Spirochetes

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They are heterogeneous group of spiral motile organisms, each one has many coils so it's like a spring shape.

They differ from other prokaryotes by the presence of axial filament which is involved with motility.

Three important genera imposed in human diseases :

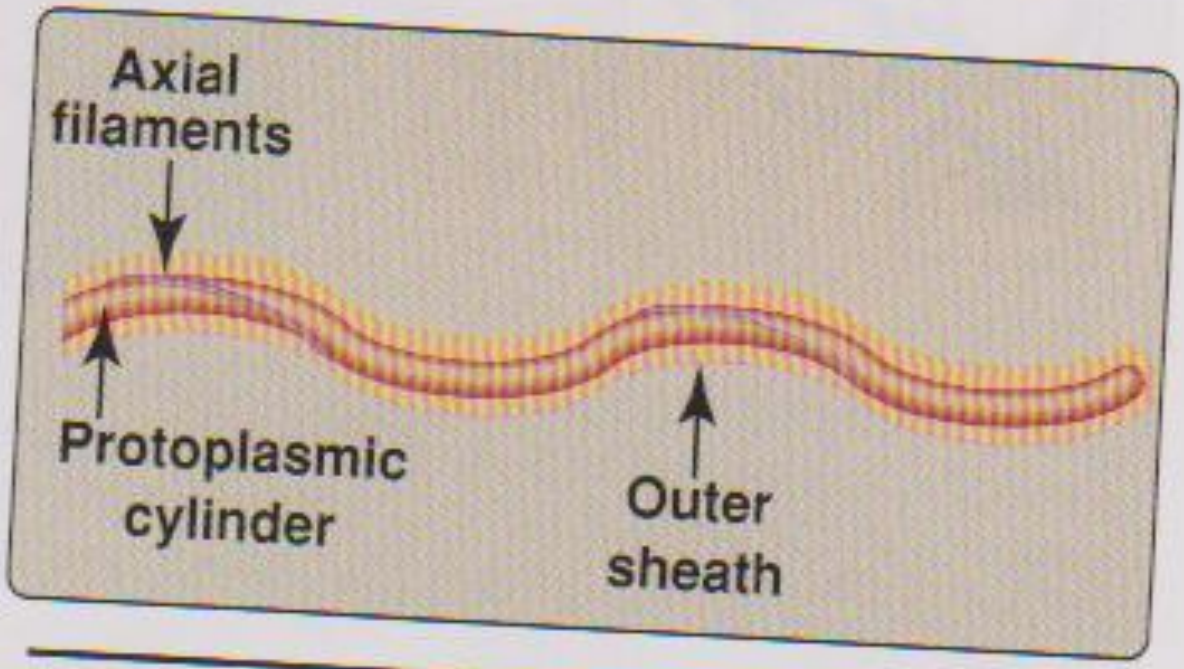


Figure 15.2

Treponema :

T. pallidum causes syphilis , other species like T. pertenu Causes yaw disease.

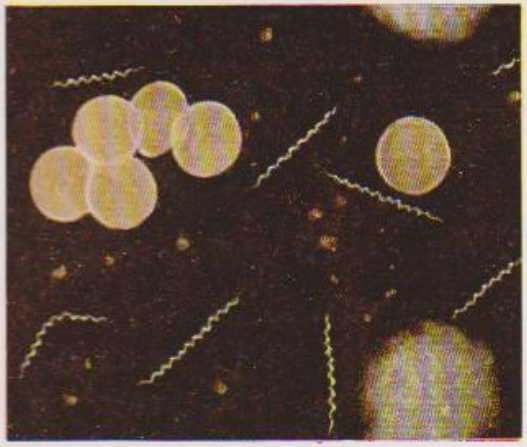
Borrelia causes relapsing fever , Lyme disease and necrotic stomatitis.

Leptospira causes systemic infections with fever and jaundice as well as meningitis.

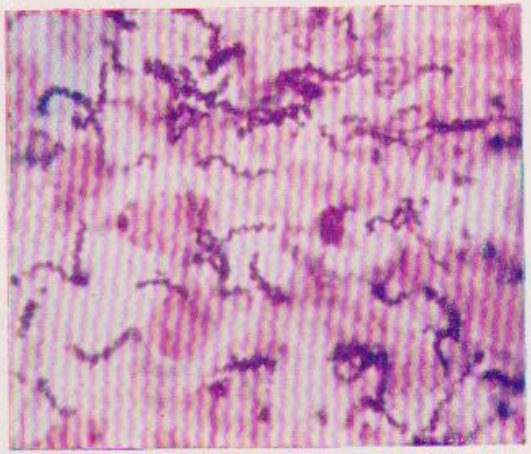
Treponema pallidum

It is delicate slender spiral filament 5-15 × 0.2 micrometer with 6-12 regular coils . Ends are pointed and actively motile rotating around the axial filament and they do not stain well with Gram stain , silver impregnation , dark field and immunoflurescent stains are used for their study.

unstained state. Cannot be demonstrated by ordinary staining techniques; silver impregnation stains may be used.



Dark-ground illumination preparation of serous exudate from primary syphilitic chancre. Seven delicately spiralled *Tr. pallidum* are seen, that on the left showing flexion. Red blood cells and part of two leucocytes are also seen in the field. ×1000.



Silver impregnation stained section of foetal liver from a case of congenital syphilis; the liver tissue is counterstained with basic fuchsin. The organisms are much rougher and thicker in appearance as compared with the dark-ground preparation and this is due to the deposition of silver. ×1000.

Culture and growth characters:

Treponema pallidum **can not grow on artificial media , in a whole blood.** ***Treponema Pallidum*** **species may remain motile for 24 hrs at 4C.**

It is easily destroyed outside the body , drying cause inactivation and kill spirochetes rapidly.

Spirochetes are sensitive to penicillin.

Antigenic structure:

Treponema pallidum antigen have not been identified though it stimulates the development of antibodies capable of staining this organism with fluorescent dyes .

It induces complement fixing antibodies, antibody like substance regain which imposed in positive reagen test .

Pathogenesis and clinical findings:

Primary syphilis:

limited to human , human infection is usually transmitted by sexual acquired syphilis natural infection with *Treponema pallidum* is contact and the lesion is on the skin and mucous membrane of genitalia however the primary lesion is intrarectal or perineal or oral mucosa

Treponema can penetrate intact mucous membranes skin through abrasion . Spirochetes multiply locally at the site of entry and reach blood through lymphatic in 2-10 weeks after infection, a papule develops at the site of infection and breaks to form ulcer clear hard chancre. The reaction is characterized by lymphocytes and plasma cells , this primary lesion always heals spontaneously.

Secondary stage:

Two to ten weeks later , the secondary lesion appears.

This stage is characterized by the presence of maculopapular rash in the anogenital region , axillas and mouth.

Chrioretinitits, hepatitis nephritis may be observed.

This type may also subside spontaneously or tertiary type arises. Both primary and secondary lesions are rich in spirochetes and highly infectious.

STAGES OF UNTREATED SYPHILIS

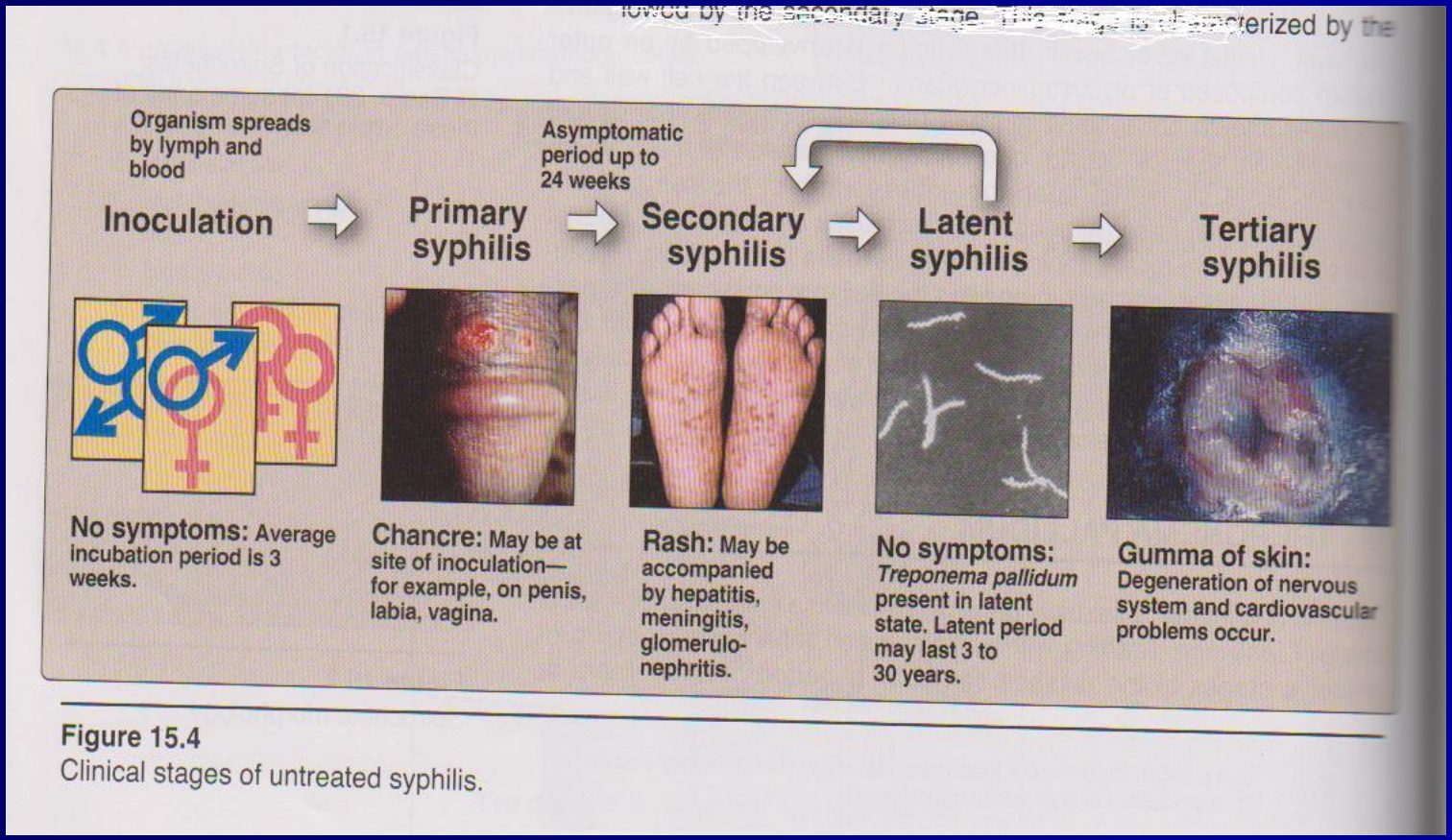


Figure 15.4
Clinical stages of untreated syphilis.

Tertiary stages:

It is characterized by the development of granulomatous lesions(gummas) of skin , bones and liver .

Lesions are seen on tongue, palate, lips also.

CNS involvement in this stage shows what is known as Tabes Dorsalis syndrome. Paresis due to damage in meninges and spinal cord.

Cardiovascular lesions as aortic aneurism may be observed also.

In this stage Treponemes are very rare there however they can be found occasionally in the eye or CNS .

Congenital syphilis :

Prenatal syphilis is established by passage of the spirochetes from mother to the fetus through placenta in the 10th -15th week of gestation.

Some infected fetuses die others are stillborn at term others are borne but develop the signs of congenital syphilis in childhood .

keratitis , saddle nose , Hutchison teeth , perostitis and variety of CNS anomalies .

Adequate treatment of mother during pregnancy prevents congenital syphilis.

Diagnosis:

1-Specimens : tissue fluid from early lesions for demonstration of spirochetes .

2-Serum for serological tests .

3-Darkfield examination of fresh smear for motility detection of the organism.

4-Fluorescent test for spirochetes detection.

Serological tests:

These are either treponemal antigens for detection of specific antibodies or non specific antigens (non treponemal antigens) for the detection of nonspecific antibodies .

1-Non treponemal antigen test

Antigens employed are lipid extract from nontreponmal mammalian tissue .

The purified cardiolipid from beef heart is a diphosphotidylglycerol .

This reacts with syphilitic reagin ,regain is a mixture of immunoglobulin and IgA characters against some antigens .

Antibodies are found in the patients serum after 2-3 weeks of untreated infection and in spinal fluid after 4-8 weeks .

two types of tests detection in the presence of reagin.

A . Flocculation tests:

VDRL (Venereal disease research laboratories)
PRP (Rapid plasma regain).

These tests are based on the clumps formation when the Antigen cardiolipin combined with regain , these tests revered negative in 6-18 weeks after effective treatment .

B. Complement fixation test CF (Wasserman test), these tests may lead to false positive result.

2- Treponemal antigen test :

1- Fluorescent treponmal antibody FTA test:

It is test employing indirect immunofluorescence (Killed *T . pallidum* and patients sera antihuman gamaglobulin) . this test shows explants specific city and sensitivity it is used for the detection of congenital syphilis due to IgM presence in the blood of newborns.

B-TpI : demonstration of *Treponema pallidum* immobilization.

T.pallidum complement fixation test .

T.pallidum hemagglutination test, VDRL and FTA test can also be performed on spinal fluid.

Treatment :

penicillin is the drug of choice . In syphilis of less than one year , penicillin levels are maintained for two weeks by single dose of penicillin G .

Tetracycline , erythromycin could be used also.

Non venereal treponemal infections

T. endemicum

This organism causes Bejel disease , occurs particularly among children and produce highly infectious skin lesions , late visceral complications are rare . penicillin is the drug of choice.

T. carateum

It causes Pinta , this disease appears to be restricted to the dark skinned races .

The primary lesions , a non ulcerating papule occurs on exposed area , months later flat hyperpigmented lesion appears on the skin . Depigmentation and hyperkeratosis takes place years after .

Late cardiovascular involvement occur very rarely .

Transmission is non venereal either by direct contact or by flies .

T. pertenu

It is endemic particularly among children in many humid hot tropical countries .

The primary lesion is ulcerating papule occurs on arms or legs . Transmission is by direct person to person between children below 15 years .

Scar formation of skin lesions and bone destruction are common . Visceral or nervous system complications are rare. Yaws represents a variant of syphilis adapted to non venereal transmission in hot climates . Penicillin is drug of choice for treatment.

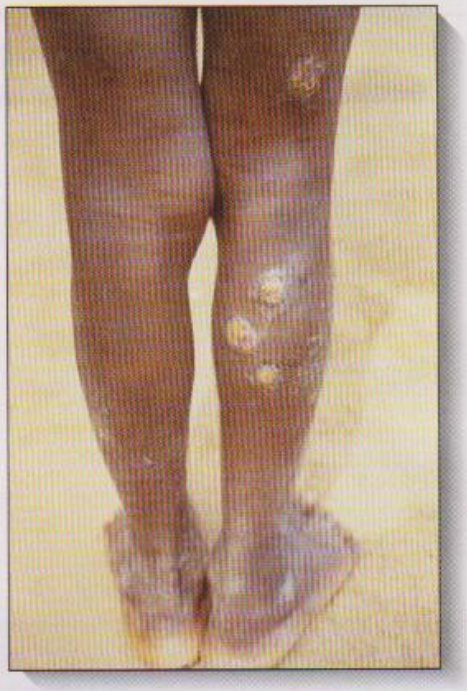


Figure 15.5
Yaws: early stage.

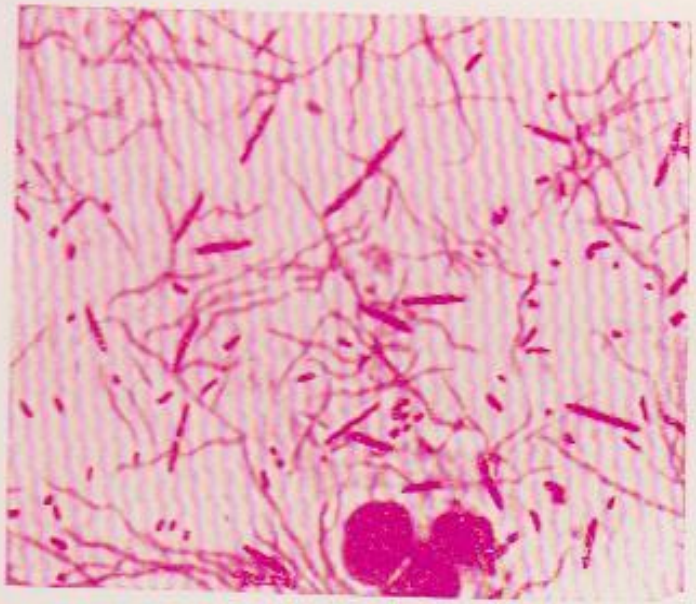
Borellia recurrentis

It is irregular spiral 10 -30× 0.3 micrometer with 5 to 7 fairly regular coils , gram negative and stains with Gemsa and Wright stain .

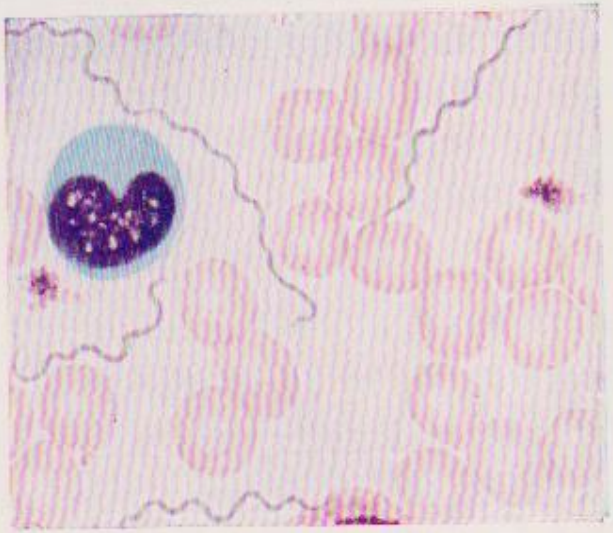
Cultivation : The organism can be cultivated in fluid media containing blood , serum or tissue

The organism survive for several months in infected blood at 4 C. In some ticks but not lice , spirochetes pass from generation to generation.

sporing. It is strictly anaerobic and



ganism can be demonstrated in stained films of tail blood 1 to 5 days later



Blood film from a case of relapsing fever in Poland; four *Borr. recurrentis* can be seen, and that above the mononuclear leucocyte appears to be dividing. Morphologically identical with other species involved in relapsing fever in various parts of the world. Film treated with Leishman's stain. ×1000.

BORRELIA DUTTONII

Pathology :

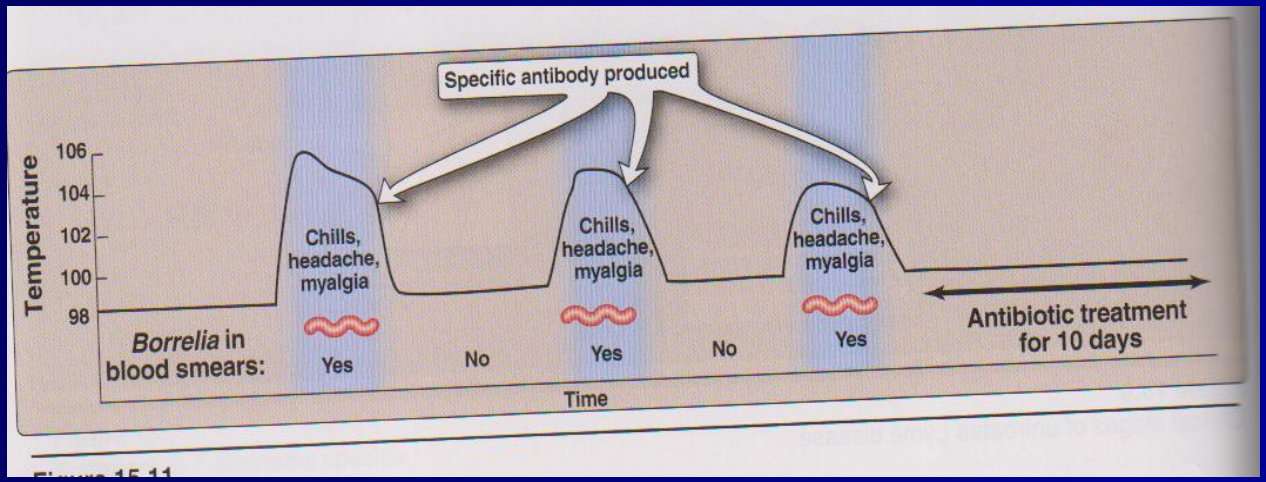
The incubation period of this infection is 3-10 days , and the onset is sudden with chills and abrupt rise of temperature . The fever persists for 3-5 days and then declines leaving the patient weak but not ill.

The febrile period lasts 4-10 days and it is followed by second attack of chills , fever , headache and malaise are clinical manifestations .

Antibodies against spirochetes appear during the febrile stage.

Fatal cases show spirochetes in great number in spleen and liver , necrotic foci in other parenchymatous organs and hemorrhagic lesions are in the kidneys and gastrointestinal tract.

Organisms have been demonstrated in spinal fluid and brain occasionally .


Specific antibody produced
Temperature
106
104
102
100
98
Chills, headache, myalgia
Chills, headache, myalgia
Chills, headache, myalgia
Borrelia in blood smears:
Yes
No
Yes
No
Yes
Antibiotic treatment for 10 days
Time

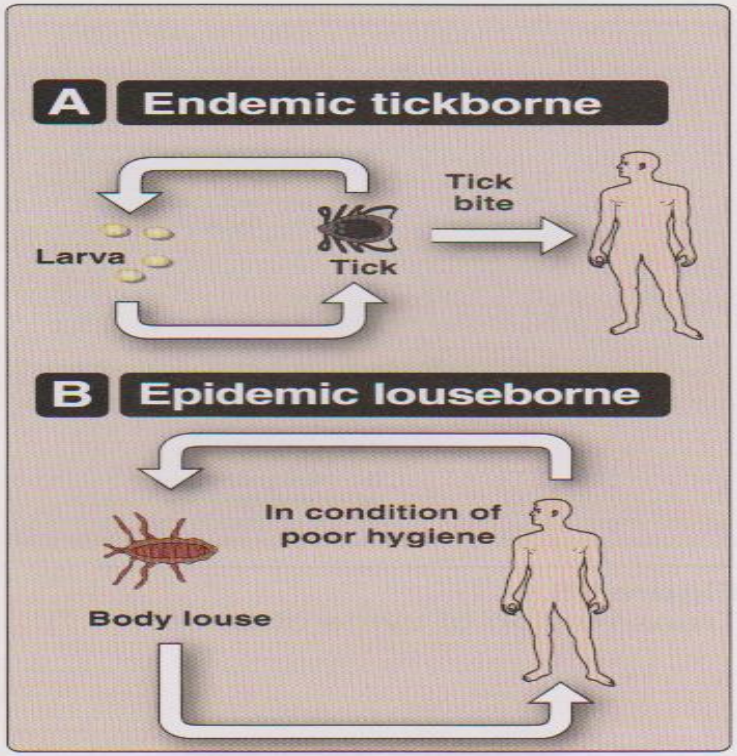


Figure 15.10
Endemic (for example, Lyme disease) versus epidemic relapsing fever by *Borrelia recurrentis*.

Diagnosis :

Blood Film : **Specimens obtained during rise of fever ,smears stained with wrights or Gemsa stain reveal large loosely coiled organisms.**

Serology :

Spirochetes grown in culture can serve as antigens to complement fixation test for the diagnosis of this disease. Shared antigenicity between this organism and Proteus OxK may develops and also a false positive VDRL test.

Immunity and treatment:

Short duration immunity follows this infection .

penicillin , erythromycin and tetracylines are effective against this organism .

Epidemiology and control :

Rodents serve as a source of infection , ticks of genus Ornithodores , lice become infected by sucking blood 4-5 days later they may serve as a source of infection.

Infection is favored by crowding , malnutrition and cold climate with low mortality .

Prevention is based on avoidance of exposure to ticks and lice and on delousing .

No vaccines are available .

Lyme disease:

It is named after **Lyme town** , it occurs in America, Australia, and Europe , it occurs in summer and represents expanding annular skin lesions .

Often there are headache , stiff neck , fever , myalgia , arthralgia and lymphadenopathy , symptoms may develops after weeks or months .

This disease is transmitted by ticks (small ixodes) which carry *Borrelia burgdoferi* which can be found in blood ,and CSF .

Treatment with penicillin or tetracyclines results in recovery.

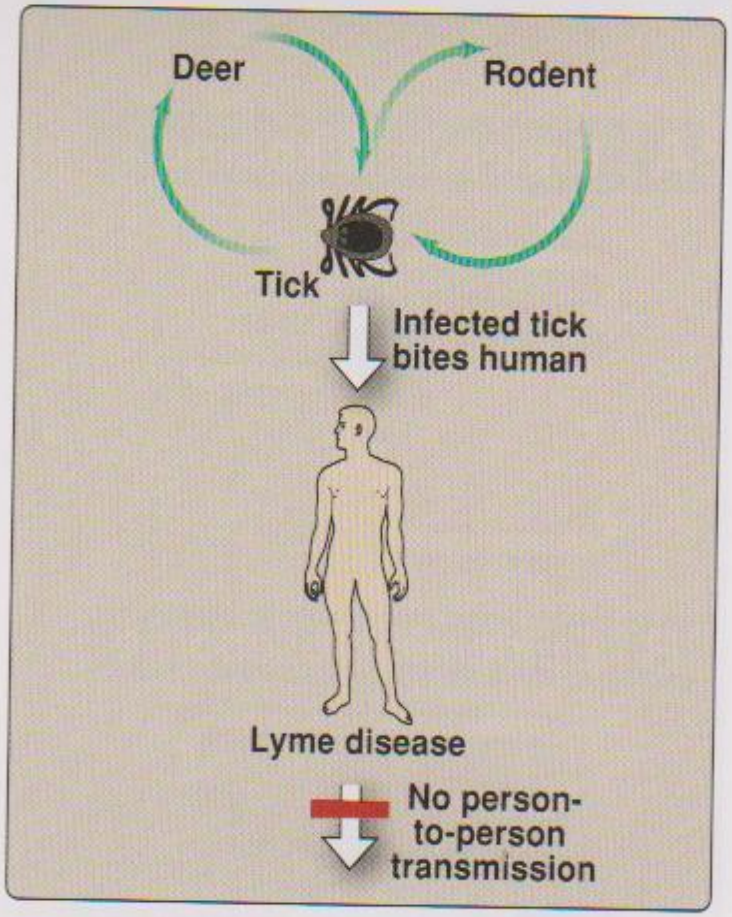

Deer
Rodent
Tick
Infected tick bites human
Lyme disease
No person-to-person transmission

Figure 15.8

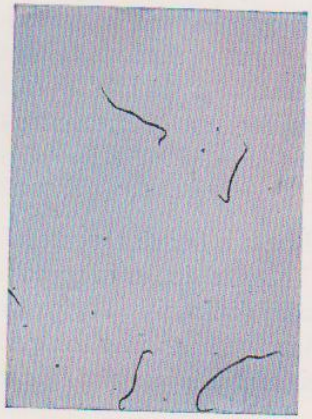
Leptospira

L. Icterohemorrhagica

Tightly coiled flexible spirochete about 5-15 micrometer length with very fine spirals and one end of the organism is often bent forming a hook .

It is actively motile by rotation , electron micrographs showed a thin axial filament and delicate membrane. It is unstainable readily with ordinary dyes but can be revealed with silver impregnation dye.

Dark-ground preparation of *L. icterohaemorrhagiae* from Stuart's medium. Both ends of the organism are recurved on the body; the very fine coils are just discernible. ×1000.



Silver impregnation stained preparation of *L. canicola* which is morphologically indistinguishable from other leptospires; in comparison with the living preparation on the left the leptospires here show a tendency to straighten and lose their characteristic hooked appearance. ×1000.

Cultural appearances. Requires special fluid media for growth, e.g.

Culture:

Leptospira grow best under aerobic condition at 28-30 C in protein rich semisolid medium known as (Fletcher medium).

Colonies are round 1-3 mm in diameter within 6-10 days .

Leptospira also grow on chick embryo . fatty acid oxidation is the source of energy in this organism as it ca not consume carbohydrates and amino acids for this purpose. They can survive for weeks in water at alkaline PH.

Antigenic structure:

A serologically active lipopolysaccharide with group reactivity has been extracted from leptospira.

Cross reactivity between leptospira isolates from humans and animals due to antigenic overlapping.

Pathogenic and clinical findings :

Human infection results from ingestion of water or food contaminated with leptospira , organisms may enter through skin abrasions or mucous membranes rarely .

After one week a variable febrile onset during which spirochetes are found in blood stream then establish themselves in parynchamytous organs particularly liver and kidneys producing hemorrhagic necrosis of tissue and resulting in dysfunction of those organs (jaundice , hemorrhage and nitrogen retention).

It is often seen as aseptic meningitis with intense headache , stiff neck and pleocytosis in CSF .

Nephritis and hepatitis may also recurrent with skin muscle and eye lesions. Intensity of infection depends on the type of the organism ,

Infections are mild or subclinical. Hepatitis is frequent in patients with leptospirosis .

It is associated with elevated serum creatin phosphokinase CPK where is normal in viral hepatitis .

Human urine may contain spirochetes in the second and third weeks of disease.

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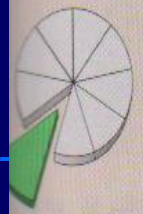


Spirochetes

Leptospira species

Leptospira interrogans

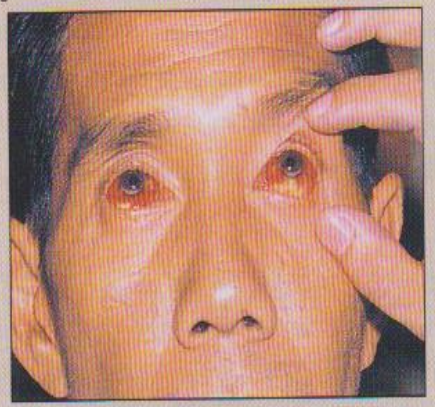
- **Gram-negative**, but stains poorly, and needs to be visualized by other means, such as dark-field examination of wet-mount preparations
- Long, slender, flexible, spiral- or corkscrew-shaped rods
- Organisms are highly motile

Leptospira interrogans

- Infectious jaundice
- Marsh fever
- Weil's disease
- Swineherd's disease

Penicillins 1 Penicillin
CEPHALOSPORINES

Tetracyclines 1 Doxycycline
AMINOGLYCOSIDES
MACROLIDES
FLUOROQUINOLONES
OTHER



Scleral hemorrhages in a jaundiced patient with leptospirosis

Figure 15.14

Diagnosis :

Specimens are blood and urine ,smears are done t o be stained with Gemsa , darkfield examination.

Culture of the whole blood or urine can be cultured on Fletcher medium or Tween 80 albumen medium .

Growth is slow and culture should be kept for several weeks.

Animal inoculation test

inoculation of young hamster or Guinea pigs with fresh plasma or urine within few days . spirochetes become demonstrable in peritoneal fluid.

Postmortem test show hemorrhagic lesions in the peritoneal cavity. Positive culture will be after 8-14 days.

Serology

Agglutinins titer is high , develops slowly in leptospira infections reaching peak 5-8 weeks later.

Antibody can be detected by slide agglutination or passive hemagglutination test.

Immunity:

Solid immunity follows infection but reinfection with different serotype of this organism occurs

Treatment

Penicillin , tetracycline have some therapeutic effect , doxycycline has prophylactic efficacy .

Control

Reducing contamination of water chances with rodent excreta and other animal sources.

Vaccination of animals

Other spirochetal infections :

Spirillum minor:

It causes one form of rat bite fever , it is very small 3-5 micrometer and rigid spiral organism . it is carried by rats and result in a local lymphadenopathy , skin rashes and fever of relapsing type . organism can be isolated from enlarged lymph node and blood.

Spirochetes of the normal mouth and mucous membrane

A number of spirochetes occur in the mouth and mucous membranes like *Borrelia vincenti* .

These organisms participates in oral opportunistic oral infections like vincents angina or trench mouth in combination with other organisms .