# Infectious Lect. 2
# 14/11/2022

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# ***Sexually Transmitted diseases:***

Syphilis :

is a chronic venereal disease with multiple presentations. The causative spirochete, *T. pallidum* is too slender to be seen in Gram stain, but it can be visualized by silver stains, dark-field examination, and immunofluorescence techniques. Sexual contact is the usual mode of spread. Transplacental transmission of *T. pallidum* occurs readily, and active disease during pregnancy results in congenital syphilis. *T. pallidum* cannot be grown in culture

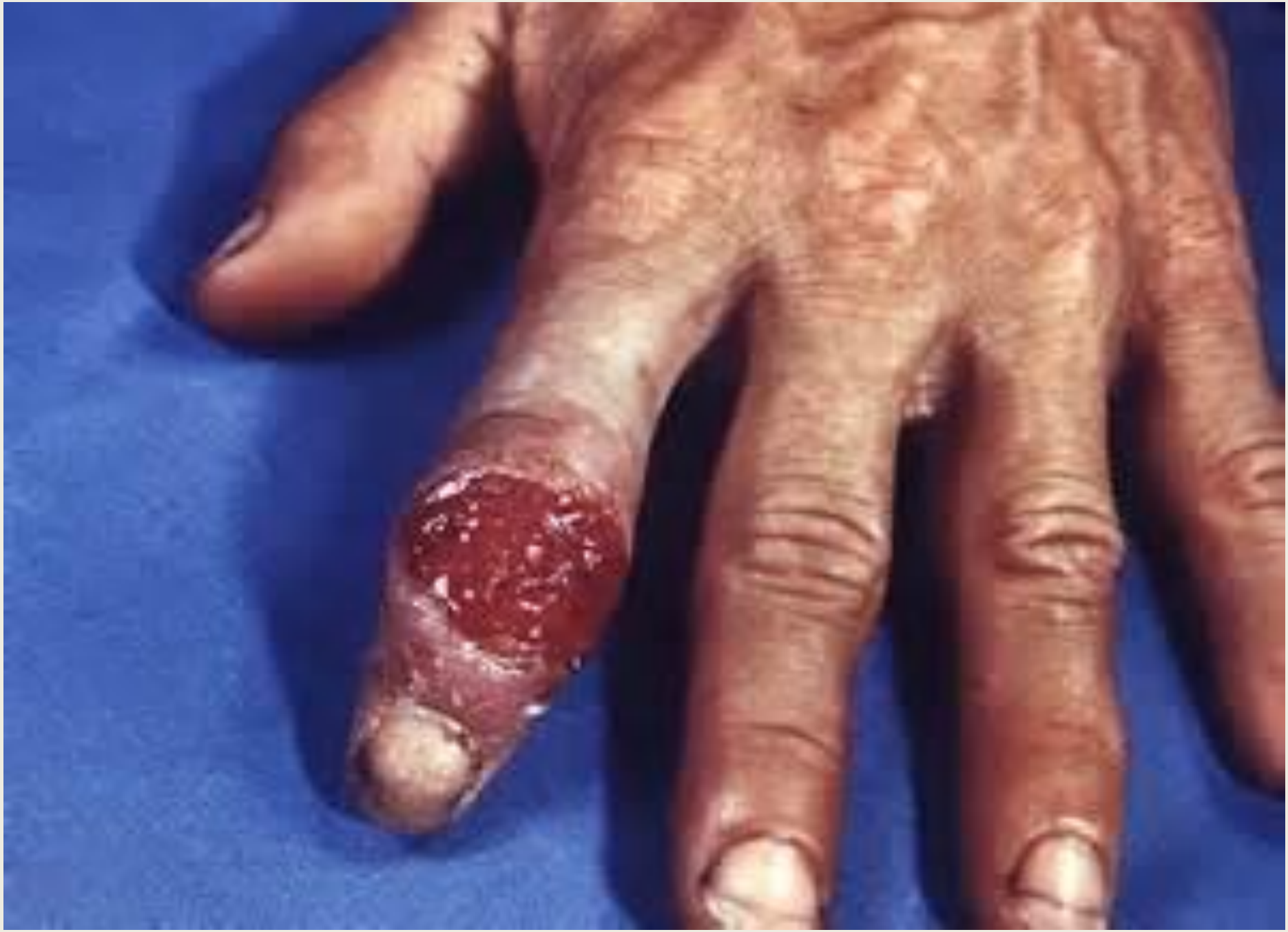
Syphilis is divided into three stages, with distinct clinical and pathologic manifestations

1-Primary Syphilis:

This stage, occurring approximately 3 weeks after contact with an infected individual, features a single firm, nontender, raised, red lesion (chancre) located at the site of treponemal invasion on the penis, cervix, vaginal wall, or anus. The chancre heals in 3 to 6 weeks with or without therapy. *Spirochetes are plentiful within the chancre and can be seen by immunofluorescent stains of serous exudate.* Treponemes spread throughout the body by hematologic and lymphatic dissemination even before the appearance of the chancre.

**Morphology**. In **primary syphilis** a chancre occurs on the penis or scrotum of 70% of men and on the vulva or cervix of 50% of women. The chancre is a slightly elevated, firm, reddened papule, up to several centimeters in diameter, that erodes to create a clean-based shallow ulcer. The contiguous induration creates a button-like mass directly adjacent to the eroded skin, providing the basis for the designation hard chancre . On histologic examination, treponemes are visible at the surface of the ulcer with silver stains (e.g., Warthin-Starry stain) or immunofluorescence techniques.

The chancre contains an intense infiltrate of plasma cells, with scattered macrophages and lymphocytes and a proliferative endarteritis . The endarteritis, which is seen in all stages of syphilis, starts with endothelial cell activation and proliferation and progresses to intimal fibrosis. The regional nodes are usually enlarged due to nonspecific acute or chronic lymphadenitis, plasma cell-rich infiltrates, or granulomas.

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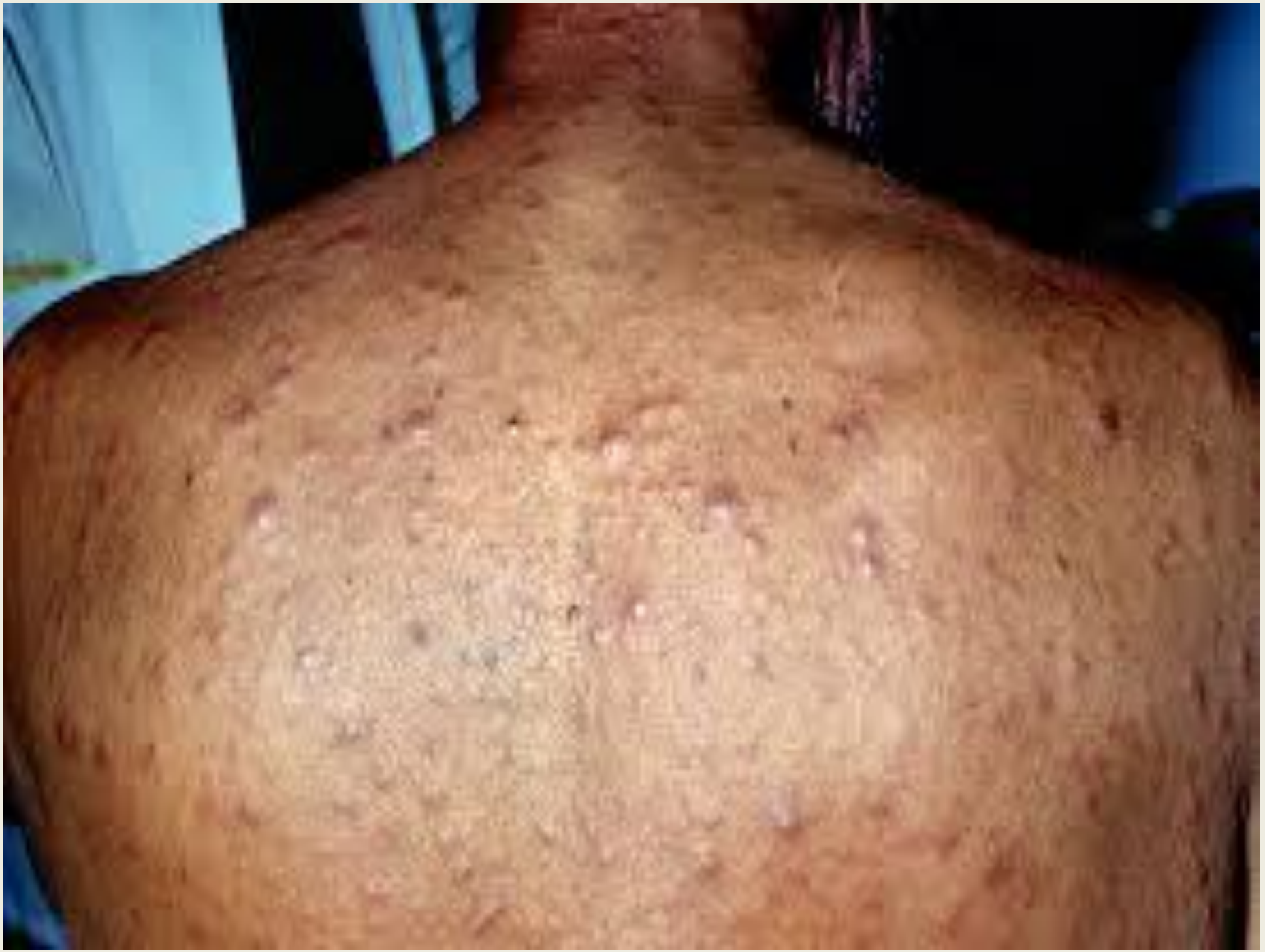
2-Secondary Syphilis:

This stage usually occurs 2 to 10 weeks after the primary chancre and is due to spread and proliferation of the spirochetes within the skin and mucocutaneous tissues. Secondary syphilis occurs in approximately 75% of untreated people. *The skin lesions, which frequently occur on the palms or soles of the feet, may be maculopapular, scaly, or pustular*. Moist areas of the skin, such as the anogenital region, inner thighs, and axillae, may have *condylomata lata*, which are broad-based, elevated plaques.

Silvery-gray superficial erosions may form on any of the mucous membranes but are particularly common in the mouth, pharynx, and external genitalia. All these painless superficial lesions contain spirochetes and so are infectious. Lymphadenopathy, mild fever, malaise, and weight loss are also common in secondary syphilis. The symptoms of secondary syphilis last several weeks, after which the person enters the latent phase of the disease. Superficial lesions may recur during the early latent phase, although they are milder.

In **secondary syphilis** :

The rash frequently consists of discrete red-brown macules less than 5 mm in diameter, but it may be follicular, pustular, annular, or scaling. Red lesions in the mouth or vagina contain the most organisms and are the most infectious. Histologically, the mucocutaneous lesions of secondary syphilis show the same plasma cell infiltrate and obliterative endarteritis as the primary chancre, although the inflammation is often less intense.

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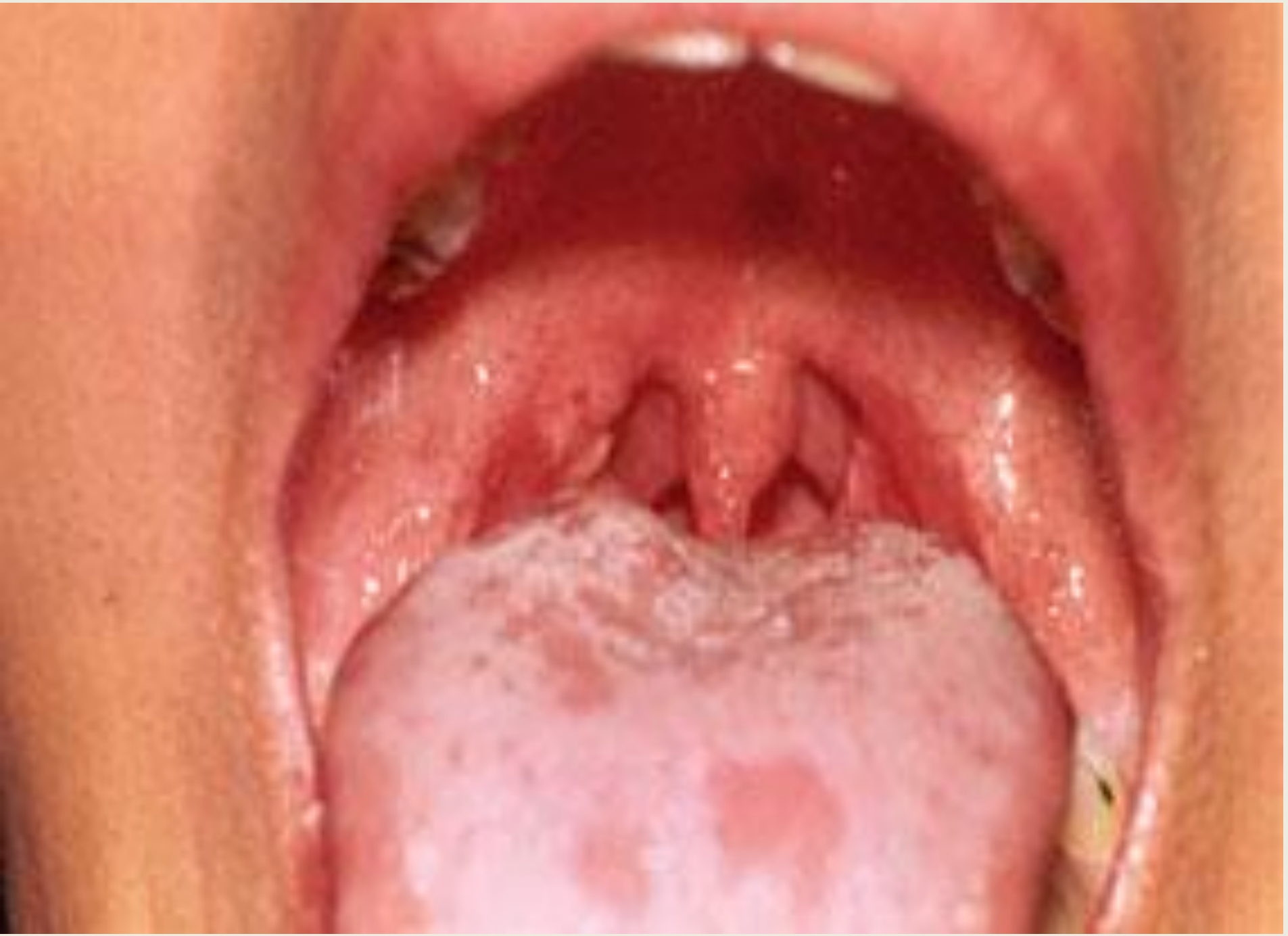
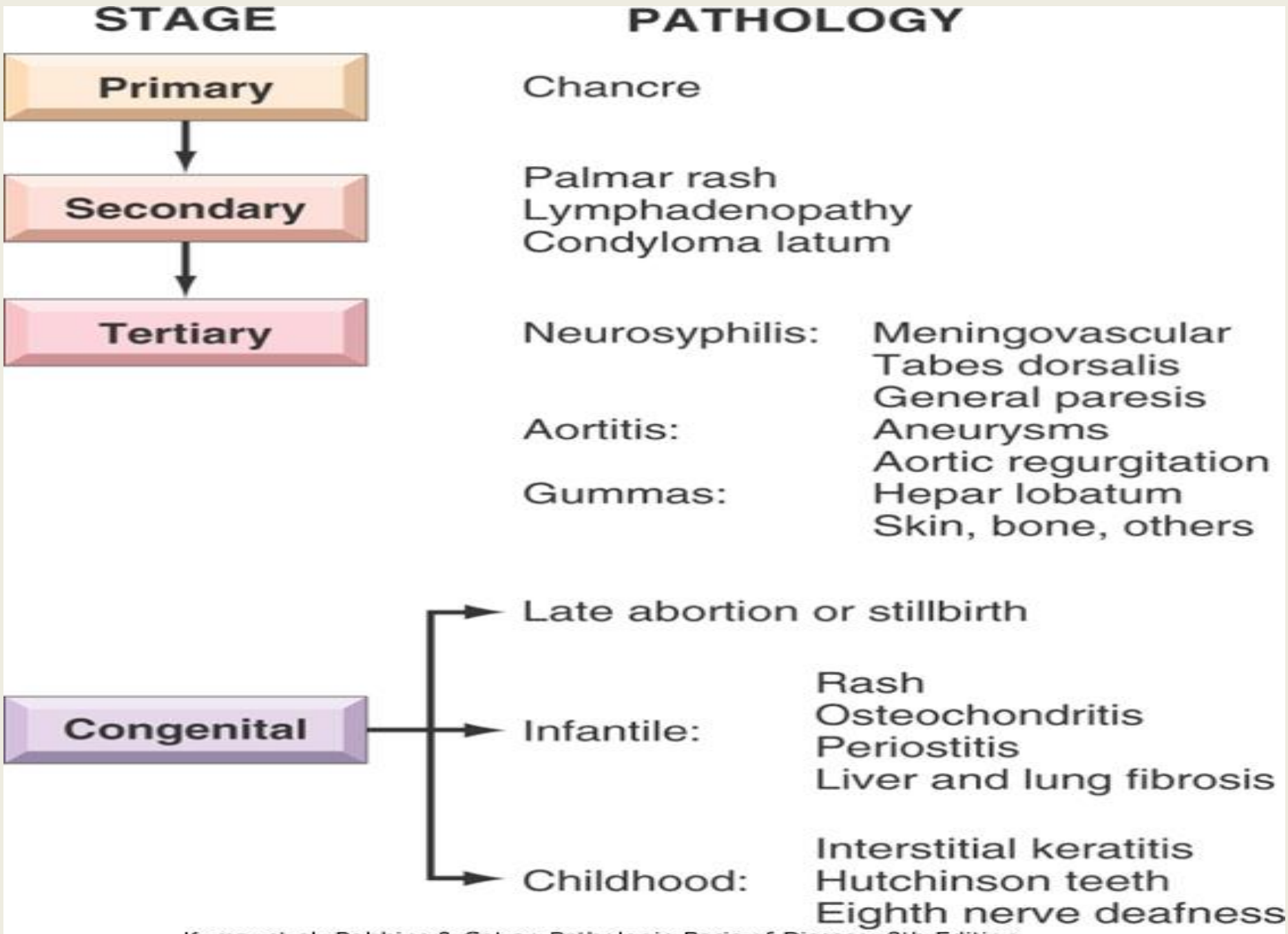


## 3-Tertiary Syphilis:

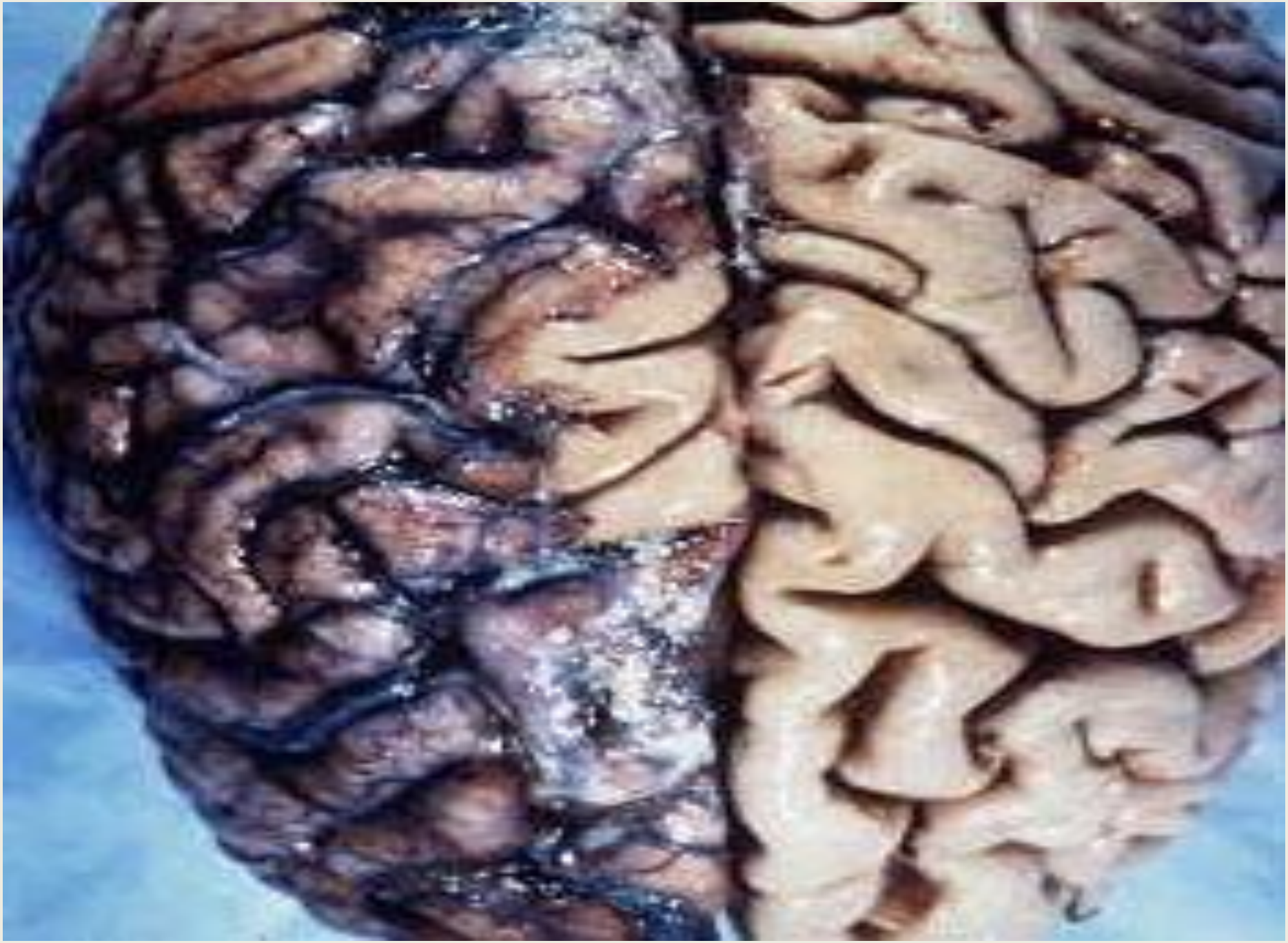
This stage is rare where adequate medical care is available, but it occurs in approximately one third of untreated patients, usually after a latent period of 5 years or more. Tertiary syphilis has three main manifestations: cardiovascular syphilis, neurosyphilis, and so-called benign tertiary syphilis. These may occur alone or in combination.



*Cardiovascular syphilis*, in the form of syphilitic aortitis, accounts for more than 80% of cases of tertiary disease. The aortitis leads to slowly progressive dilation of the aortic root and arch, which causes aortic valve insufficiency and aneurysms of the proximal aorta

*Neurosyphilis* :

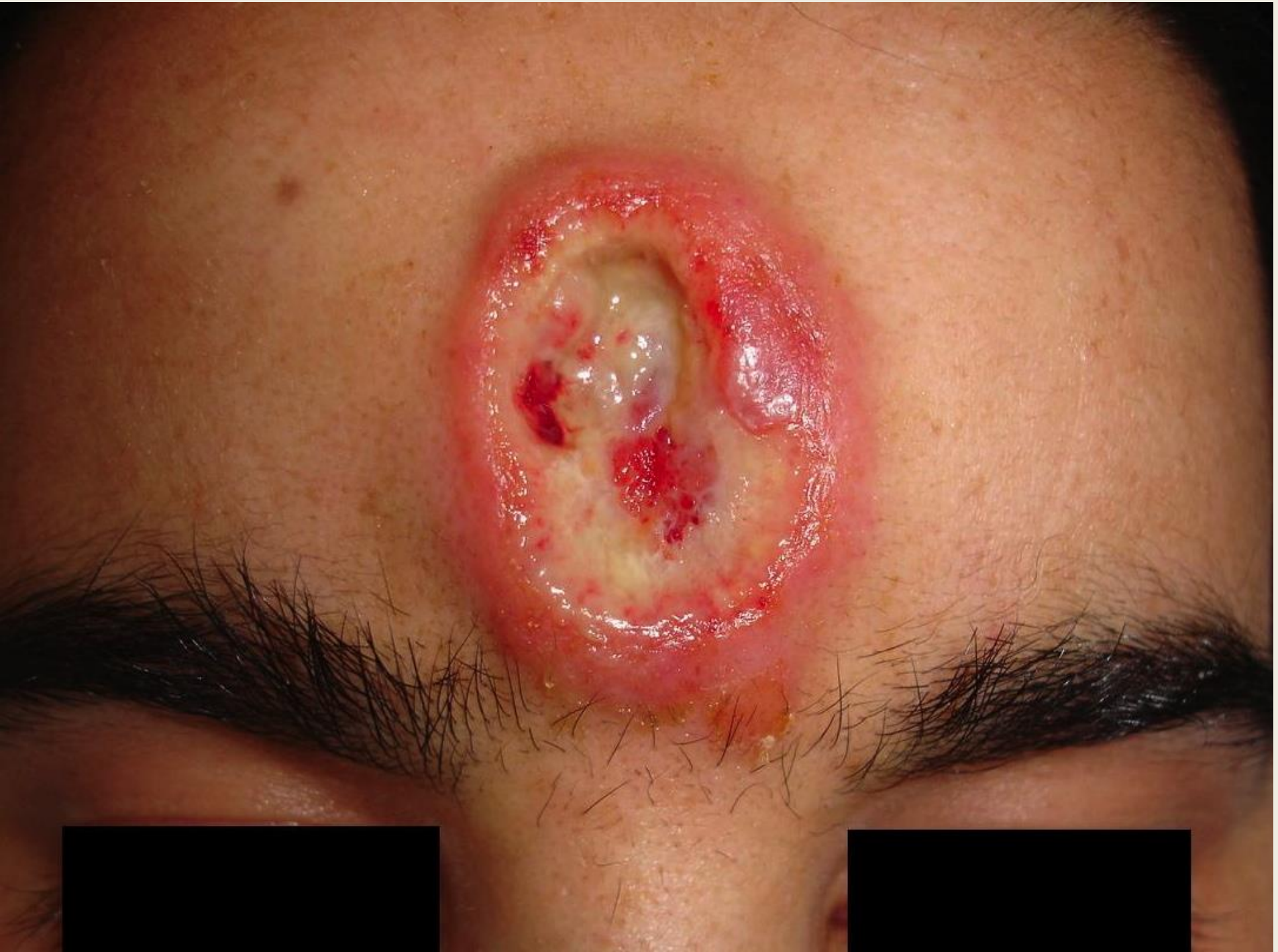
may be symptomatic or asymptomatic. Symptomatic disease manifests in several ways, including chronic meningovascular disease, tabes dorsalis, and a generalized brain parenchymal disease called *general paresis*. Asymptomatic neurosyphilis, which accounts for about one third of neurosyphilis cases, is detected when a patient's CSF exhibits abnormalities such as pleocytosis (increased numbers of inflammatory cells), elevated protein levels, or decreased glucose. Antibodies stimulated by the spirochetes, can also be detected in the CSF, and this is the most specific test for neurosyphilis. Antibiotics are given for a longer time if the spirochetes have spread to the CNS, and so patients with tertiary syphilis should be tested for neurosyphilis even if they do not have neurologic symptoms



So-called *benign tertiary syphilis* is characterized by the formation of gummas in various sites. Gummas are nodular lesions probably related to the development of delayed hypersensitivity to the bacteria. They occur most commonly in bone, skin, and the mucous membranes of the upper airway and mouth, although any organ may be affected. Skeletal involvement characteristically causes local pain, tenderness, swelling, and sometimes pathologic fractures. Involvement of skin and mucous membranes may produce nodular lesions or, rarely, destructive, ulcerative lesions that mimic malignant neoplasms. Gummas are now very rare because of the use of effective antibiotics and are seen mainly in individuals with AIDS

**Tertiary syphilis** most frequently involves the aorta; the CNS; and the liver, bones, and testes. The aortitis is caused by endarteritis of the vasa vasorum of the proximal aorta. Occlusion of the vasa vasorum results in scarring of the media of the proximal aortic wall, causing a loss of elasticity. There may be narrowing of the coronary artery ostia caused by subintimal scarring with resulting myocardial ischemia.

**Neurosyphilis** takes one of several forms, designated meningovascular syphilis, tabes dorsalis, and general paresis . **Syphilitic gummas** are white-gray and rubbery, occur singly or multiply, and vary in size from microscopic lesions resembling tubercles to large tumor-like masses. They occur in most organs but particularly in skin, subcutaneous tissue, bone, and joints. In the liver, scarring as a result of gummas may cause a distinctive hepatic lesion known as hepar lobatum . On histologic examination, the gummas have centers of coagulated, necrotic material and margins composed of plump, palisading macrophages and fibroblasts surrounded by large numbers of mononuclear leukocytes, chiefly plasma cells. Treponemes are scant in gummas and are difficult to demonstrate



Congenital syphilis occurs when *T. pallidum* crosses the placenta from an infected mother to the fetus. Maternal transmission happens most frequently during primary or secondary syphilis, when the spirochetes are most numerous. Because the manifestations of maternal syphilis may be subtle, routine serologic testing for syphilis is mandatory in all pregnancies. Intrauterine death and perinatal death each occurs in approximately 25% of cases of untreated congenital syphilis.

Manifestations of congenital disease are divided into:

1- early (infantile)

2-late (tardive) syphilis.

depending on whether they occur in the first 2 years of life or later. Early congenital syphilis is often manifested by nasal discharge and congestion (snuffles) in the first few months of life. A desquamating or bullous rash can lead to sloughing of the skin, particularly of the hands and feet and around the mouth and anus. Hepatomegaly and skeletal abnormalities are also common.

Nearly half of untreated children with neonatal syphilis will develop late manifestations, which are discussed below.

The rash of **congenital syphilis** is more severe than that of adult secondary syphilis. It is a bullous eruption of the palms and soles of the feet associated with epidermal sloughing. **Syphilitic osteochondritis and periostitis** affect all bones, but lesions of the nose and lower legs are most distinctive. Destruction of the vomer causes collapse of the bridge of the nose and, later on, the characteristic saddle nose deformity. Periostitis of the tibia leads to excessive new bone growth on the anterior surfaces and anterior bowing, or saber shin. There is also widespread disturbance in endochondral bone formation. The epiphyses become widened as the cartilage overgrows, and cartilage is found in displaced islands within the metaphysis.

The liver is often severely affected in congenital syphilis. Diffuse fibrosis permeates lobules to isolate hepatic cells into small nests, accompanied by the characteristic lymphoplasmacytic infiltrate and vascular changes. Gummas are occasionally found in the liver, even in early cases. The lungs may be affected by a diffuse interstitial fibrosis. In the syphilitic stillborn, the lungs appear pale and airless (pneumonia alba). The generalized spirochetemia may lead to diffuse interstitial inflammatory reactions in virtually any other organ (e.g., the pancreas, kidneys, heart, spleen, thymus, endocrine organs, and CNS).

The late manifestations of congenital syphilis include a distinctive **triad of interstitial keratitis, Hutchinson teeth, and eighth-nerve deafness**. In addition to interstitial keratitis, the ocular changes include choroiditis and abnormal retinal pigmentation. Hutchinson teeth are small incisors shaped like a screwdriver or a peg, often with notches in the enamel. Eighth-nerve deafness and optic nerve atrophy develop secondary to meningovascular syphilis.

# Pathogenesis

1- *T. pallidum* has never been grown in culture (it lacks genes for making nucleotides, fatty acids, and most amino acids).

2-the intense inflammatory infiltrate suggest that the immune response plays a role in the development of these lesions.

3-The immune response to *T. pallidum* reduces the burden of bacteria, but it may also have a central role in the pathogenesis of the disease.

4-The T cells that infiltrate the chancre are $T_H1$ .

5-The antibody response does not eliminate the infection.

6-The outer membrane of *T. pallidum* seems to protect the bacteria from antibody binding.

Laboratory diagnosis of syphilis

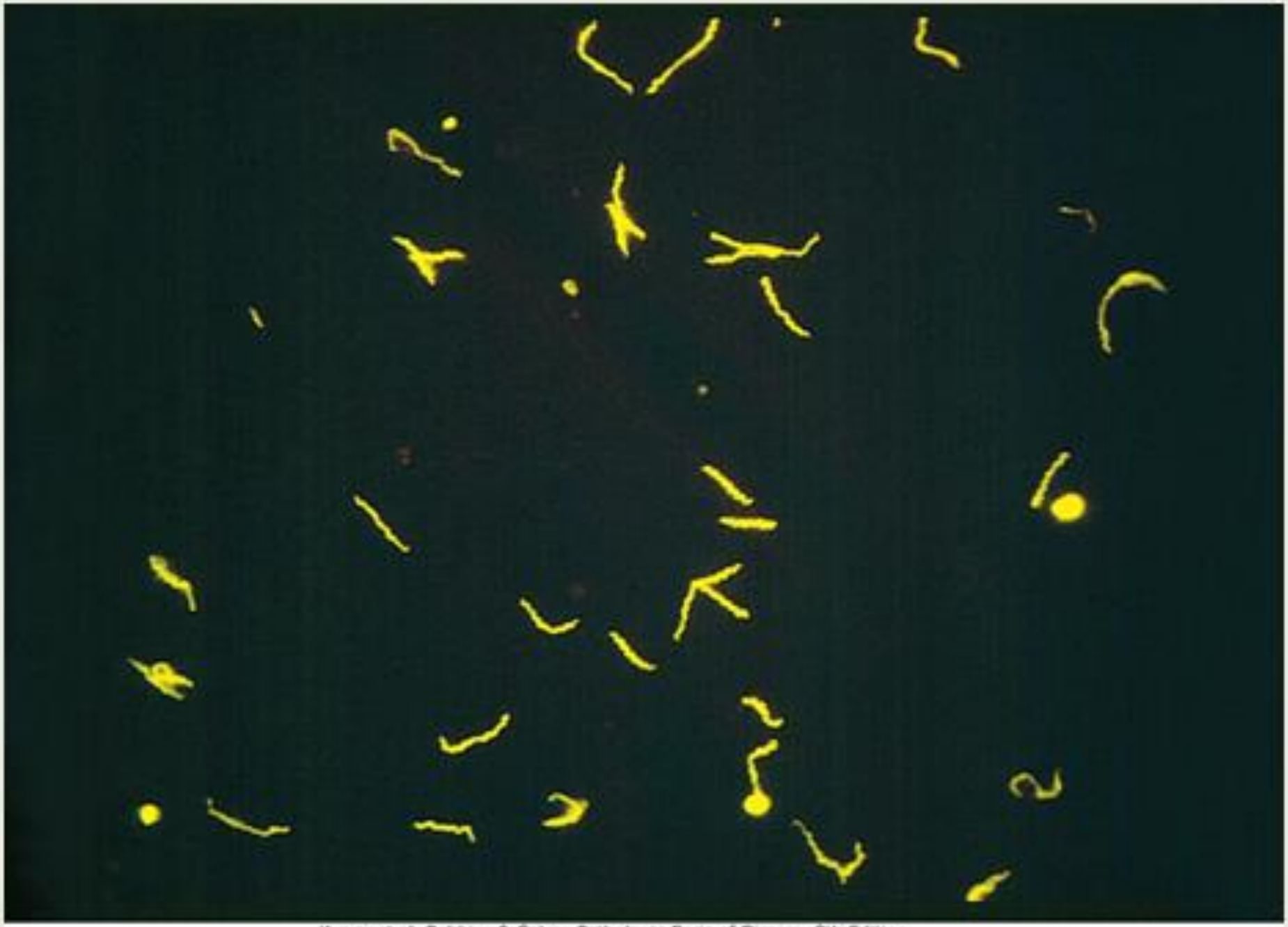
As T. pallidum cannot be grown in vitro, laboratory diagnosis hinges on microscopy and serology.

A- Microscopy

Exudate from the primary chancre should be examined by either:

1-dark-field microscopy immediately after collection.

2-ultraviolet (UV) microscopy after staining with fluorescein-labeled anti-treponemal antibodies.



B-Serology:

1-***Non-specific tests (non-treponemal tests) for syphilis are the VDRL and RPR tests (***the Venereal Disease Research Laboratory test and the rapid plasma reagin test).

2-***Commonly used specific tests for syphilis are the treponemal antibody test, FTA-ABS test and the MHA-TP (***the fluorescent treponemal antibody absorption , microhemagglutination assay for *T. pallidum* ).

it should be noted that antibiotic treatment of syphilis, in patients with a high bacterial load, can cause a massive release of endotoxins, resulting in a cytokine storm that manifests with high fever, rigors, hypotension, and leukopenia. This syndrome, called the Jarisch-Herxheimer reaction, is seen not only in syphilis but in other spirochetal diseases, such as Lyme disease, and can be mistaken for drug allergy.

***Granuloma Inguinale:***

Its other venereal disease, the causative agents are bacteria called ***Calymmato bacterium donavani***

These bacteria are intracellular bacteria, the infection occur by sexual intercourse, there is chronic ulcerative lesion in which extensive ulcer occur in skin and sub-cutanious tissues.

The ulceration involves the skin of external genetalia, tests, scrotum, penis, perineum, anogenital region and healing of this ulcer occurs by formation of fibrous tissues and extensive scaring.

The organism can be seen inside macrophages as small drops called ***Donavan body***, the inguinal lymph nodes are either normal or slightly enlarge.

***Lympho granuloma venereum:***

Its other venereal disease cased by ***Chlamydia trachomatis***, this cause extensive ulceration in genital area, and healing also occurs by extensive scar formation.

In addition, the inguinal lymph nodes are very enlarging and later lymph node may be suppurated.

The inflammation may also extended to pelvis and pelvic organ and peri-rectal tissues and again healing of these inflammation cause fibrosis of lymphatic which may lead to lymphatic obstruction , this will lead to stasis, therefore this patient also develop condition called ***elephantiasis*** , in which scrotum of male become swallow and enlarge also uvula in female become swallow and enlarge .

***Trichomonas vaginalis:***

This is a sexually transmitted, anaerobic, flagellated protozoan parasite that present in trophozoit only. It adheres to and cause superficial lesion in the mucosal surface of male and female genital tracts without invasion.

In females it causes itching and watery vaginal discharge exacerbated by menstruation and pregnancy.

***Gonorrhea:***

This is caused by ***Neisseria gonorrhea***, which is pyogenic encapsulated Gram-negative diplococcus.

***Pathogenesis:***

1. The bacteria are a facultative intracellular pathogen that bind to and invades epithelial calls through cell binding sites (receptors) and pili.

2. Its internalization depends on rearrangement of host cell actin filament.

3. Capsular polysaccharides contributed to the virulence by inhibiting phagocytosis.

4. Secretion of a protease that cleaves IgA.

5. Release of peptidoglycans and endotoxins, which induce host cell secretion of TNF , which may cause shock and multi-system failure.

***Morphology:***

The reaction is an Exudative purulent one. This is followed by granulation tissue formation, plasma cell infiltration and fibrosis.

***In men,*** there is infection of urethral meatus, 2-7 days after exposure. This is manifested by a muco-purulent discharge.

Spread of infection occurs to the posterior urethra, epididymis, prostate and seminal vesicle.

Chronic inflammation may lead to strictures and sterility.

***In women, It*** usually

- The urethral inflammation is less prominent.
- Abscess involve Bartholine gland.
- Cervicitis.
- Sever form of salpingitis and its distention with pus or formation of tubo-ovarian abscesses and pelvic peritonitis with adhesions (pelvic inflammatory diseases).
- Gonococcus bactermia leads to arthritis-dermatitis syndrome.
- Conjunctivitis may also occur.

***Diagnosis:***

This is made by urethral smear to demonstrate polymorph nuclear leucocytes laden with gram-negative diplococci.

***Trichomoniasis:***

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In females it causes itching and watery vaginal discharge exacerbated by menstruation and pregnancy.

It's also cause urethritis both in males and females, the mucosa and sub mucosa of this areas show infiltration with lymphocytes, plasma cells and polymorph nuclear leucocytes.

This organism can be seen in fresh smears as rapidly motile flagellated forms.

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