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 **2017**

**Genital Ulcer**

**Causes:**

**ST causes**: herpes genitalis, chancre (primary syphilis), chancroid, lymphogranuloma venereum (LGV), and granuloma inguinale (Donovanosis).

**Non ST causes**: Behcet disease, fixed drug eruption, trauma, malignancy as SCC, and chronic infections as TB.

**Syphilis**

**Definition:**

Syphilis is a STI caused by a spirochetal bacterium, Treponema *pallidum*, also called "Lues" or "Cupid's disease (Roman mythology god of love)".

**Mode of Transmission:**

The infection is usually acquired through sexual contact with infected lesions or body fluids; less commonly, transplacentally; and rarely through blood transfusion, or inoculation with contaminated instruments (as tattooing or IV drug users).

**Microbiology:**

***Treponema pallidum*** is a Gram negative, fragile, spiral bacterium (spirochete) with corkscrew rotation motility. It can be observed only by dark-field microscope, and unable to be cultured in vitro.

*T. pallidum* can cause the following diseases:

**1. Syphilis:** caused by *T. pallidum**pallidum*.

**2. Bejel** (endemic syphilis): caused by *T. pallidum* *endemicum*. Transmitted non sexually, and has features of secondary syphilis without presence of the primary stage. Bejel is endemic in some areas in Saudi Arabia, Iraq, and Syria.

**3. Yaws**: caused by *T. pallidum* *pertenue*. It is a tropical disease characterized by an infection of the skin, bones, and joints.

**4. Pinta**: caused by *T. pallidum* *carateum* (vitiligo-like presentation).

**Classification and Stages:**

There are two types of syphilis **congenital** and **acquired**.

The **Acquired Syphilis** passes through four distinct clinical stages:

**1.** Primary stage (chancre).

**2.** Secondary stage (skin, mucous membrane, and systemic eruption).

**3.** Latent stage (history of syphilis **+** absence of signs and symptoms **+** positive serology).

It is divided into early latent (less than one year) and late latent (1 year or longer).

**4.** Tertiary stage (skin, mucous membrane, and visceral).

**Early syphilis** (within the first 2 years of infection, more infectious) including the primary, secondary, and early latent stages.

**Late syphilis** (after 2 years of infection, less infectious) including late latent and tertiary syphilis.

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**Natural Course of Untreated Syphilis:**

  **50%** **50%**  **75%**  (**1/3**) Remission

Exposure Primary Secondary Early latent Late latent (**1/3**) Remain latent

 (**1/3**) Tertiary

 Relapse to Secondary

 **25%**

**A**- **Acquired Syphilis:**

**Primary Syphilis (Chancre):**

The syphilitic ulcer (chancre) appear in the genital area after 9-90 days (3 weeks in **50%**) after exposure to infected partner at the site of initial contact. Chancre is usually solitary, painless, hard, and indurated; the base is clean with a scant yellow serous discharge (typical chancre occur in **50%** of patients). Extragenital chancres accrue in 5% of cases. The chancre usually heals with scarring after 3-6 weeks.

Painless, hard, discrete regional lymphadenopathy occurs in 1-2 weeks; which never coalesce or suppurate unless there is mixed infection.

**Secondary Syphilis:**

**I- Cutaneous findings:** most eruptions are macular and/or papular**;** nodular, follicular, and pustular eruptions occur infrequently.

The skin changes of syphilis can mimic many other skin diseases "great imitator", but the lesions of secondary syphilis have certain characteristics that differentiate them:

**1.** There is little or no fever at onset.

**2.** Pain or itching is minimum or absent.

**3.** Lesions are non inflammatory, develop slowly.

**4.** There is a marked tendency to polymorphism.

**5.** Usually bilateral symmetrical, with characteristic palms and soles involvement.

**6.** The color is characteristic, resembling a "clean-cut ham" (coppery tint).

Hair loss: small irregular patches of hair loss ("moth eaten" alopecia).

Malignant syphilis: wide spread lesions that become necrotic and ulcerated, associated with toxicity, fever, arthralgia. Most patients are immunocompromised.

**II- Mucous membrane findings**: are extremely infectious, including: codylomata lata (smooth, papillated, or covered with cauliflower-like vegetations), oral mucous patches, pharyngitis and laryngeal involvement which may produce hoarseness.

**III- Systemic findings:**

Ophthalmologic: iritis, is the most common eye complication.

Auditory: sensorineural hearing loss.

Musculoskeletal: back pain, arthralgias, arthritis, tenosynovitis, and bursitis.

Haematologic: anaemia, leukocytosis, relative lymphopenia, and elevated ESR.

Renal: acute membranous glomerulonephritis.

Neurological: asymptomatic or symptomatic (headache and meningeal irritation).

Hepatic and gastric.

**Differential Diagnosis of Secondary Syphilis:**

**Skin eruption:** pityriasis rosea, guttate psoriasis, lichen planus, pityriasis versicolor, drug eruptions, and viral eruptions.

**Condylomata lata:** genital warts, and haemorrhoids.

**Oral lesions:** aphthous ulcers, and candidiasis.

**Alopecia "Moth eaten":** alopecia areata, and tinea capitis.

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**Tertiary Syphilis**:

**I- Cutaneous lesions**: in opposite to the secondary syphilis; the lesions are few, asymmetrical, slowly growing, destructive and heals with scar, and this stage is less infectious and the microorganisms are few within these lesions.

They can be divided into 2 types:

**1.** Nodular and noduloulcerative lesions: may be psoriasiform.

**2.** Gummas (a form of granuloma): are non-tender pink to dusky-red nodules or plaques. They favor sites of previous trauma, scalp, and forehead, but may arise anywhere in the body.

**II- Mucous membranes lesions**: Discrete gummas or diffuse gummatous infiltration may involve mucous membranes, especially the palate, nasal mucosa, tongue, tonsils, and pharynx. The lesions ulcerate and are disfiguring. Destruction of the nasal cartilage and bone (saddle nose) are the disease hallmark. Oral leukoplakia may occur, and may progress to SCC in **50%** of cases.

**III- Visceral (systemic findings):** cardiovascular syphilis and neurosyphilis {asymptomatic or symptomatic (headache, fever, stiff neck, confusion, and seizures)}.

**B**- **Congenital Syphilis:**

• *T.pallidum* can be transmitted to the fetus in utero from an infected mother (usually with early syphilis), this transmission usually occurs after the forth month of gestation.

• The ability of the mother to infect the fetus diminishes with further pregnancies.

• Approximately **25%** of infants from mothers with untreated primary or secondary syphilis die in utero. Of those infants born (**75%**), **one-half** develop the disease,  **one-forth** are seropositive without clinical manifestations, and **one-forth** are not infected.

• Congenital syphilis divided into:

**Early**: presenting within the first 2 years of life (usually after the third week).

**Late**: presented after the age of 2 years.

**Stigmata of Congenital Syphilis:**

1. Ophthalmic: corneal clouding.
2. Oral: Hutchinson teeth (notched, peg-shaped upper incisors) and high-arched palate.
3. Nose: saddle nose.
4. Orthopedic: frontal bossing, saber shin, and thickened medial clavicle.
5. Neurologic: 8th cranial nerve palsy.
6. Positive serology for syphilis.

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**Diagnosis of Syphilis:**

1. History and examination.
2. Dark-field microscopy: in which the specimen (usually taken from the base of a chancre) appears bright against a dark background. Mostly useful in early disease when the serological tests still negative.
3. Serological tests.
4. PCR.
5. Biopsy: rarely needed.

**Serological Tests of Syphilis:** classified into two main groups:

**A**- **Non-specific (lipoidal or non treponemal) tests:**

These tests are directed against the phospholipids in the cell wall of the microorganisms, including two important tests:

**1.** Venereal disease research laboratory (**VDRL**).

**2.** Rapid plasma regain (**RPR**) tests.

• These tests become positive 3-6 weeks after infection (after 3 weeks in **50%**).

• Remain strongly positive throughout the secondary phase, and usually become negative after treatment, so can be used to monitor response to therapyand follow up.

• They are used for screening purposes and have a high degree of sensitivity but relatively low specificity.

• These tests give quantitative as well as qualitative results, so all reactive samples are titrated to determine the highest reactive dilution. A fourfold change in titer is considered significant clinically.

• When these tests are positive, verification should be done by the specific tests.

**B**- **Specific (treponemal) tests:**

These tests are directed against the treponaeml antigens include:

1. *T. pallidum* haemagglutination test (**TPHA**): available in Iraq.
2. Reiter protein complement fixation test (**RPCF**).
3. Fluorescent treponemal antibody absorption test (**FTA/ABS**).
4. *T. pallidum* immobilization test (**TPI**).

•These tests become positive earlier than the non specific tests.

•A patient who has a reactive treponemal test usually will have a reactive test for a life time, regardless of treatment or disease activity, so these tests should not be used to assess response to treatment or follow up.

• They are not used for screening purposes.

• These tests cannot be titrated.

**False reactions:**

**False**-**positive reactions:** (positive non-specific test with negative specific test), may occur with collagen vascular disease, advancing age, narcotic drug use, chronic liver disease, several chronic infections such as TB, and several acute infections such as herpes.

**False-negative** **reactions:** may occur if the patient has been used topical or systemic antibiotics, or due toProzone phenomenon (caused by excessive amount of antibody).

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**Treatment of Syphilis:**

**Penicillin** **remains the treatment of choice for all stages of syphilis.**

• **Early syphilis:**

Single IM injection of 2.4 Million U benzathin penicillin G, if penicillin allergic, doxycycline 100 mg orally twice daily for 2 weeks.

• **Late syphilis:**

IM injection of 2.4 MU benzathin penicillin G once a week for 3 weeks, if penicillin allergic, doxycycline 100 mg orally twice daily for one month.

• **Congenital syphilis:**

Crystalline penicillin G 200 000 U/Kg/d IV or 50 000 U/6h IM for 10-14 days.

• Sexual partner(s) should be treated.

• No proven alternatives to penicillin are available for treating:

**1.** Neurosyphilis.

**2.** Congenital syphilis.

**3.** HIV infected patient.

**4.** Pregnant patient.

These patients should be skin tested and desensitized if the test is positive.

• **Jarisch-Herxheimer Reaction:** a complex allergic response to antigens released from dead microorganism can complicate the treatment of syphilis. A transient acute febrile reaction with head ache and myalgia may develop within 24 hours of therapy. It occurs in of **50%** of patients with early syphilis.

**Follow Up:**

All patients should be followed after treatment, this done by clinical examination and by measuring the VDRL titer (a 4 fold decrease in titer suspected after 6 months of therapy), as follows:

• **Early syphilis:**

1. Every 3 months in the 1st year.
2. Every 6 months in the 2nd year.
3. Yearly thereafter.

• **Late syphilis:** yearly.

• **Neurosyphilis:** every 6 months by measuring the blood and CSF level.

**Signs of Relapse:**

1. Clinical.
2. Serological (4 fold increase).
3. Transplacental infection.
4. Infection of the partner.

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**Chancroid**

It is a common and endemic in many of the world's poorest regions such as areas of Africa, and Asia, but it is rare in Iraq. It is caused by *haemophilus ducreyi* which is short gram negative bacillus.

**Clinical Features:**

In reverse to chancre, the ulcer of chancroid is painful, tender, deep, soft, bleed easily with purulent base, with short IP (3-5 days). Multiple ulcers appear on the genitalia from autoinoculation (highly infectious ulcer).

Usually heal with scarring after months.

Unilateral or bilateral painful inguinal lymphadenopathy (which may matted together) develops in about 50% of patients.

**Investigation:**

Smear: the gram negative bacilli are usually found in small clusters or parallel chains of two or three organisms (the "school-of-fish" pattern).

Culture: using modified Muller-Hinton agar.

**Treatment:**

Single dose of azithromycin 1 gm orally, or cefriaxone 250 mg IM; or erythromycin 500 mg orally four times daily for 7 days.

**Lymphogranuloma Venereum (LGV)**

It is a rare STI, caused by *chlamydia trachomitis*, characterized by transient small ulcer on the genital area followed in one to two months by painful swelling of inguinal and perirectal LN, which is often accompanied by mild constitutional symptoms. The inguinal ligament often forms a cleft between the enlarged inguinal LN "groove sign". Early treatment with doxycycline is curable.

**Granuloma Inguinale (Donovanosis)**

It is a rare STI, caused by *klebsiella granulomatis* (gram-negative bacillus), characterized by intracellular inclusions in macrophages referred to as Donovan bodies. It usually affects the skin and mucous membranes in the genital region, results in nodular lesions that evolve into ulcers. This disease is treated by azithromycine, doxycycline, or metheprim.

"Best Regards"

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