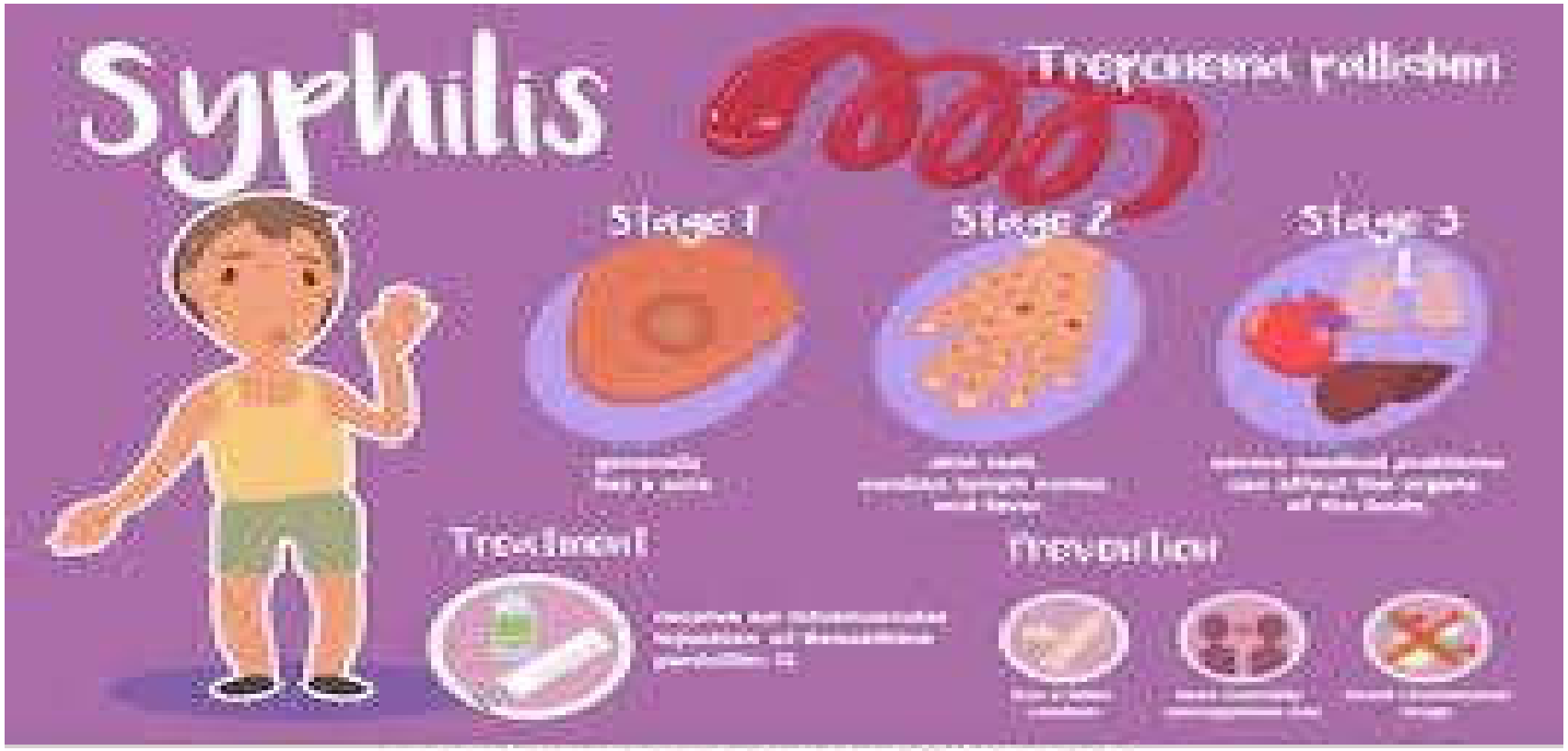
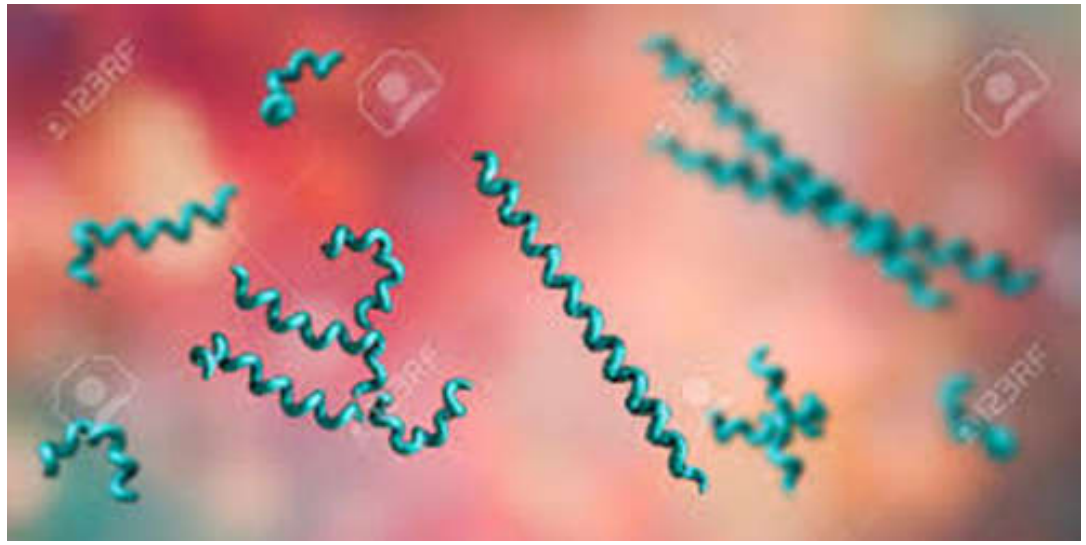
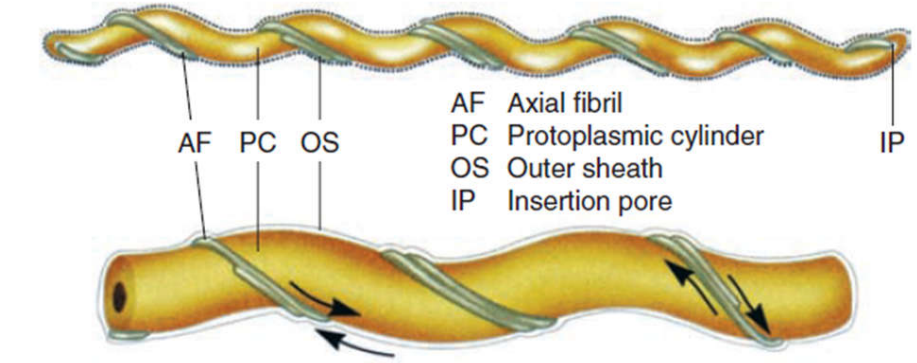
Genito-Urinary System

Syphilis



- Spirochetes are bacteria with a spiral morphology
  - Small, motile, gram –ve, slender, helically coiled, flexible
  - Intracellular flagella(endoflagella)



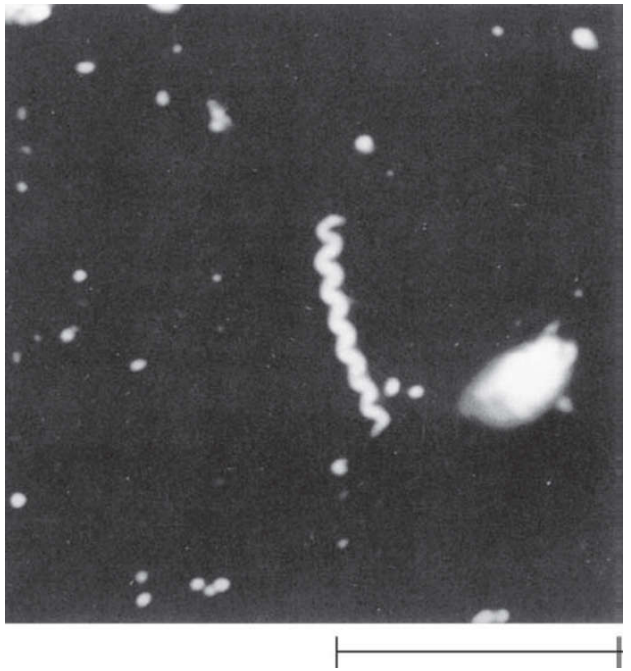


(A1)

(A2)

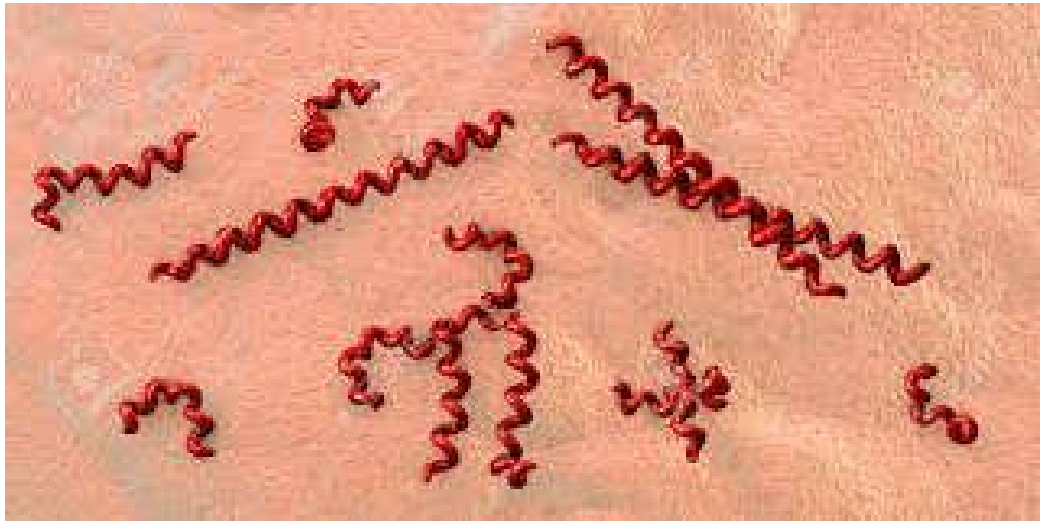
- Syphilis
  - Treponema pallidum subspecies pallidum
- yaws
  - treponema pallidum pertenue
- Lyme disease
  - Borrelia bacterium

- Many spirochetes are difficult to see by routine microscopy.
  - Gram negative, many either take stains poorly or are too thin (0.15 µm or less) to fall within the resolving power of the light microscope.
- Only darkfield microscopy, immunofluorescence, or special staining techniques can demonstrate these spirochetes.



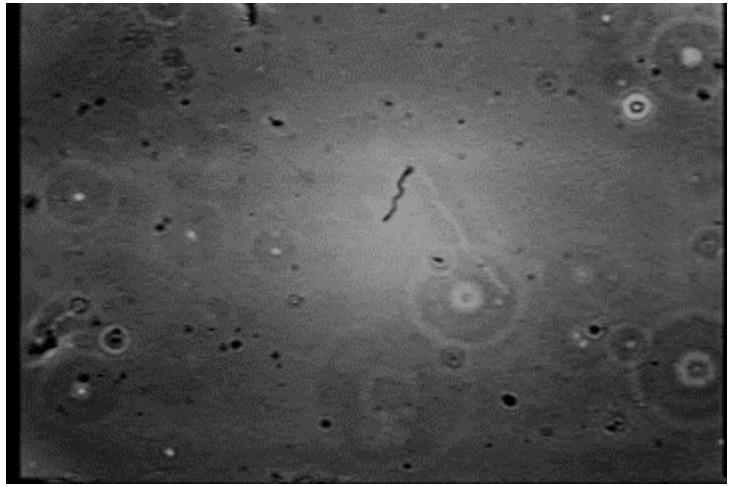
Treponema pallidum

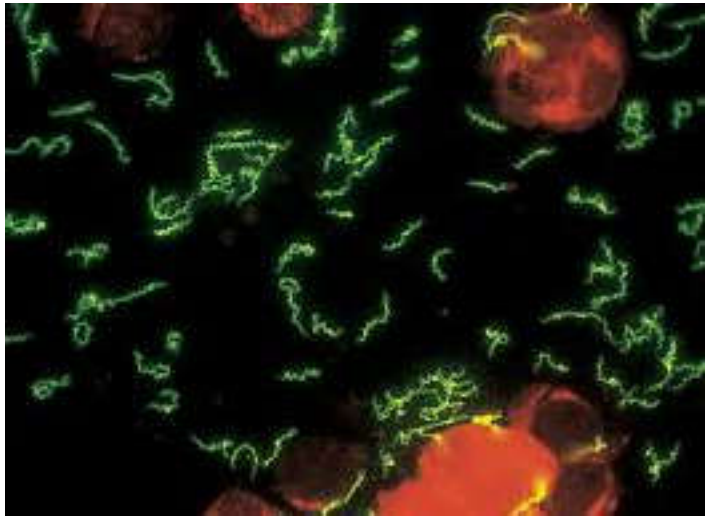
- *T. pallidum* is the causative agent of syphilis, a venereal disease first recognized in the 16th century.
- *T. pallidum* is a slim (0.15 µm) spirochete 5-15 µm long with regular spirals that resemble corkscrews .

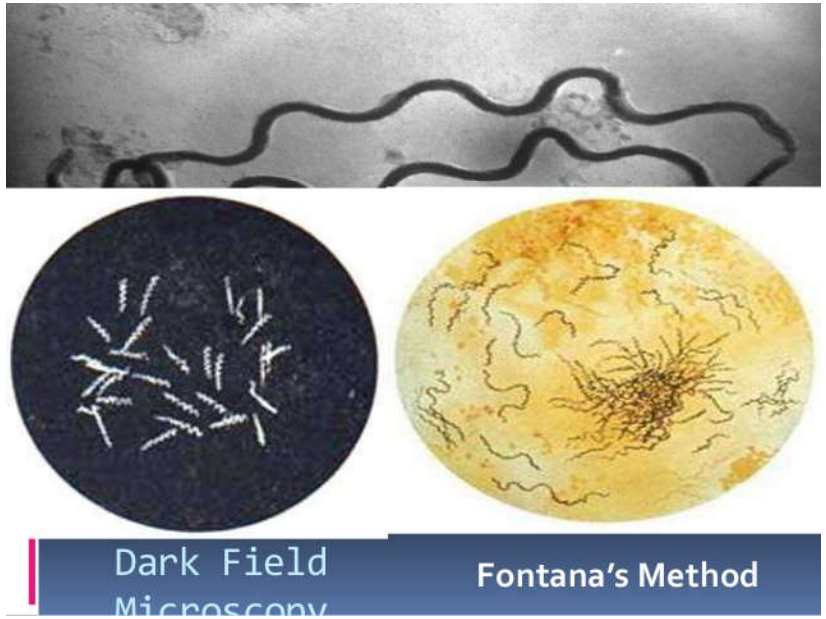


Treponema pallidum

- It is readily seen only by immunofluorescence, darkfield microscopy, or silver impregnation histologic techniques.
- Live *T. pallidum* cells show characteristic slow, rotating motility with sudden 90-degree angle flexion.







- inability to grow the organism in culture.
- It multiplies for only a few generations in cell cultures and is difficult to subculture.
  - cultured mammalian cells.
- Small genome
- Few structures or product
- The sluggish growth (mean generation time more than 30 hours)
- lacks lipopolysaccaride (LPS) and contains few proteins.

- extremely susceptible to any deviation from physiologic conditions.
- It dies rapidly on drying
- is readily killed by a wide range of detergents and disinfectants.
- The lethal effect of even modest elevations of temperature (41° to 42°C) was the basis of fever therapy early in the last century.

EPIDEMIOLOGY

- Treponema pallidum is an exclusively human pathogen
- Infection is acquired from direct sexual contact with a person who has an active primary or secondary syphilitic lesion

- Less commonly,
  - Non-genital contact with a lesion (e.g., of the lip),
  - sharing of needles by intravenous drug users,
  - transplacental transmission to the fetus within approximately the first 3 years of the maternal infection.
- Late disease is not infectious.
- Syphilis remains a major public health problem, with12 million new cases annually.

Sex

Genital ulcer
(lesion at the point of entry)

weeks later

Secondary syphilis

Generalized
maculopapular rash

years to decades

Tertiary syphilis

Focal lesions

Sex

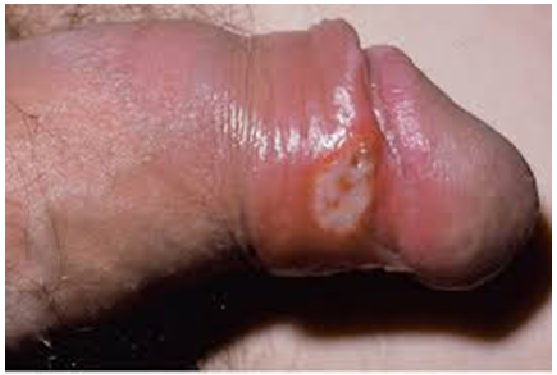
3 weeks (3 to 90d)

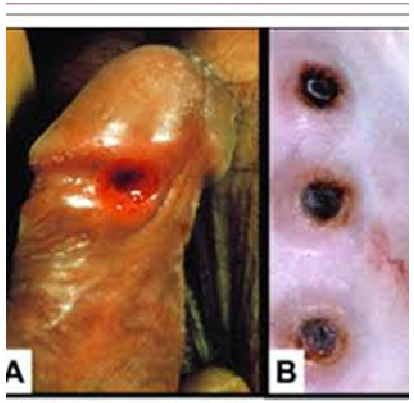
The primary syphilitic lesion

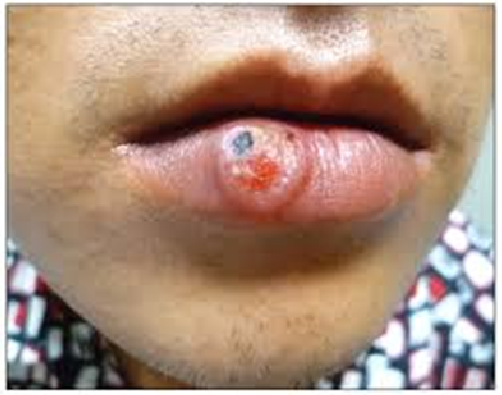
Genital ulcer
(lesion at the point of entry)

Papule…ulcer,,,,indurated and ulcerates but remains painless (chancre).

- heals spontaneously after 4 to 6 weeks.
- Firm, nonsuppurative, painless enlargement of the regional lymph nodes
  - 1 week of the primary lesion and may persist for months.







Primary Syphilis

Sex

Genital ulcer
(lesion at the point of entry)

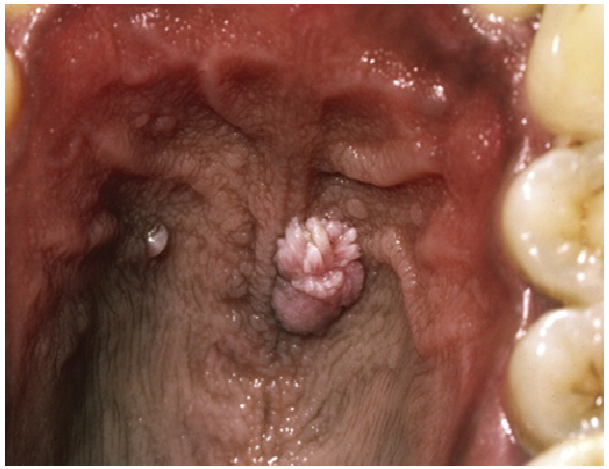
2 to 8 weeks after the chancre

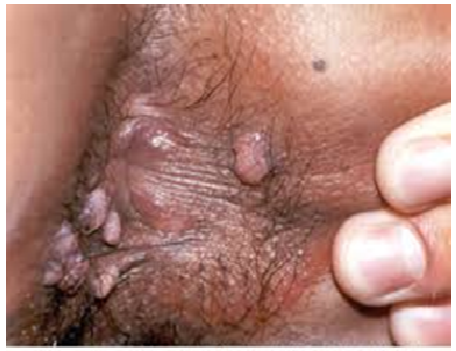
Secondary syphilis

Generalized maculopapular rash

About 1/3 of patients condylomata lata,

- painless mucosal warty erosions
- usually develop in warm, moist sites such as the genitals and perineum.





Source: Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow: Current Medical Diagnosis and Treatment 2020
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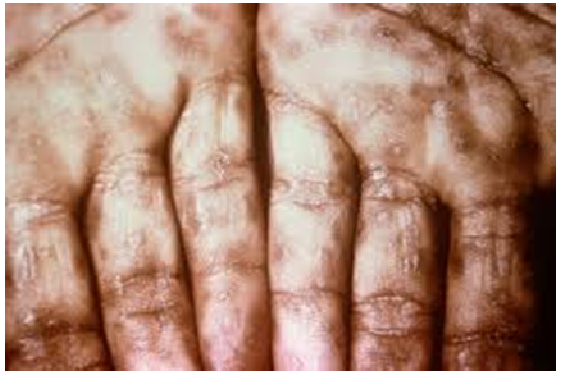
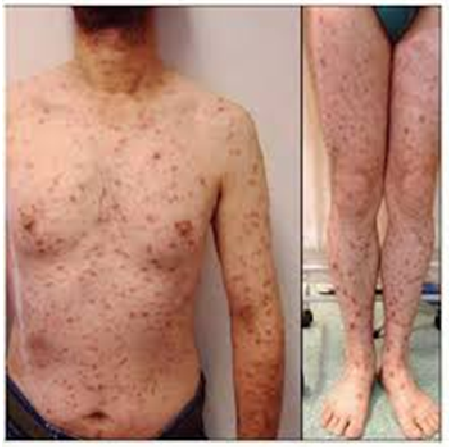
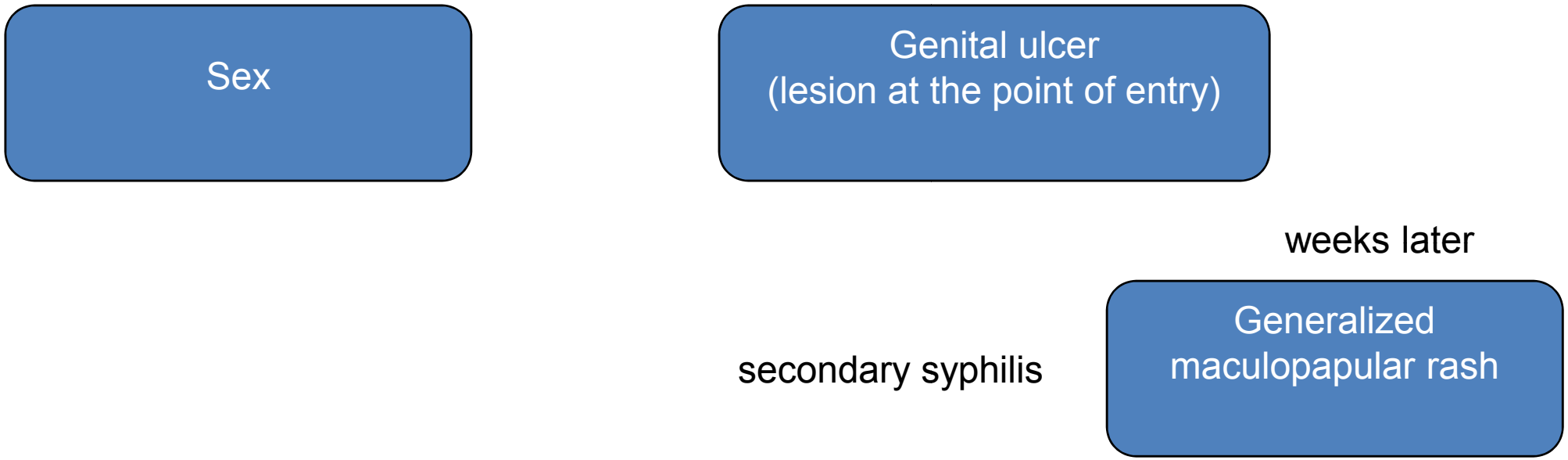
- Symmetric non itchy muco -cutaneous maculopapular rash
- generalized non-tender lymph node enlargement
- fever and malaise.
- Skin lesions are distributed on the trunk and extremities, often including the palms, soles, and face.





All the lesions are highly infectious



1/3: They resolve spontaneously after a few days to many weeks,
2/3: The illness enters the latent state

Latent Syphilis

- It is by definition a stage where there are no clinical manifestations but continuing infection is evidenced by serologic tests.
- In the first few years latency (early phase) may be interrupted by progressively less severe relapses of secondary syphilis.

Latent Syphilis

- In late latent syphilis (>4 years) relapses cease.
- Transmission is possible from relapsing secondary lesions by transfusion or other contact with blood.
- Mothers throughout latency may transmit it to their fetus.
- About one third of untreated cases do not progress beyond this stage.

Tertiary Syphilis

- Another one third of patients with untreated syphilis develop tertiary syphilis.
- The manifestations may appear as early as 5 years after infection but characteristically occur after 15 to 20 years.

- The inflammatory response to immune complexes, spirochetal lipoproteins, and complement in arteriolar walls accounts for some of the injury in syphilitic lesions.
- The granulomatous nature of the lesions (Gumma) in late syphilis is consistent with injury caused by delayed-type hypersensitivity responses prolonged by persistence of the spirochetes.
- In all of this, no toxins, virulence factors, or other molecules can yet be linked with specific features of syphilis.

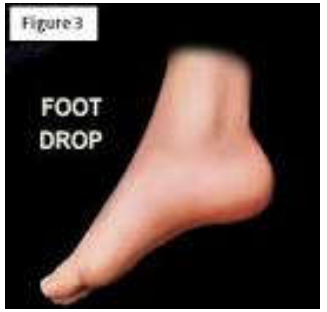
Tertiary Syphilis

- The manifestations depend on the body sites involved the most important of which are the **nervous** and **cardiovascular** systems.

Tertiary Syphilis

- **Neurosyphilis**
  - Neurosyphilis is due to the damage produced by a mixture of meningovasculitis and degenerative parenchymal changes in virtually any part of the nervous system.

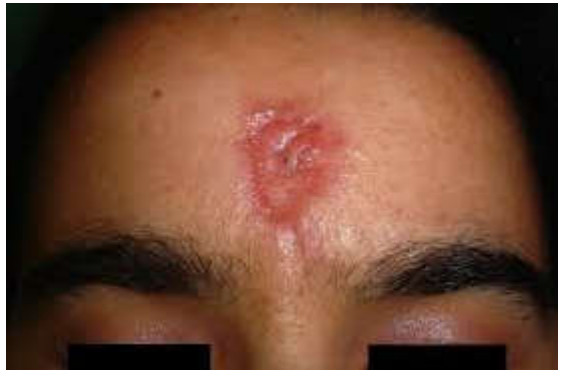
- Cortical degeneration of the brain
  - mental changes ranging from decreased memory to hallucinations or frank psychosis.
- In the spinal cord demyelination of the posterior columns, dorsal roots, and dorsal root ganglia produces a syndrome called **tabes dorsalis**
  - which includes ataxia, wide-based gait, foot slap, and loss of the sensation.



- The most advanced CNS findings include a combination of neurologic deficits and behavioral disturbances called **paresis.**
  - (personality, affect, reflexes, eyes, sensorium, intellect, speech

- **Cardiovascular syphilis**
  - arteritis involving the vasa vasorum of the aorta
  - dilatation of the aorta and aortic valve ring leading to aneurysms of the ascending and transverse segments of the aorta and/or aortic valve incompetence.

- A localized, granulomatous reaction to *T. pallidum* infection called a **gumma** may be found in skin, bones, joints, or other organ.
- Any clinical manifestations are related to the local destruction as with other mass-producing lesions, such as tumors.

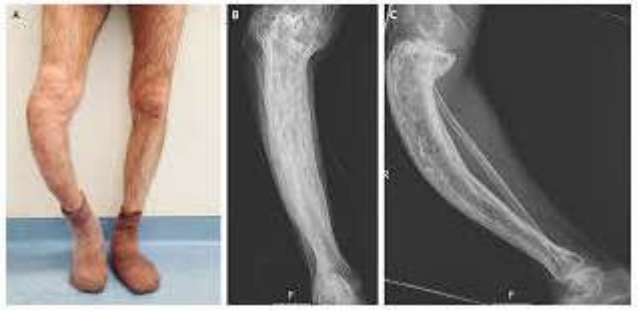


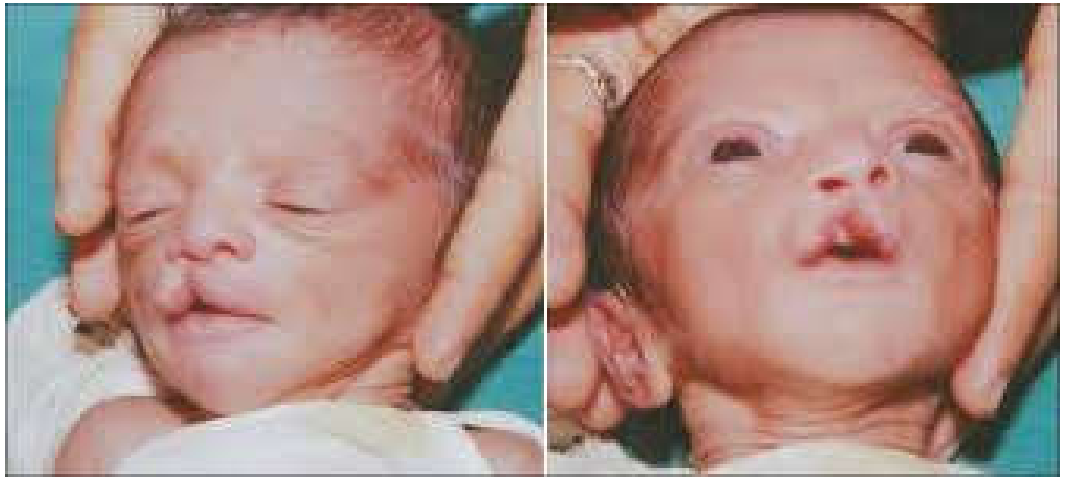
Congenital Syphilis

- Fetuses are susceptible to syphilis only after the fourth month of gestation.
- Routine serologic testing is performed in early pregnancy and should be repeated in the last trimester in women at high risk of acquiring syphilis.
- Untreated maternal infection may result in fetal loss or congenital syphilis.

Congenital Syphilis

- Bone involvement produces characteristic changes in the architecture of the entire skeletal system (**saddle nose, saber shins, Hutchinson teeth, hearing loos**). Anemia, thrombocytopenia, and liver failure are terminal events.





DIAGNOSIS

Microscopy

- *T. pallidum* in primary and secondary lesions can be seen by darkfield microscopy.
  - It requires experience and fluid from deep.
  - A negative test does not exclude syphilis.
- Darkfield microscopy of oral and anal lesions is not recommended
  - because of the risk of misinterpretation of other spirochetes present in the normal flora.

DIAGNOSIS

Microscopy

- Direct fluorescent antibody methods have been developed but are available only in certain centers.

Serologic Tests

- Most cases of syphilis are diagnosed serologically using serologic tests that detect antibodies directed at either lipid or specific treponemal antigens.
- The former are called non-treponemal tests, and the latter are referred to as treponemal tests.
- Their use in screening, diagnosis, and therapeutic evaluation of syphilis has been refined over many decades.

Non-treponemal tests	Treponemal tests
• Antibody directed against cardiolipin (lipid complex) (reagin)	• antibody specific to T. pallidum
• Rapid plasma regain • Venereal Disease Research Laboratory (VDRL)	• Fluorescent treponemal antibody (FTA-ABS) • T pallidum hem-agglutination (TPHA) • the microhem-agglutination test for T. pallidum (MHA-TP).
• Nonspecific*	• Specific
• Sensitivity and low cost :preferred for screening ○ if positive, they must be confirmed by one of the more specific treponemal tests	• not useful for screening ○ Positive result confirms RPR and VDRL
• following treatment	• They are not useful for following therapy (once positive, they usually remain so for life)
▪ With successful antibiotic therapy nontreponemal serologies slowly revert to negative.	• The treponemal IgM tests are useful in establishing the presence of an acute infection in infants (congenital syphilis

- *in a variety of auto-immune diseases or in diseases involving substantial tissue or liver destruction, such as lupus erythematosus, viral hepatitis, infectious mononucleosis, and malaria.
- False-positive results can also occur occasionally in pregnancy and in patients with HIV infection

TREATMENT AND PREVENTION

- *T. pallidum* remains exquisitely sensitive to **penicillin**, which is the preferred treatment in all stages.
- In primary, secondary, or latent syphilis persons hypersensitive to penicillin may be treated with **tetracyclines**, **erythromycin**, or **cephalosporins.**

TREATMENT AND PREVENTION

- In penicillin-hypersensitive patients with neurosyphilis or congenital syphilis be **desensitized** rather than use an alternate antimicrobial.
- Safe sex practices are as effective for syphilis prevention.
- No vaccine is available so far.