
Chapter 18. Miscellaneous Bacterial Infections

Table of Contents

SPIROCHETES	1
<i>Treponema pallidum</i> (Syphilis)	1
Nonvenereal <i>Treponema</i> species	5
<i>Borrelia</i> species	5
<i>Leptospira interrogans</i>	5
RICKETTSIAE AND RELATED GENERA	6
Clinical Manifestations	7
Laboratory Diagnosis	7
CHLAMYDIAE	8
Clinical Manifestations	8
Laboratory Diagnosis	8
Prevention	9
MYCOPLASMA	9

CHAPTER PREVIEW

- Spirochetes: *Treponema*, *Borrelia* and *Leptospira*
- Rickettsiae and Related Genera
- Chlamydiae
- *Mycoplasma*

SPIROCHETES

Spirochetes are thin, flexible, elongated spirally coiled helical bacilli; e.g. *Treponema*, *Borrelia* and *Leptospira*.

Treponema pallidum (Syphilis)

Treponema pallidum is the causative agent of a sexually transmitted infection called as syphilis. It is a genitoulcerative disease, transmitted by sexual contact, but rarely by non-venereal modes such as direct contact, blood transfusion or transplacental transmission. The incubation period is about 9-90 days.

Clinical Stages

The clinical course of syphilis passes through four clinical stages.

1. **Primary syphilis:** It is characterized by:

- *Genital ulcer:* Painless, firm, non-suppurative genital ulcers (called hard chancre), and

- *Lymphadenopathy* (usually inguinal): Painless firm, non-suppurative, and often bilateral.
2. **Secondary syphilis:** It usually develops 6–12 weeks after the healing of the primary lesion. It presents as:
 - *Skin rashes* on palms and soles
 - Mucosal patches
 - *Condylomata lata:* Mucocutaneous papules are seen in the perianal region, vulva, and scrotum.
 3. **Latent syphilis:** It is a clinically silent phase between secondary and late syphilis. It is characterized by the absence of clinical manifestations with positive serological tests for syphilis
 4. **Late syphilis:** It occurs several decades after the initial infection, and is associated with skin, CVS, and CNS manifestations
 - *Skin lesions* are called gummata: They are destructive granulomatous lesions
 - *CVS manifestations:* It is characterized by aneurysm of ascending aorta and aortic regurgitation
 - *CNS manifestations:* Common manifestations include—chronic meningitis, general paresis of the insane, and tabes dorsalis.

Congenital syphilis: Mother-to-fetus transmission can lead to the development of various congenital manifestations such as—Hutchinson's teeth (notched central incisors), mulberry-shaped molar, saddle nose, etc.

Laboratory Diagnosis

Syphilis is mainly diagnosed by the following diagnostic modalities.

Direct Microscopy

Treponemes can be demonstrated from the superficial lesions of primary, secondary, and congenital syphilis. The surface of the genital ulcer is cleaned with saline, gentle pressure is applied at the base of the lesion, and a drop of exudate is collected on a slide and examined by any of the following methods:

- Dark ground microscopy (DGM) (*Fig. 18.1A*)
- Direct fluorescent antibody staining for *T. pallidum* (DFA-TP)
- Silver impregnation staining—such as Levaditi stain and Fontana stain: *Treponema* do not take up ordinary stains as they are extremely thin and delicate. Therefore, silver impregnation methods can be used to increase their thickness (*Fig. 18.1B*).

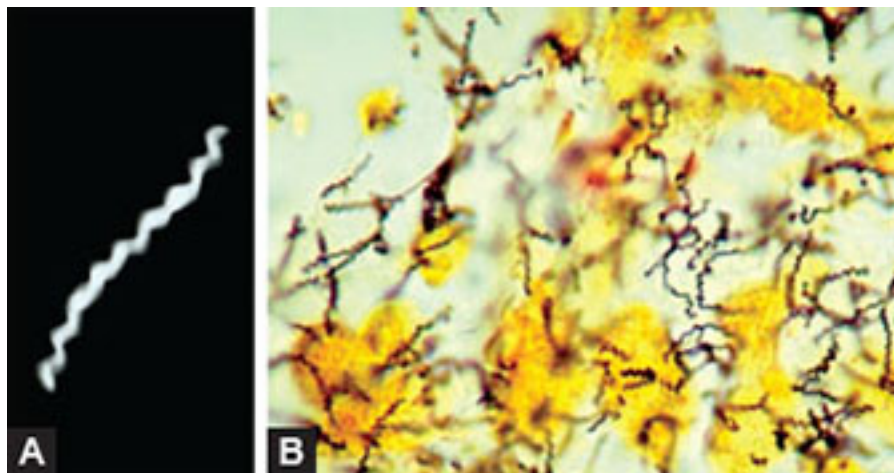
Cultivation

Pathogenic treponemes including *T. pallidum* cannot be grown in artificial culture media but are maintained by subcultures in susceptible animals such as rabbit testes (e.g. Nichols strain).

Serology (Antibody Detection)

As microscopy is difficult and culture methods are not available, antibody detection methods are of paramount importance in the diagnosis of syphilis. Depending upon the type of antigen used, two types of tests are available to detect antibodies in a patient's sera.

Figs. 18.1 A and B. Direct microscopy of *T. pallidum*: A. Dark ground microscope; B. Silver impregnation method.



Source: Public Health Image Library, A. ID# 2043; B. ID# 836, Centers for Disease Control and Prevention (CDC), Atlanta (with permission).

Non-treponemal Tests

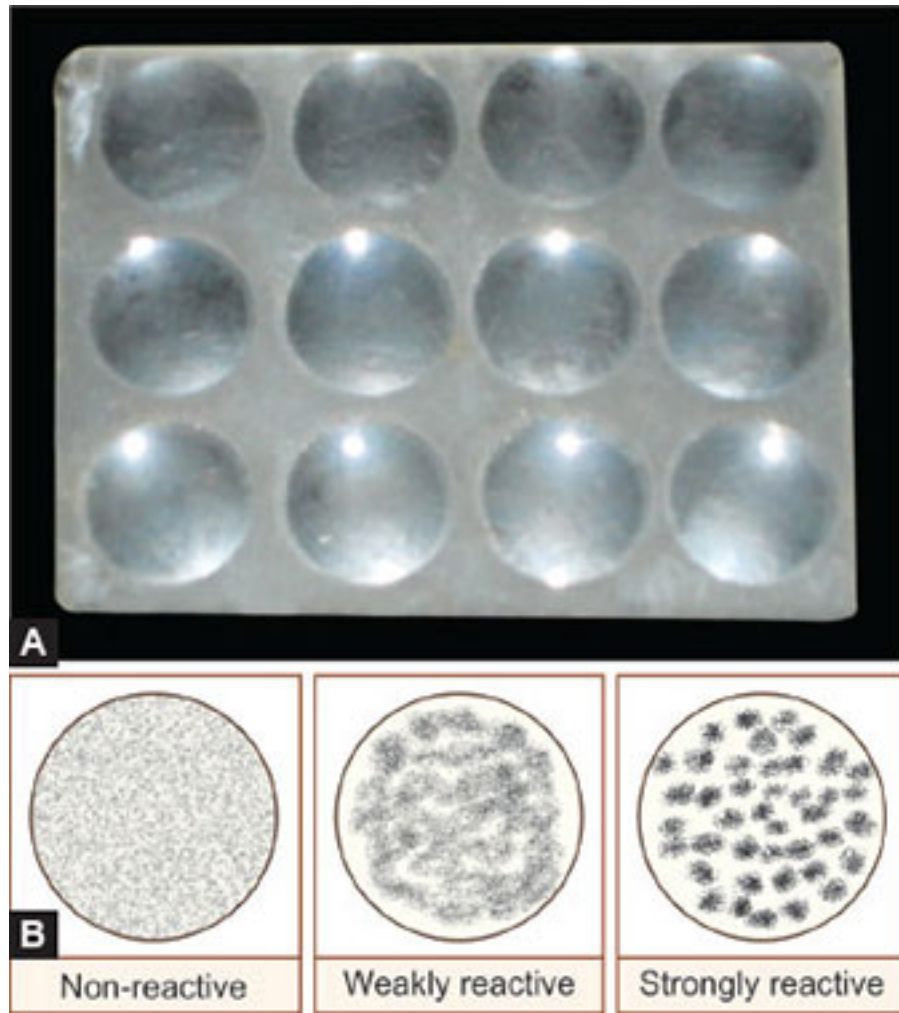
These tests detect non-specific reagin antibody by using cardiolipin antigen derived from the bovine heart. These tests work on the principle of slide flocculation (precipitation reaction).

- **Venereal disease research laboratory (VDRL) test:** The patient's serum is mixed with a drop of VDRL antigen on a concave slide, which is then mixed by rotating the slide. A positive test is indicated by the formation of medium to large clumps of Ag-Ab complexes; visualized by focusing the slide under the microscope (Figs. 18.2A and B)
- **Rapid plasma reagin (RPR):** It is similar to the VDRL test, except that it does not require a microscope to take the reading. RPR is preferred to test individual samples (less sample load); whereas VDRL is preferred when samples are tested in batches (large sample load).

Treponemal Tests

These tests detect species-specific antibody by using *T. pallidum*-specific antigen; which is polysaccharide in nature. Various tests are:

Figs. 18.2A and B. A. VDRL slide; B. VDRL test results.



Source: Department of Microbiology, JIPMER, Puducherry (with permission).

- TPI: *T. pallidum* immobilization test
- FTA-ABS: Fluorescent treponemal antibody absorption test
- TPHA: *T. pallidum* hemagglutination test
- TPPA: *T. pallidum* particle agglutination test
- Western blot and enzyme immunoassay.

TREATMENT

Syphilis

Penicillin is the drug of choice for treating all stages of syphilis. Doxycycline can be used alternatively in case of penicillin allergy.

Nonvenereal Treponema species

Endemic or nonvenereal treponematoses are caused by three close relatives of *T. pallidum*; producing primary mucocutaneous lesions in non-genital sites (e.g. extremities, oral mucosa).

- *T. pertenue*: Causes yaws
- *T. endemicum*: Causes endemic syphilis
- *T. carateum*: Causes pinta.

Borrelia species

Most of the species of *Borrelia* occur as commensals on the buccal and genital mucosa. Few are pathogenic to man, such as:

- *B. recurrentis* causes epidemic relapsing fever
- *B. duttonii* and *B. hermsii* cause endemic relapsing fever
- *B. burgdorferi* is the agent of Lyme disease
- *B. vincentii* causes Vincent's angina in association with fusiform bacilli.

Leptospira interrogans

Leptospira interrogans is the causative agent of leptospirosis; a zoonotic disease transmitted, by direct contact with the urine of infected animals such as rodents.

Leptospira interrogans is antigenically complex and comprises 26 serogroups; which are further typed into >300 serovars. The serogroups and serovars differ in their geographical distribution and severity of infection.

Clinical Manifestations

Leptospira interrogans produces two types of illnesses.

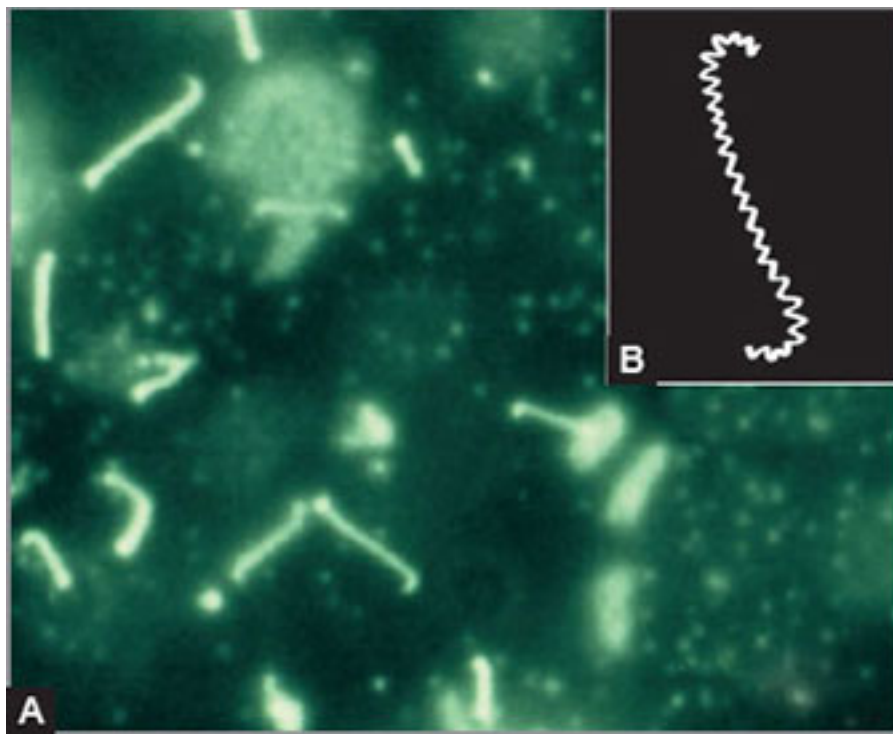
- The majority (90%) of leptospirosis cases present as mild anicteric febrile illness
- Few cases (10%) progress to severe form hepatorenal hemorrhagic syndrome or *Weil's disease*; characterized by icterus, high-grade fever, hemorrhagic manifestations, and impaired renal functions.

Laboratory Diagnosis

Laboratory diagnosis of leptospirosis involves the following modalities. Specimens include blood and CSF (in the early stage) and urine (in the late stage).

- **Dark ground microscopy** of clinical specimens such as blood or CSF reveals spirally coiled bacilli (tightly) with hooked ends (*Figs. 18.3A and B*)
- **Culture**: Can be performed on special media such as Ellinghausen-McCullough-Johnson-Harris (EMJH) medium and incubated at 30°C for 4–6 weeks
- **Serology for antibody detection**: Various tests are available such as:
 - *Genus specific tests*: Latex agglutination test, ELISA, ICT (immunochromatographic test)

Figs. 18.3A and B. *Leptospira interrogans* (spirally coiled bacilli with hooked ends):
A. Dark ground microscopy of the mount following microscopic agglutination test; B. Schematic diagram (viewed under a dark-ground microscope).



Source: A. Public Health Image Library/ID#: 2888/ Mrs M Gatton, Centers for Disease Control and Prevention (CDC), Atlanta (with permission).

- *Serovar specific test: Microscopic agglutination test.* It serves as the gold standard reference method for the diagnosis of leptospirosis.

TREATMENT

Leptospirosis

Oral doxycycline is given for mild leptospirosis; whereas severe cases are treated with penicillin.

RICKETTSIAE AND RELATED GENERA

Rickettsiaceae comprise of two genera—*Rickettsia* and *Orientia*; both possess the following properties:

- They are obligate intracellular organisms
- They are not cultivable in artificial media, although they can grow in cell lines, or by animal and egg inoculation
- They are transmitted by arthropod vectors, such as tick, mite, flea, or louse.

The various members of Rickettsiae are:

- *R. prowazekii*: It is the causative agent of epidemic typhus, transmitted by louse

- *R. typhi*: It causes endemic typhus, transmitted by flea
- *R. rickettsii*: It is the causative agent of Rocky Mountain spotted fever, transmitted by tick
- *R. conorii*: It causes Indian tick typhus, transmitted by tick
- *R. akari*: It is the causative agent of rickettsialpox, transmitted by mite
- *Orientia tsutsugamushi*: It is the causative agent of scrub typhus, transmitted by mite.

Clinical Manifestations

For all Rickettsiae, the final target site is the endothelial cells. Clinically the rickettsial infections may manifest as a combination of one or more of the following features—fever, rashes, headache, myalgia, eschar, lymphadenopathy, etc.

Other genera related to Rickettsia are:

- **Ehrlichia**: It produces an acute febrile illness called ehrlichiosis, transmitted by ticks. It infects leukocytes such as granulocytes, monocytes; producing intracellular inclusions, called *morula*
- **Coxiella burnetii**: It causes *Q fever*, transmitted by inhalational mode; characterized by atypical pneumonia, hepatitis and on chronic stage, produces endocarditis. Rashes are typically absent
- **Bartonella**: It has three important species, which are associated with distinct clinical conditions
 - *B. bacilliformis* is the causative agent of a systemic disease called Carrion's disease and a local cutaneous lesion called verruga peruana
 - *B. quintana* causes trench fever
 - *B. henselae* is the agent of cat-scratch disease.

Laboratory Diagnosis

Laboratory diagnosis of rickettsial infection includes:

- **Weil Felix test**: It is a heterophile agglutination test, where rickettsial antibodies are detected by using non-specific cross-reacting *Proteus* antigens such as OX2, OX19, and OXK antigens
 - In epidemic and endemic typhus—sera agglutinate mainly with OX19 and sometimes with OX2
 - In tick-borne spotted fever—antibodies to both OX19 and OX2 are elevated
 - In scrub typhus—antibodies to OXK are raised
 - The test is negative in rickettsialpox, Q fever, ehrlichiosis and bartonellosis.
- **Specific antibody detection test**, e.g. indirect immunofluorescence test and ELISA.

TREATMENT

Rickettsial infections

Doxycycline is the drug of choice in the majority of rickettsial infections.

CHLAMYDIAE

Chlamydiae are obligate intracellular bacteria that cause a spectrum of diseases in man infecting the eye, genital organs, and lungs.

Clinical Manifestations

Chlamydiae have three pathogenic species infecting man, which are associated with various clinical manifestations.

Chlamydia trachomatis

Chlamydia trachomatis comprise of 19 serovars, which cause various infections in man such as:

- **Trachoma:** It is a type of chronic keratoconjunctivitis, caused by serotypes A, B, and C
- **Genital chlamydia:** Caused by serotypes D to K, presents as urethral discharge (urethritis) and mucopurulent cervicitis, etc.
- **Inclusion conjunctivitis:** Caused by serotypes D to K. It presents mucopurulent discharge from the eyes. It can affect adults (swimming pool conjunctivitis) or neonates (ophthalmia neonatorum)
- **Infant pneumonia:** Caused by serotypes D to K, presents as interstitial pneumonia in infants
- **LGV (lymphogranuloma venereum):** It is a sexually transmitted infection, caused by serotypes L1, L2, and L3. It is characterized by painless genital ulcers and painful inguinal lymphadenopathy.

Chlamydia psittaci

It is a pathogen of birds. Infection in man can range from mild influenza-like syndrome to fatal atypical pneumonia. It comprises of several serotypes.

Chlamydia pneumoniae

It is an exclusively human pathogen, that causes atypical interstitial pneumonia. It is also associated with the pathogenesis of atherosclerosis. It has only one serotype.

Laboratory Diagnosis

Specimens collected depend upon the types of infection associated— (1) Scrapings or swabs from infected sites: Urethral swab for urethritis, endocervical swab for cervicitis, or conjunctival swabs for ocular infections, (2) Nasopharyngeal aspirate and respiratory secretions for suspected pneumonia, or (3) Bubo aspirate for LGV.

- **Microscopy:** Useful for detection of chlamydial inclusion bodies. Common staining methods used are Gram staining, Lugol's iodine, and direct immunofluorescence test
- **Antigen detection:** Enzyme immunoassays are available for the detection of LPS antigens
- **Culture:** It was the gold standard method in the past. Various culture methods available are:
 - Egg inoculation (yolk sac)
 - Mice inoculation
 - Cell line culture by using McCoy, HeLa (for *C. trachomatis*), or HEP2 (for *C. pneumoniae*).

- **Nucleic acid amplification tests (NAAT)**, e.g. PCR
 - This is considered as the most sensitive and specific method
 - Currently the diagnostic assay of choice for chlamydial infections.
- **Serology (antibody detection)**: Two formats are available
 - ELISA using group-specific LPS antigen
 - Micro-immunofluorescence test detects antibody against species and serovar-specific MOMP (major outer membrane protein) antigen of *C. trachomatis*.

TREATMENT

Chlamydial infections

- Azithromycin is the drug of choice
- Alternatively, doxycycline, tetracycline, erythromycin or ofloxacin can be used.

Prevention

Control measures for the prevention of chlamydial genital infections include:

- Periodic screening of high-risk groups, such as young women having multiple sex partners
- Treatment of both the sex partners
- Use of barrier methods of contraception such as condoms
- Abstain from sex till 7 days after starting the treatment.

MYCOPLASMA

Mycoplasmas are the smallest microbes capable of free-living in the environment. They lack rigid cell wall and therefore, are resistant to cell wall-acting antibiotics such as beta-lactams.

- **M. pneumoniae** is the pathogenic species, which is the causative agent of *primary atypical pneumonia* (community acquired pneumonia)
 - *Clinical manifestations*: *M. pneumoniae* produces upper respiratory tract infection (manifests as pharyngitis, tracheobronchitis), *atypical pneumonia* (community acquired interstitial pneumonia) and extrapulmonary manifestations (e.g. septic arthritis, Guillain–Barre syndrome or neurologic manifestations)
 - *Laboratory diagnosis* involves detection of antibodies (e.g. ELISA) or isolation of the organism in specific culture media such as PPLO broth
 - *Treatment*: Macrolides are the drug of choice.
- **Urogenital mycoplasmas** include *M. hominis*, *M. genitalium* and *Ureaplasma urealyticum*. They cause urethritis.

EXPECTED QUESTIONS

1. I. Write short notes on:

1. Clinical manifestations of syphilis.
2. Laboratory diagnosis of syphilis.
3. Leptospirosis.
4. Infections produced by Chlamydiae.
5. Rickettsial infections.

2. II. Multiple Choice Questions (MCQs):

1. **Weil's disease is caused by___?**
 - a. *Leptospira interrogans*
 - b. *Borrelia recurrentis*
 - c. *Orientia tsutsugamushi*
 - d. *Mycoplasma pneumoniae*
2. **VDRL test is done for___?**
 - a. Leptospirosis
 - b. Lyme disease
 - c. Scrub typhus
 - d. Syphilis
3. **Primary atypical pneumonia is caused by ___?**
 - a. *Leptospira interrogans*
 - b. *Borrelia recurrentis*
 - c. *Mycoplasma pneumoniae*
 - d. *Orientia tsutsugamushi*
4. **Lyme disease is caused by___?**
 - a. *Leptospira interrogans*
 - b. *Borrelia recurrentis*
 - c. *Borrelia vincenti*
 - d. *Borrelia burgdorferi*

Answers

1. a	2. d	3. c	4. d
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