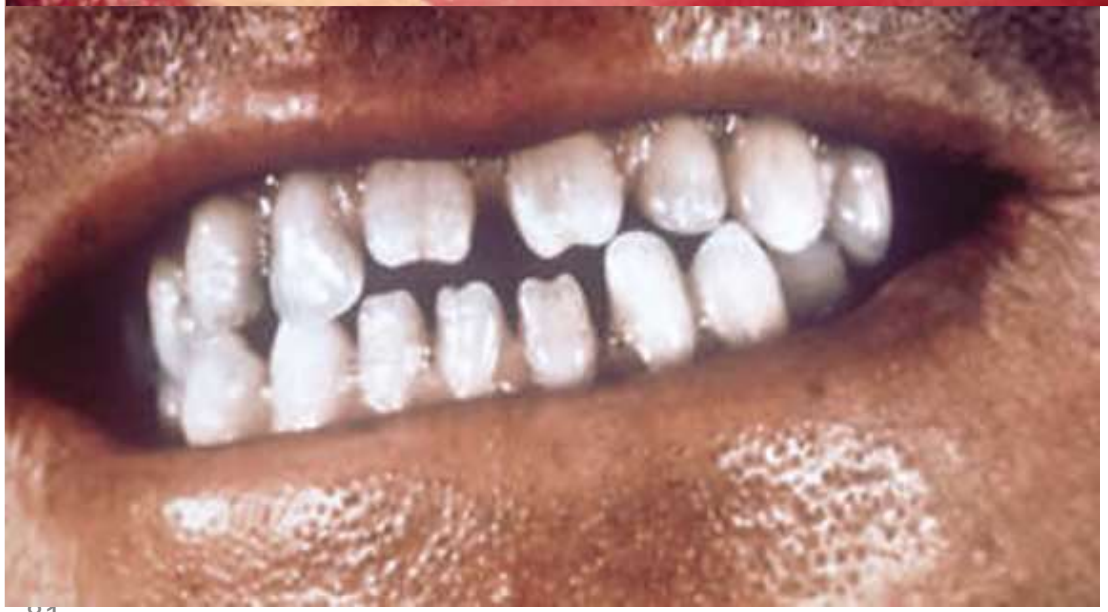
Early congenital syphilis showing serous nasal discharge from nasopharyngitis – ‘syphilitic snuffles

Perioral rhagades are linear scars that result from ulcerations that appear during early congenital syphilis and persist to adulthood. The presence of small, notched, peg shaped upper incisors (Hutchinson teeth) is also part of the late congenital syphilis triad.









Hutchinn's incisors

DIAGNOSTIC TESTS

DIRECT DETECTION OF T. PALLIDUM

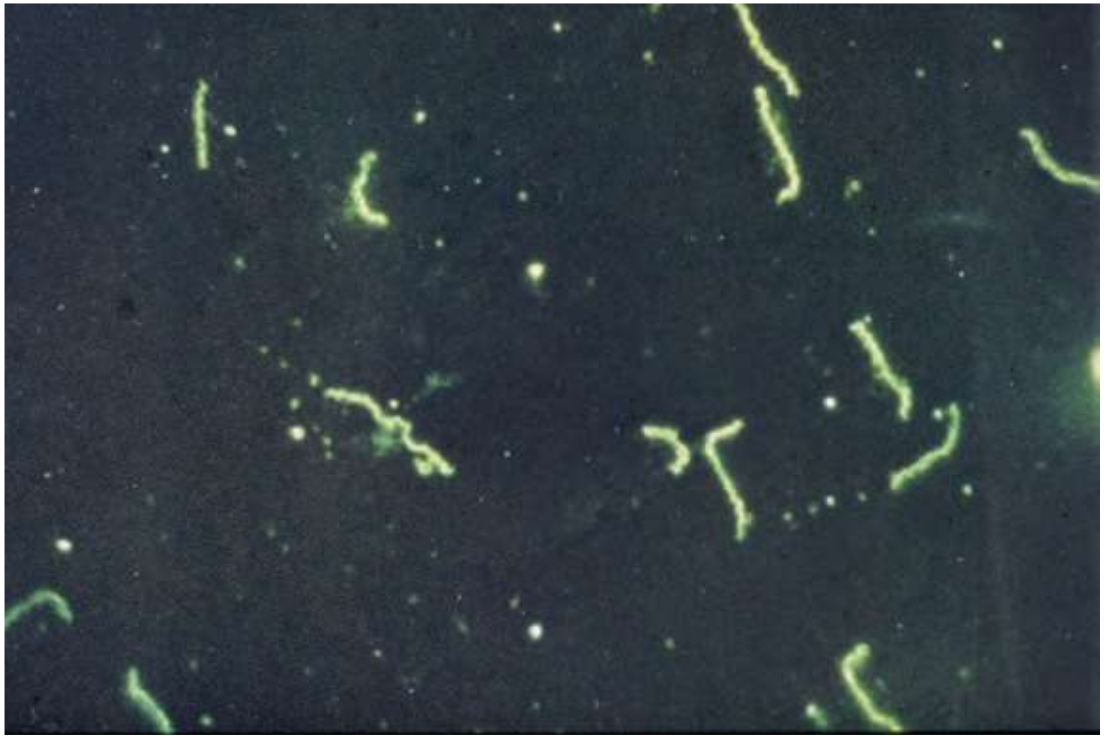
1) DARKFIELD MICROSCOPY.

- It is the diagnostic test of choice in chancres, moist lesions of secondary syphilis (condylomata lata and mucous patches), and the discharge from rhinitis in congenital syphilis.
- Darkfield examination will often be positive before serologic tests become reactive
- Because nonpathogenic treponemes are normally present in the oral cavity and can be mistaken for T. pallidum, darkfield microscopy cannot be used to test oral lesions.

DARKFIELD MICROSCOPY.

- The number of T. pallidum organisms in secondary syphilis lesions except for mucous patches and condyloma lata is generally not sufficient to allow darkfield diagnosis.
- Sensitivity is approximately 74%–79%, but declines as minutes elapse, as dead treponemes cannot exhibit the motility required for diagnosis. Of note, prior application of a topical antibiotic to a lesion can give in a false-negative darkfield specimen.

Treponema pallidum on dark ground microscopy.



DIAGNOSTIC TESTS

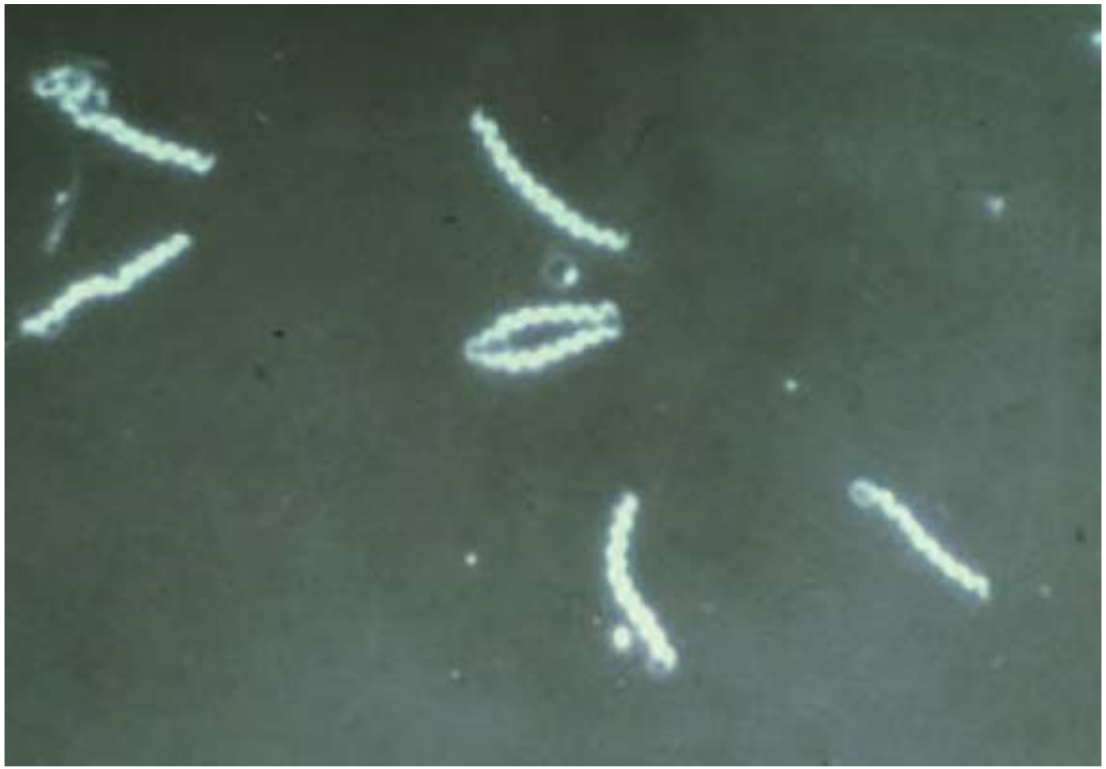
2) DIRECT FLUORESCENCE ANTIBODY TEST:

- The exudate is smeared on a glass slide and stained with fluorescein-labeled anti-T. pallidum immunoglobulin.
- In contrast to darkfield microscopic examination, the smear can be held for later evaluation and oral or anal lesions can be examined because only T. pallidum is stained. The sensitivity of the test is 73%–100%.

3) MOLECULAR TESTS.

- In research settings, polymerase chain reaction (PCR-based methods) have been used to detect T. pallidum DNA from lesions

Immunofluorescent image of Treponemal pallidum.



SEROLOGY

Serologic tests for syphilis include

- **nontreponemal tests**, which detect IgG and IgM antibodies
- **treponemal tests**, which detect antibodies to T. pallidum itself.
- correct serologic diagnosis of syphilis requires both types of test.

NONTREPONEMAL SEROLOGIC TESTS

- The two most widely used nontreponemal tests are the **Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests**.
- The VDRL and RPR begin to become reactive 4–5 weeks after infection, with 100% sensitivity by approximately 12 weeks, and revert to nonreactive in 25%–30% of cases during late latent syphilis.

NONTREPONEMAL SEROLOGIC TESTS

- Results can be qualitative or quantitative. Quantitative results are reported as titer, which refers to serial dilutions of serum by a factor of 2 (1:2, 1:4, 1:8, and so on).
- Because of the importance of using nontreponemal titers to assess response to treatment, a titer for each person diagnosed with syphilis must be obtained on the day-of-treatment.
- In most persons, following appropriate treatment, nontreponemal titers will revert to nonreactive.

NONTREPONEMAL SEROLOGIC TESTS

- False-negative results occur during very early infection or in latent and late syphilis.
- In a small percent of secondary syphilis cases, very high antibody titers inhibit test reactivity, producing a false-negative result, called the prozone phenomenon.
- To exclude the prozone phenomenon the test must be repeated with diluted serum.
- Biologic false-positive results make approximately 1% of reactive nontreponemal tests and usually have low titers (<1:8). Ex: Lyme disease; Cytomegalovirus; mononucleosis; Hepatitis; Malaria; connective tissue diseases; Drug abuse

TREPONEMAL SEROLOGIC TESTS

Examples of treponemal serologic tests include the

- T. pallidum particle agglutination (TPPA) test,
- Microhemagglutination assay for T. pallidum (MHA-TP),
- fluorescent treponemal antibody absorption assay(FTA-ABS),
- T. pallidum haemagglutination test (TPHA),
- various treponemal enzyme immunoassays (EIAs) and immunochemiluminescence assays.

TREPONEMAL SEROLOGIC TESTS

- These tests, which use whole or fragments of T. pallidum as antigen, directly detect infection with T. pallidum.
- a reactive treponemal test result rules out the possibility of a biologic false positive reaction on a nontreponemal test.
- Persons who have had syphilis usually will have reactive treponemal test results for life, even after successful treatment.
- The tests are highly specific and sensitive during the secondary and the late phases of the disease.
- Treponemal test titers do not correlate with, and are not used to monitor, disease activity.

CONGENITAL SYPHILIS

The diagnosis of congenital syphilis can prove to be difficult for the following three reasons:

- 1. T. pallidum is non-cultivatable and often difficult to demonstrate in clinical specimens.
- 2. Serological analysis is complicated by the presence of transplacentally acquired maternal antibodies.
- 3. The majority of live born infants have no evidence of infection

Evaluation of neonates for congenital syphilis

The following investigations should be carried out in children born to seropositive mothers with no documented treatment at least 4 weeks before delivery, if a non-penicillin regimen was administered, or if relapse or reinfection is suspected:

- Examination for stigmata of congenital syphilis.
- X-ray of long bones for evidence of periostitis.
- CSF examination.
- Dark-field microscopy and/or PCR from exudates of suspicious lesions or fluids.

TREATMENT AND FOLLOW-UP

- penicillin G is the recommended treatment for all stages of syphilis
- Penicillin-allergic persons with syphilis who are not pregnant and do not have neurosyphilis may be treated with doxycycline
- Pregnant women who are penicillin-allergic must be desensitized to and treated with penicillin, which is the only drug that is known to cross into the placenta and treat infection in the fetus.
- Reports of treatment failures and resistance to macrolides including azithromycin

TREATMENT AND FOLLOW-UP

- Treatment success is generally defined as a fourfold decline in serologic nontreponemal titer (or reversion to nonreactive result) following appropriate treatment. An example of a fourfold decline in titer is a 1:64 titer declining to 1:16 or lower, or a 1:16 titer declining to 1:4 or lower.
- **A fourfold titer increase** following appropriate treatment **indicates reinfection or treatment failure**—the latter in some cases associated with neurosyphilis
- If treatment failure cannot be ruled out, the patient should be treated with 7.2 millions units of benzathine penicillin G (divided in three weekly doses); CSF examination should be performed to determine whether neurosyphilisis present, and, if it is, the patient should be treated for neurosyphilis as well.

COMPLICATIONS OF TREATMENT

- ***The Jarisch–Herxheimer reaction* is** a self-limited clinical syndrome consisting of fever, headache, flare of mucocutaneous lesions, lymphadenopathy, pharyngitis, malaise, myalgia, and leukocytosis.
- It occurs within 12 hours of initiating therapy and resolves within 24–36 hours
- Patients should be warned about the possibility of developing this reaction before receiving treatment
- The pathogenesis of the Jarisch–Herxheimer reaction is unknown, but is thought from dying T. pallidum organisms
- **Anaphylaxis** from administration of penicillin injection is a life-threatening emergency.