

# Spirochaetes

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# Spirochaetes

- Elongated, motile, flexible bacteria twisted spirally along the long axis are termed as Spirochetes
- Speira meaning coil and chaite meaning hair.

# Classification



## Spirochaetales (Order)

Spirochaetaceae

Leptospiaceae

Spirochaeta

Cristispira

Borrelia Treponema

Leptospira

# Spirochaetales *Associated* *Human Diseases*

<u>Genus</u>	<u>Species</u>	<u>Disease</u>
<i>Treponema</i>	<i>pallidum</i> ssp. <i>pallidum</i>	Syphilis
	<i>pallidum</i> ssp. <i>endemicum</i>	Bejel
	<i>pallidum</i> ssp. <i>pertenue</i>	Yaws
	<i>carateum</i>	Pinta
<i>Borrelia</i>	<i>burgdorferi</i>	Lyme disease (borreliosis)
	<i>recurrentis</i>	Epidemic relapsing fever
	Many species	Endemic relapsing fever
<i>Leptospira</i>	<i>interrogans</i>	Leptospirosis (Weil's Disease)

# Treponema

- Trepos meaning turn and nema meaning thread.
- Treponemes are short, slender spiral organism having pointed or rounded ends.
- Cause following diseases in human beings.  
Venereal syphilis : *T. pallidum*  
Endemic syphilis : *T. endemicum*  
Yaws : *T. pertenue*  
Pinta : *T. carateum*

# Treponema pallidum

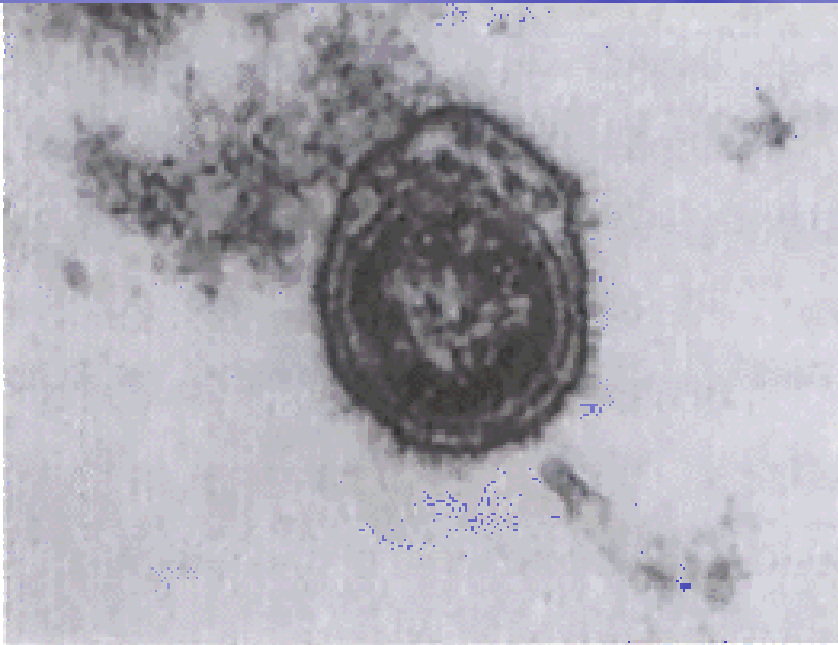
- Causative agent of syphilis, discovered by Schaudin and Hoffmann(1905).

## Morphology :

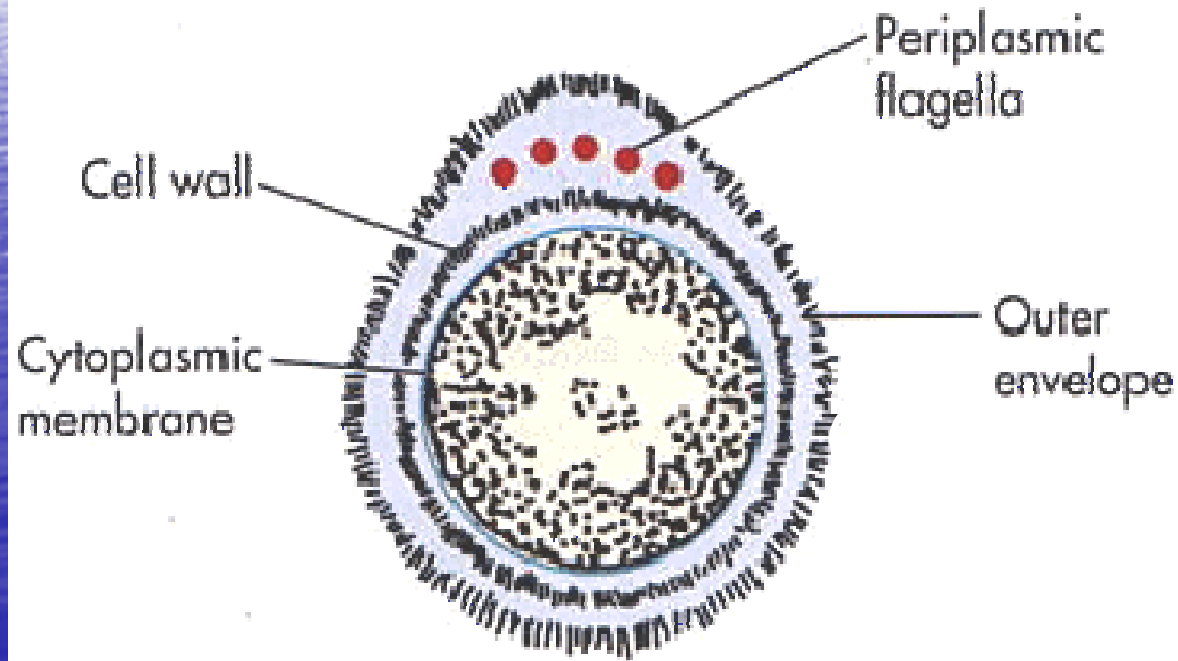
thin, delicate, spirochete with tapering ends, measuring 4 – 14  $\mu\text{m}$  long and 0.1-0.2 $\mu\text{m}$  wide. It has about 10 regular sharp coils.

The length of the coil is about 1 $\mu\text{m}$ .

- It is actively motile, exhibiting rotation around the long axis, backward and forward movements, and flexion of the whole body.
- Ultrastructurally , the cytoplasm is surrounded by a trilaminar cytoplasmic membrane, enclosed by a cell wall containing peptidoglycan which gives the cell rigidity & shape.



# *Cross-Section of Spirochete with Periplasmic Flagellas*





- External to this is the lipid rich outer membrane layer.
- Originating from each end of the cell, three or four endoflagella wind round the axis of the cell in the space between the cell wall and outer membrane layer.
- These endoflagella do not protrude outside & remain within the outer membrane layer. This endoflagella presumed to be responsible for motility although there is no direct evidence for this.

- T pallidum can not be seen under the light microscope but can be made out by

- Negative staining by India ink

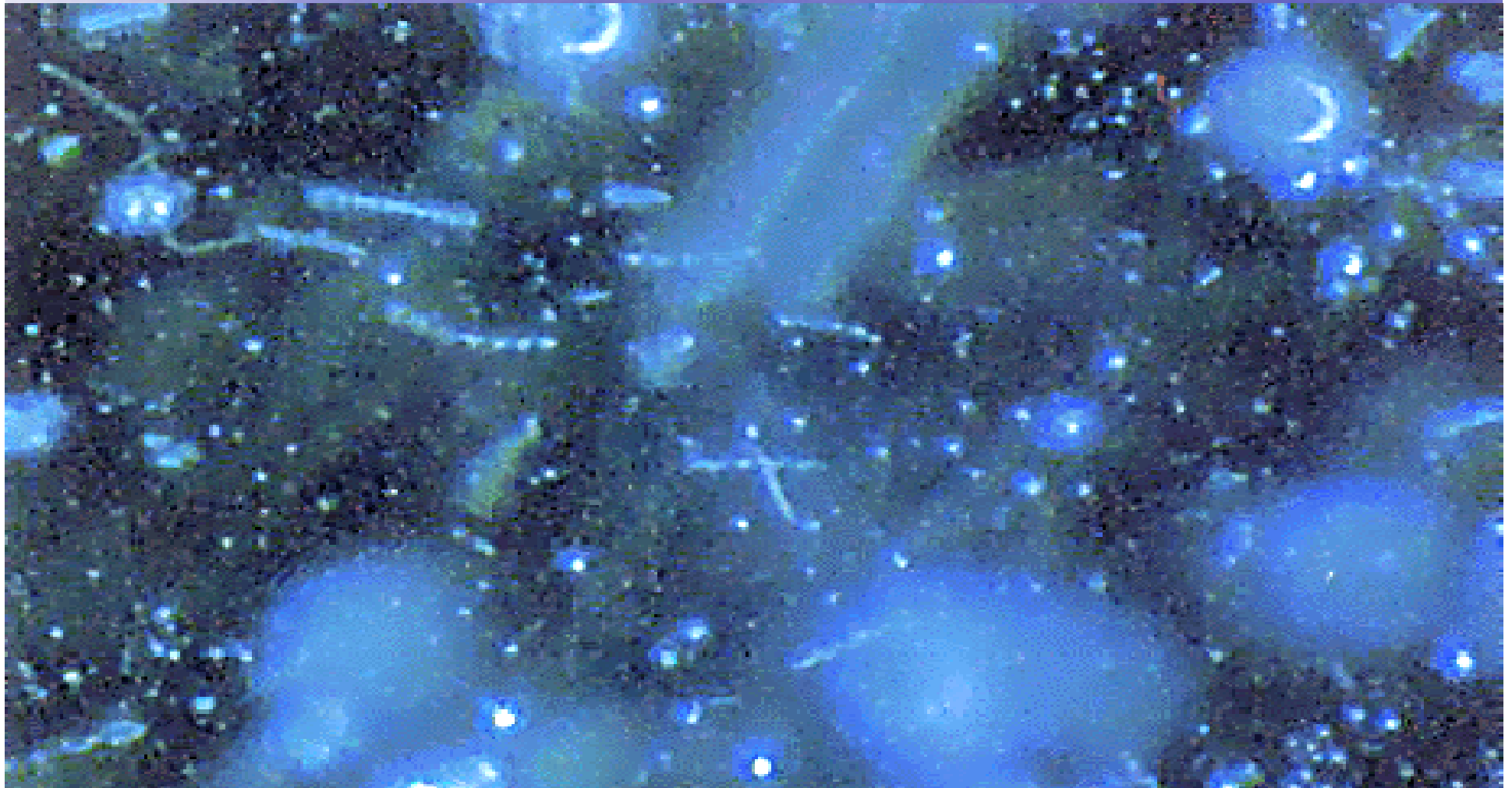
Dark ground illumination

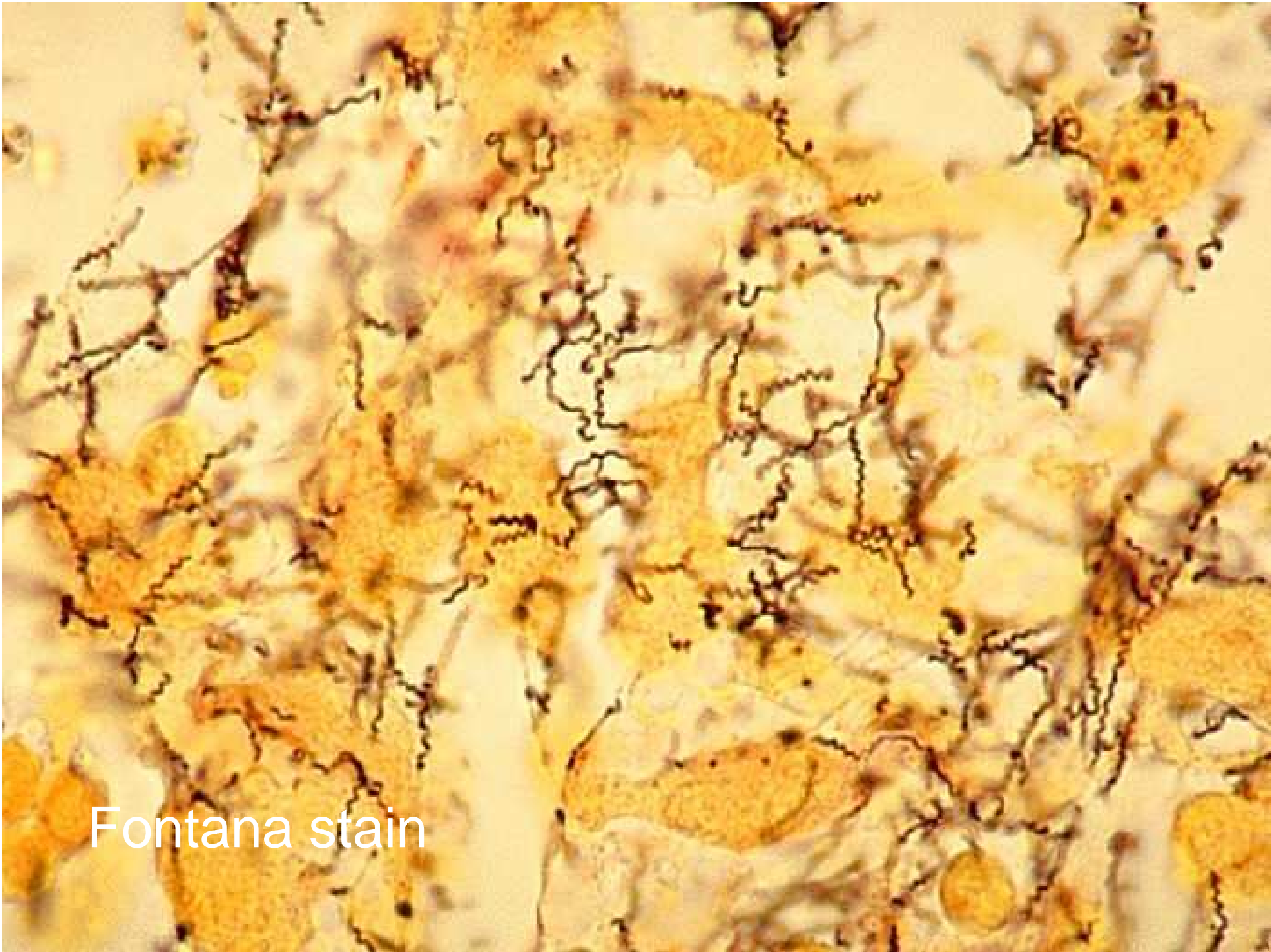
Silver impregnation methods

Fontana method for films

Levaditi method for tissue sections.

# *Microscopic Examination of Treponema pallidum*





Fontana stain

# Cultivation

- Pathogenic treponemes do not grow in artificial culture media.
- Nonpathogenic treponemes Reiter strain grows well in thioglycollate medium .
- *T. pallidum* can be maintained in motile & virulent form in complex media under anaerobic condition.
- Virulent *T. pallidum* ( Nichole's strain ) have been maintained for many decades by serial testicular passage in rabbits.

# Resistance

- Very delicate, being readily inactivated by drying or heat.
- Killed in 1 – 3 days at 0 - 4°C.
- Inactivated by contact with oxygen, distilled water, soap, antibiotics.

# Antigenic Structure

- Complex
- Induces three types of antibodies
- Reagin antibodies- cardioliipid antigen
- Group antigen
- Species specific polysaccharide antigen

# *Pathogenesis of Syphilis*

- **Tissue destruction and lesions are primarily a consequence of patient's immune response**
- **Syphilis is a disease of blood vessels and of the perivascular areas**
- **In spite of a vigorous host immune response the organisms are capable of persisting for decades**
  - Infection is **neither fully controlled nor eradicated**
  - In **early stages**, there is an inhibition of cell-mediated immunity
  - Inhibition of CMI abates in **late stages** of disease, hence late lesions tend to be localized



## ***Pathogenesis (cont.)***

### ***Primary Syphilis***

- Primary disease process involves **invasion of mucus membranes, rapid multiplication & wide dissemination** through perivascular lymphatics and systemic circulation
  - Occurs **prior to development of the primary lesion**
- 10-90 days (usually 3-4 weeks) after initial contact the host mounts an **inflammatory response at the site of inoculation** resulting in the hallmark syphilitic lesion, called the **chancre (usually painless)**
  - Chancre changes from hard to ulcerative with profuse **shedding of spirochetes**
  - Swelling of capillary walls & regional lymph nodes w/ draining
  - Primary lesion heals spontaneously by fibrotic walling-off within two months, leading to false sense of relief

# Primary Syphilis: Signs and Symptoms

- Painless ulcerative lesion on genitals lips, tongue, pharynx
- Regional lymphadenopathy



Ulceration on penis

# *Pathogenesis (cont.)*

## *Secondary Syphilis*

- Secondary disease 2-6 months after primary lesion
- Widely disseminated **mucocutaneous rash**
- **Secondary lesions** of the skin and mucus membranes are **highly contagious**
- Generalized immunological response



***Generalized  
Mucocutaneous  
Rash of  
Secondary  
Syphilis***

# *Pathogenesis* (cont.)

## *Latent Stage Syphilis*

- Following secondary disease, host enters latent period
  - First 4 years = **early latent**
  - Subsequent period = **late latent**
- **About 40% of late latent patients progress to late tertiary syphilitic disease**

## *Pathogenesis (cont.)*

### *Tertiary Syphilis*

- Tertiary syphilis characterized by **localized granulomatous dermal lesions (gummas)** in which few organisms are present
  - Granulomas reflect containment by the immunologic reaction of the host to chronic infection
- Late **neurosyphilis** develops in about 1/6 untreated cases, usually more than 5 years after initial infection
  - Central nervous system and spinal cord involvement
  - Dementia, seizures, wasting, etc.
- **Cardiovascular** involvement appears 10-40 years after initial infection with resulting myocardial insufficiency and death

# *Pathogenesis (cont.)*

## *Congenital Syphilis*

- Congenital syphilis results from **transplacental infection**
- *T. pallidum* **septicemia in the developing fetus and widespread dissemination**
- **Abortion, neonatal mortality, and late mental or physical problems** resulting from scars from the active disease and progression of the active disease state

# Laboratory diagnosis

Diagnostic Test	Method or Examination
Microscopy	Darkfield Direct fluorescent antibody staining
Culture	Not available
Serology	Nontreponemal tests Venereal Disease Research Laboratory (VDRL) Rapid plasma reagin (RPR) Treponemal tests Fluorescent treponemal antibody absorption (FTA-ABS) Microhemagglutination test for <i>Treponema pallidum</i> (MHA-TP)



# Direct Demonstration

- Dark-ground Microscopy
- Stained preparation
- Tissue biopsy
- PCR

# Serological Reaction

- Standard test for syphilis (Non treponemal test)
- Nonspecific
- Cardiolipin antigen
- Wasserman test :
- Kahn test :
- VDRL test
- RPR test
- TRUST
- EIA

- Advantage of RPR test over VDRL
    - 1) Commercially available ready to use kit
    - 2) Unheated serum is tested
    - 3) Reaction can be read visually
    - 4) Either plasma or serum can be used
- \*Disadvantage : can not be used with CSF

- Disadvantage of nonspecific test:
- Biological false positive: occur in about 1% of normal serum.

1) Acute reaction

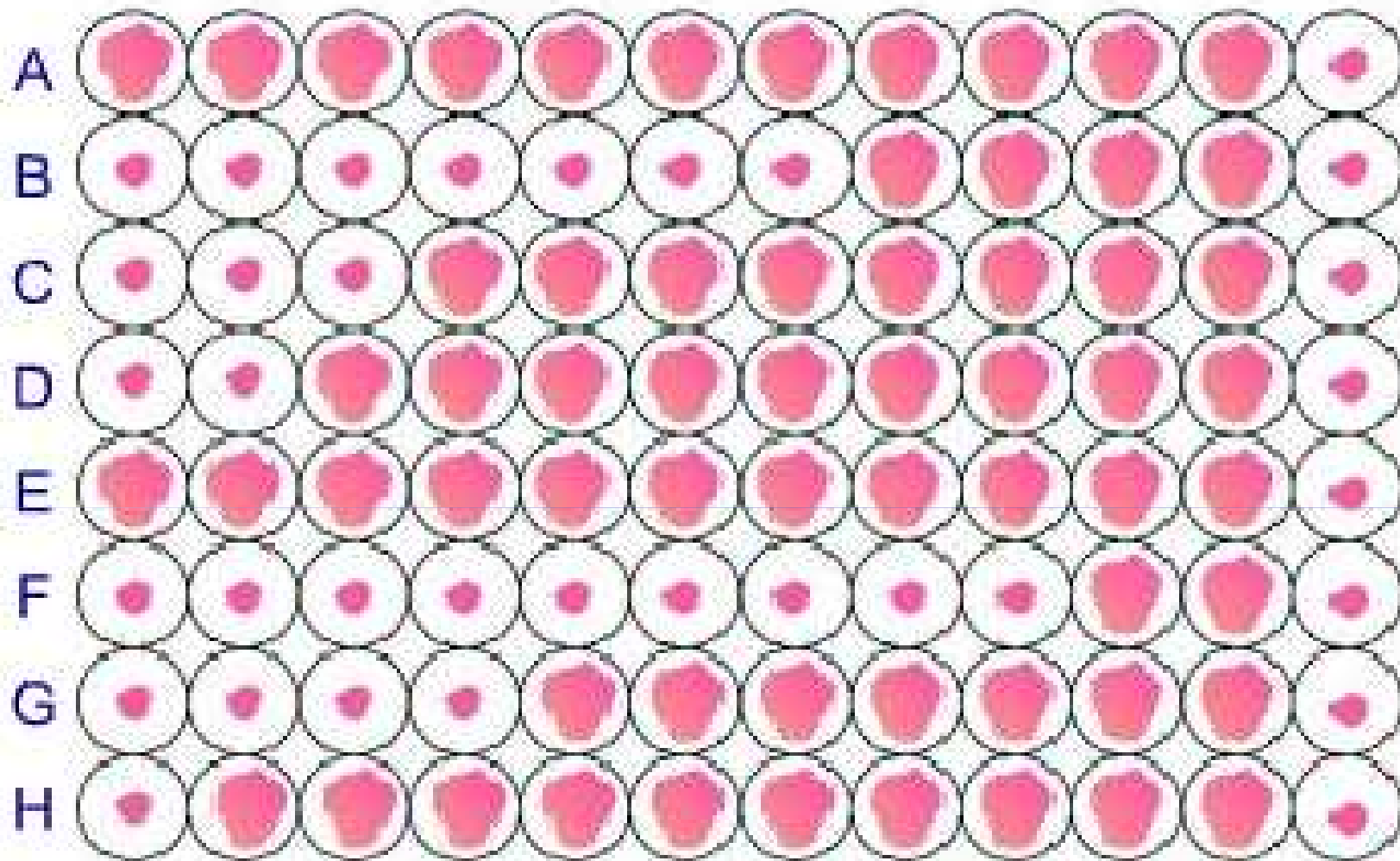
2) Chronic reaction

Group specific treponemal test: Reiter protein complement fixation test (RPCF)

- Treponemal test (Specific test):used virulent Nichol's strain of T pallidum
- FTA-ABS test
- TPHA
- TPI
- EIA

# Frequency of reactive serological reaction

Stage	VDRL/RPR	FTA-ABS	TPHA
Primary	60 – 75%	85- 100%	65-85%
Secondary	100 %	100 %	100 %
Latent/Late	60-70%	95-100%	95-100%



TPHA

- Diagnosis of congenital syphilis:
  - 1) Prenatal diagnosis is made by detection of maternal infection.
  - 2) In the infant by demonstration of T. palladium in skin lesion or in the CSF, or by detection of specific IgM antitreponemal antibodies



# ***Epidemiology of *T. pallidum****

- Transmitted from direct **sexual contact** or from **mother to fetus**
- **Not highly contagious** (~30% chance of acquiring disease after single exposure to infected partner) but transmission rate dependent upon stage of disease
- **Long incubation period** during which time host is non-infectious

- Treatment :  
Penicillin is the drug of choice
- Tetracycline or Erythromycin may be used.

# Non venereal treponemal disease

- **Bejel, Yaws & Pinta**
- **Primitive tropical and subtropical regions**

# *Treponema pallidum* ssp. *endemicum*

## ➤ **Bejel** (endemic syphilis)

- **Initial lesions:** nondescript oral lesions
- **Secondary lesions:** oral papules and mucosal patches
- **Late:** gummas (granulomas) of skin, bones & nasopharynx

## ➤ **Transmitted person-to-person by contaminated eating utensils**

## ➤ **Primitive tropical/subtropical areas** (Africa, Asia & Australia)

# *Treponema pallidum* ssp. *pertenue*

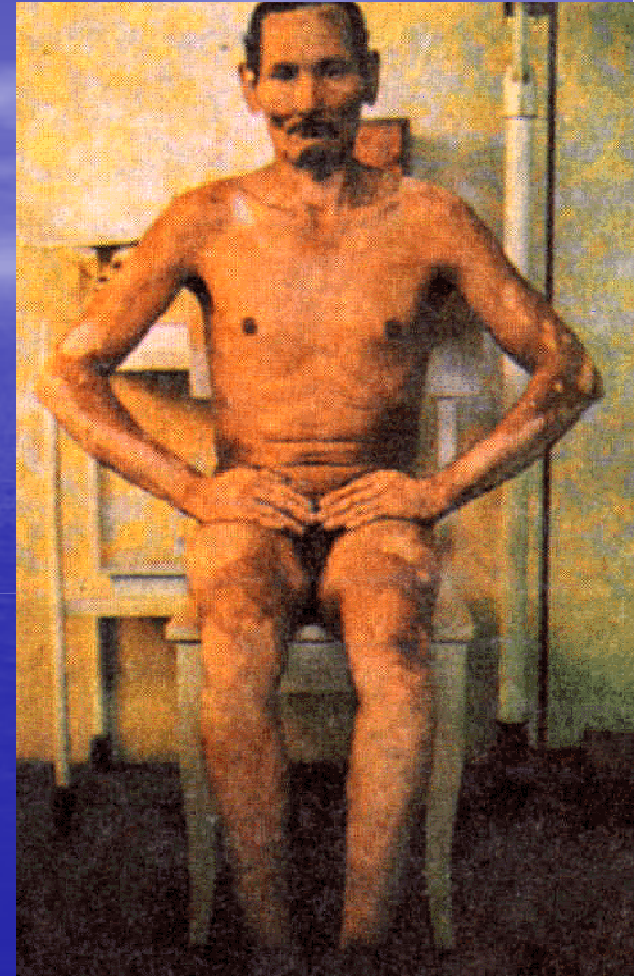
- **Yaws:** granulomatous disease
  - Early: skin lesions (see below)
  - Late: destructive lesions of skin, lymph nodes & bones
- Transmitted by direct contact with lesions containing abundant spirochetes
- Primitive tropical areas (S. America, Central Africa, SE Asia)




**Papillomatous Lesions of Yaws:** painless nodules widely distributed over body with abundant contagious spirochetes.

# *Treponema carateum*

- **Pinta:** primarily restricted to skin
  - 1-3 week incubation period
  - Initial lesions: small pruritic papules
  - Secondary: enlarged plaques persist for months to years
  - Late: disseminated, recurrent hypopigmentation or depigmentation of skin lesions; scarring & disfigurement
- **Transmitted by direct contact with skin lesions**
- **Primitive tropical areas**  
(Mexico, Central & South America)



**Hypopigmented Skin Lesions of Pinta:** depigmentation is commonly seen as a late sequel with all treponemal diseases



***Review of  
Treponema pallidum  
ssp. pallidum***

# ***General Characteristics of Treponema pallidum***

- Too thin to be seen with light microscopy in specimens stained with Gram stain or Giemsa stain
  - Motile spirochetes can be seen with **darkfield microscopy**
  - Staining with **anti-treponemal antibodies labeled with fluorescent dyes**
- **Intracellular pathogen**
- **Cannot be grown in cell-free cultures in vitro**
  - Koch's Postulates have not been met
- **Do not survive well outside of host**
  - Care must be taken with clinical specimens for laboratory culture or testing



