The causative factor of syphilis is Treponema pallidum (TP), family motile Spirochaetaceae, which is very common all over the world. TP can be transmitted via close sexual contact or transplacentally (vertical way). Also, syphilis can be acquired or congenital, both of them having early and late stages. TP invades the host body through the breaches in the squamous or columnar epithelium affecting lymphatic nodes and disseminates with the blood stream to all parts of the body.

Definition and Background of Syphilis

Syphilis is a chronic systematic disease which is easily treated in its early stages, but neglected cases very often lead to grave consequences and death consequently. Treponema pallidum is the causative factor of syphilis described in 1905-1910 by Schaudinn and Hoffman; Wasserman described the blood test for long-term forms of infection.

The first outbreak of the illness was described in 1495 when French soldiers invaded Naples and came down with a deadly disease, which they called “great pox”; the whole Europe was devastated with the sickness with incidences of thousands of death.

During the First World War, syphilis had become a serious reason for the disability and absence from duty in the US Army, over 10,000 men were discharged, and 7 million lost
person-days.

This illness has changed names over time: “French disease”, “Spanish fever” so forth. At the beginning there wasn’t any efficient treatment for syphilis. For this reason, sporadic epidemic outbreaks occurred in different corners of the world.

**Mercury** was administered by the Esculaps of early medicine as the remedy against this infection; however, this chemical element appeared to be very toxic and became the reason of severe consequences or even death.

**Etiology of Syphilis**

Pathogenic treponemes are associated with the following 4 diseases:

- Venereal syphilis, caused by T. pallidum pallidum
- Yaws, caused by T. pallidum pertenue
- Endemic syphilis (bejel), caused by T. pallidum endemicum
- Pinta, caused by T. carateum

**Ways of transmission**

- Sexual contact
- Transplacental/congenital syphilis (vertical way, 50-80% of neonates are exposed to the infection)
- Contact with contaminated blood (while transfusion) and tissues
- Personal contact is a very rare way.

**Types of syphilis**

- Acquired
- Congenital

**Epidemiology of Syphilis**

**United States**

CDC analyzed data obtained from the National Notifiable Diseases Surveillance System (NNDSS), for cases of primary and secondary syphilis diagnosed during 2005-2013 among homosexual, bisexual and other men having sex with men (MSM), the figure accounted for 5.3 cases in 100,000 of population, which is twice as many as it was in the period between 2005 and 2013 (2.9).

The highest prevalence was in Western regions. Among Hispanics (53.4%, from 1,291 in 2009 to 1,980 in 2012) and whites (38.1%, 2,449 to 3,381), when compared with blacks (21.2%, 2,267 to 2,747). By age group, the greatest percentage increases occurred among MSM aged 25–29 (53.2%, 1,073 to 1,644). Nonwhite women tend to contract syphilis more than white females (13.3 times to 4 times accordingly).

**International**

In the developing world and sub-Saharan Africa as well as in Venezuela, syphilis has become a major public health problem; this illness has no racial predilection, however **socioeconomic factors** play a pivotal role in the spread of the disease. The
highest incidence of Syphilis is observed in South and Southeast Asia, then in Sub-Saharan Africa and third highest in Latin America and Caribbean.

Sex: Men are prone to contract syphilis more frequently than women. Also, syphilis has a strong affiliation with HIV infection, in drug users and those who tend to practice promiscuity in their sexual contacts.

Age: adolescents and young adults are at risk of infection with TP due to their reckless attitude towards sex and drugs.

**Clinical Presentation of Syphilis**

**History**

It is vital to collect the whole history of a particular patient in order to determine or assume the stage of the disease: **thorough sexual and social history**, including the number of sexual partners, condom use, history of STDs in the patient and their partners, intravenous (IV) drug use, and exposure to blood products.

![Image: “Primary stage syphilis sore (chancre) on the surface of a tongue.” by Centers for Disease Control and Prevention (CDC) – http://www.cdc.gov/std/syphilis/images.htm#. License: Public Domain](image)

**Physical examination**

**Primary** (10-90 days after exposure to the pathogen)

- Hard chancre on genitals
- Painless regional lymphadenopathy

**Secondary** (4-10 weeks after the first manifestation)

- General: fever, fatigue, pain in joints, sore throat, headache, anorexia, neck stiffness and polylymphadenopaty.
- Skin: red or brown maculopapular non-itchy rash
- Mucosa: patches, “snail track” ulcers on the place of TP penetration.

**Late stages** (tertiary) occur if there is inappropriate treatment or late administration of the medicines and progresses to tertiary syphilis.
- Late benign: gummas (bone and viscera)
- **Heart** and vessels: affected aorta (inflammation of the wall and regurgitation)
- **Neurosyphilis**: meningovascular lesion, paralysis of the insane and tabes dorsalis

If without treatment, symptoms and signs adate over 3-12 weeks, in 20% may recur in early latency period (2 years)

**Congenital syphilis**

- Stillbirth or retardation of physical and mental development
- "Snuffles" nasal infection
- Appearance of skin like in secondary syphilis

Late stages become apparent after 2 years age.
“Stigmata”: abnormalities of long bones, sabre tibia
- Hutchinson’s teeth
- Eyes problems: keratitis, uveitis, facial gummas
- CNS disease

Differential Diagnosis of Syphilis

- Chancroid
- Condyloma acuminata
- Cystitis in females
- Dermatologic manifestations of herpes simplex
- Drug eruptions
- Genital warts in emergency medicine
- Granuloma inguinale (donovanosis)
- Herpes zoster
- HIV disease
- Lymphogranuloma venereum
- Urethritis
- Urinary tract infection in males
- Urinary tract infections in pregnancy.
- Varicella-zoster virus
- Yaws

Diagnosis of Syphilis

Laboratory studies

<table>
<thead>
<tr>
<th>Stages</th>
<th>Length of exposure to bacterium</th>
<th>Primary syphilis</th>
<th>Secondary syphilis (skin symptoms)</th>
<th>Tertiary syphilis (neurological problems)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time after contact with infected person</td>
<td>Day 1</td>
<td>10 to 90 days</td>
<td>6 weeks to 6 months</td>
<td>10 to 30 years</td>
</tr>
</tbody>
</table>

**Antibody tests**

  - Highly informative (sensitive); nontreponemal antibodies are not found after 3 years adequate treatment.
  - Same as primary stage
  - VDRL is performed on CSF and administered in the diagnostics of neurosyphilis.

  - Specific; followed by nontreponemal antibody test in order to determine active and past infection.
  - Same as primary stage
  - The CSF FTA-ABS is used for diagnostics of neurosyphilis.

**Direct detection tests** (much less common):
<table>
<thead>
<tr>
<th>Microscopic exam, Darkfield exam: a sample taken from the chancre is studied in a special microscopic examination</th>
<th>Detection of the bacteria in the biomaterial</th>
<th>N/a</th>
<th>N/a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymerase chain reaction (PCR)</td>
<td>Detection of the bacteria in the biomaterial</td>
<td>Genetic material in blood</td>
<td>Detects genetic material in blood and/or CSF sample</td>
</tr>
</tbody>
</table>

Imaging studies
- CT as well as MRI detect numerous infarcts in the brain tissue in neurosyphilis.
- X-ray examination is informative when there is severe lesion of the bones suspected.

Staging of Syphilis

**Acquired**
- Primary syphilis
- Secondary syphilis
- Late (tertiary) stage
- Quaternary syphilis (nowadays extremely rare case owing to appropriate medication and diagnostics)

**Congenital**
- Early stages
- Late stages

Management of Syphilis

**Pharmacotherapy**

<table>
<thead>
<tr>
<th>Stages</th>
<th>First-line treatment</th>
<th>Alternative treatment</th>
<th>Treatment options for pregnant patients</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary, secondary, or early syphilis</td>
<td>Intramuscular benzathine penicillin G 2.4×10^6 U as single dose</td>
<td>Single 2 g dose of azithromycin (second choice treatment), Azithromycin contraindicated for homosexual male partners and in pregnancy. Ceftriaxone 1 g daily for 10 days.</td>
<td>According to CDC, pregnant women with a history of allergy should be desensitized and still get penicillin because erythromycin can’t pass the placenta and is not effective.</td>
<td>3, 6, 9, 12 and 24 months</td>
</tr>
</tbody>
</table>
Neurosyphilis

Intravenous aqueous penicillin G 4×10⁶ U q4 hours or continuous infusion for 10-14 days

Procaine penicillin G 2.4×10⁶ U daily with oral probenecid 500 mg q.i.d. for 10-14 days. Another option is ceftriaxone 2 g IM or IV daily for 10-14 days.

Congenital syphilis

Neonates with normal CSF: intramuscular benzathine penicillin G 50,000 U/kg in a single dose. Neonates with abnormal CSF and babies with CNS involvement: intramuscular aqueous procaine penicillin G 50,000 U/kg/day for 10 days.

3, 6, 9, 12 and 24 months

Surgical intervention

It is not required for the direct treatment unless there are severe complications which lead to the secondary infection of the skin and bone lesions and tertiary syphilis.

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