41 Spirochetes

INTRODUCTION

Elongated, motile, flexible bacteria twisted spirally along the long axis are termed **spirochetes** (from *speira*, meaning coil and *chaite*, meaning hair). They are structurally more complex than other bacteria. A characteristic feature is the presence of varying numbers of **endoflagella** (axial filament), which are polar flagella wound along the helical protoplasmic cylinder, and situated between the outer membrane and cell wall.

Spirochetes vary widely in size, some being as long as 500 μm and others as short as 5 μm. They are Gram negative. Many are free-living saprophytes, while some are obligate parasites. They may be aerobic, anaerobic or facultative. Reproduction is by transverse fission.

Spirochetes belong to the order Spirochetales, comprising two families (Fig. 41.1):

- Spirochetaceae containing the genera *Spirochaeta*, *Cristispira*, *Treponema* and *Borrelia*
- Leptospiraceae containing the genus *Leptospira*

Human pathogens are found in the genera *Treponema*, *Borrelia* and *Leptospira*. Members of the genus *Spirochaeta* are saprophytes found in water and sewage, while *Cristispira* are found in molluses.

TREPONEMA

Treponemes *(trepos,* meaning to turn, and *nema,* meaning thread) are relatively short, slender spirochetes with fine spirals and pointed or rounded ends. Some of them are pathogenic, while others occur as commensals in the mouth, intestines and genitalia. Pathogenic treponemes have not been successfully cultivated in cell free media, though commensals may be grown in artificial media.

Treponemes cause the following diseases in humans:

- Venereal syphilis (*T.pallidum*)
- Endemic syphilis (*T.pallidum* [*T.endemicum*])

- Yaws (*T.pertenue*)
- Pinta (*T.carateum*)

They are almost identical in their morphology, antigenic structure and other features, though there are differences in the clinical features and natural history of the diseases they produce. It has been suggested that the pathogenic treponemes represent only evolutionary variations of a single species and that the diseases caused by them, though different clinically and epidemiologically, should be considered as part of a continuous spectrum of **treponematoses**. Accordingly, the species *T.pallidum* is now considered to include three subspecies—*pallidum* causing venereal syphilis, *endemicum* causing endemic syphilis and *pertenue* causing yaws.

TREPONEMA PALLIDUM

Clinical Case 1 A 20-year-old male who works as a truck driver presented to the Skin and Venereal Disease clinic with a genital ulcer which was painless for the previous 10 days. He had had unprotected sexual contact with a commercial sex worker about two weeks previously. On examination, the ulcer was found to be circumscribed, indurated and partially healed. The inguinal lymph nodes were enlarged. A diagnosis of syphilis was made and the serum sent for a VDRL test. This was reactive at 1:64 dilution. The patient was treated with penicillin.

Treponema pallidum, the causative agent of syphilis, was discovered by Schaudinn and Hoffmann (1905) in the chancres and inguinal lymph nodes of syphilitic patients. The name *pallidum* refers to its pale staining.

Morphology

It is a thin, delicate spirochete with tapering ends, about 10 µm long (range 4–14 µm) and 0.1–0.2 µm wide. It has about ten regular spirals, which are sharp and angular, at regular intervals of about 1 µm (Fig. 41.1). It is actively motile, exhibiting rotation around the long axis, backward and forward movements, and flexion of the whole body. During motion, secondary curves appear and disappear in succession but the primary spirals are unchanged.

T.pallidum cannot be seen under the light microscope in wet films but can be discerned by negative staining with Indian ink. Its morphology and motility can be seen under the dark ground or phase contrast microscope. It does not take ordinary bacterial stains but stains a light rose-red with prolonged Giemsa staining. It can be stained by **silver impregnation** methods. **Fontana's method** is useful for staining films and **Levaditi's method** for tissue sections.

Ultrastructurally, the cytoplasm of *T.pallidum* is surrounded by a trilaminar cytoplasmic membrane, enclosed by a cell wall containing peptidoglycan which gives the cell rigidity and shape. 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, to interdigitate at its centre. Unlike the flagella of other bacteria, these endoflagella do not protrude outside, but remain within the outer membrane layer.

Saprophytic spirochetes are generally coarser in appearance, lack the uniform spirals with regular spacing, and show lashing motility.

Cultivation

Pathogenic treponemes do not grow in artificial culture media.

- The cultivable strains are the non-pathogenic treponemes, showing morphological and antigenic similarities with *T.pallidum*. The best known of these is the **Reiter strain**, which has been widely used as the antigen in group-specific treponemal tests for the diagnosis of syphilis. The Reiter treponeme grows well in thioglycollate medium containing serum. It is now classified as *T.phagedenis*.

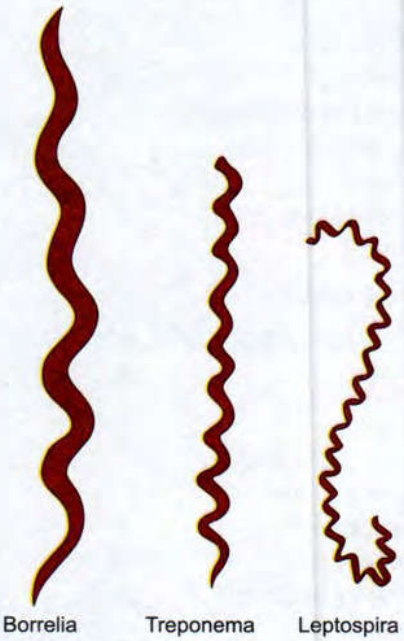

Fig. 41.1 Schematic representation of comparative morphology of different spirochetes

- Virulent *T.pallidum* strains cannot be cultivated in artificial media but have been maintained for many decades by serial testicular passage in rabbits. One such strain (**Nichol's strain**), isolated from the brain of a fatal case of general paralysis of the insane in 1912, is still being propagated and used for diagnostic and research purposes.

Resistance

T.pallidum is very delicate, being readily inactivated by drying or by heat (41–42°C in one hour). Hence fomites are of little importance in the transmission of infection. It is killed in 1–3 days at 0–4°C, so transfusion syphilis can be prevented by storing blood for at least four days in the refrigerator before transfusion. Stored frozen at –70°C in 10% glycerol, or in liquid nitrogen (–130°C), it remains viable for 10–15 years. It is inactivated by contact with oxygen, distilled water, soap, arsenicals, mercurials, bismuth, common antiseptic agents and antibiotics.

Antigenic structure

The antigenic structure of *T.pallidum* is complex. Treponemal infection induces at least three types of antibodies:

- The first is the **reagin antibody** that reacts in the standard or non-specific tests for syphilis, such as Wassermann, Kahn and VDRL, in which a hapten extracted from beef heart is used as the antigen. This lipid hapten is known as **cardiolipin** and is chemically a diphosphatidyl glycerol. This lipid has been detected in *T.pallidum* but it is not known whether the reagin antibody is induced by the cardiolipin that is present in the spirochete or that released from damaged host tissues.
- The second is a **group antigen** found in *T.pallidum* as well as in non-pathogenic cultivable treponemes like the Reiter treponeme.
- The third antigen, probably polysaccharide in nature, is **species specific**. The antibody to this antigen is demonstrated by specific *T.pallidum* tests which are positive only with the sera of patients infected with pathogenic treponemes.

Pathogenicity

Natural infection with *T.pallidum* occurs only in human beings. Experimentally, monkeys may be infected. A disease resembling syphilis can be produced experimentally in chimpanzees, with typical lesions of primary and secondary syphilis. Rabbits can be infected by intradermal or intratesticular inoculation, the former giving rise to chancre and the latter to syphilomas. Serial passage in rabbits does not appear to reduce the virulence of the spirochete to human beings, as evidenced by several accidental infections in laboratory workers caused by the Nichol's strain. Hamsters are also susceptible.

SYPHILIS

Syphilis can be acquired by the venereal or non-venereal route or be congenital or acquired.

1. **Venereal syphilis** is acquired by sexual contact. The spirochete enters the body through minute abrasions on the mucosa or skin. Infectivity of a patient to the sexual partner is maximum during the first two years of the disease—the primary, secondary and early latent stages. After five years, the risk is considered minimal. The infective dose is small—as few as 60 treponemes are capable of infecting 50 per cent of human volunteers. It multiplies at the site of entry. Its generation time is 30–33 hours. Clinical disease sets in after an incubation period of about a month (range 10–90 days). The clinical manifestations fall into three stages: primary, secondary and tertiary.
   - The **primary lesion** in syphilis is the **chancre** at the site of entry of the spirochete (Fig. 41.2). In all but a few, the chancre is genital. Other common sites are the mouth and nipples. The chancre is a painless, relatively avascular, circumscribed, indurated, superficially ulcerated lesion. It is known as '**hard chancre**' to distinguish it from the non-indurated lesions of 'soft chancre' caused by *H.ducreyi,* and as Hunterian chancre named after John Hunter who produced the lesion on himself experimentally and described the evolution of the disease. The chancre is covered by a thick, glairy exudate rich in spirochetes. The regional lymph nodes are swollen, discrete, rubbery and non-tender. Even before the chancre appears, the spirochetes spread from the site of entry into the lymph and bloodstream, so the patient may be infectious during the late incubation period. The chancre invariably heals in about 10–40 days, even without treatment, leaving a thin scar. Persistent or multiple chancres may be seen in HIV-infected or other immunodeficient patients (*Case* 1).

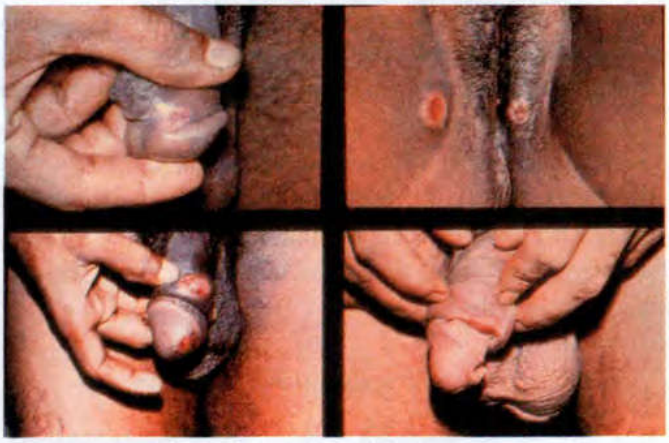

Fig. 41.2 Penile chancre of primary syphilis, yaws and pinta

- **Secondary syphilis** sets in 1–3 months after the primary lesion heals. During this interval, the patient is asymptomatic. The secondary lesions are due to widespread multiplication of the spirochetes and their dissemination through the blood. Roseolar or papular skin rashes, mucous patches in the oropharynx and condylomata at the mucocutaneous junctions are the characteristic lesions. Spirochetes are abundant in the lesions and consequently the patient is most infectious during the secondary stage. There may also be ophthalmic, osseous and meningeal involvement. Secondary lesions are highly variable in distribution, intensity and duration but they usually undergo spontaneous healing, in some instances taking as long as four or five years.
- After the secondary lesions disappear, there is a period of quiescence known as **latent syphilis**. Diagnosis during this period is possible only by serological tests. In many cases, this is followed by natural cure but in others, after several years, manifestations of tertiary syphilis appear. These consist of cardiovascular lesions including aneurysms, chronic granulomata (gummata) and meningovascular manifestations. Tertiary lesions contain few spirochetes and may represent manifestations of delayed hypersensitivity.

2. **Late tertiary** or quanternary syphilis in a few cases, a late tertiary stage may develop, presenting with neurological manifestations such as tabes dorsalis, or general paralysis of the insane may develop several decades after the initial infection.

In syphilis acquired **non-venereally** (as occupationally in doctors or nurses), the natural evolution is as in venereal syphilis, except that the primary chancre is extragenital, usually on the fingers. In the rare instances where syphilis is transmitted by blood transfusion, the primary chancre does not occur.

3. In **congenital syphilis**, where infection is transmitted from mother to fetus transplacentally, the manifestations and course are different. Transplacental transmission can take place at any stage of pregnancy. A woman with early syphilis can infect her fetus much more commonly (75–95 per cent) than one with syphilis of over two years' duration (35 per cent). The lesions of congenital syphilis usually develop only after the fourth month of gestation, the time when fetal immune competence starts appearing. This suggests that the pathogenesis requires an immune response from the fetus. Congenital syphilis can be prevented if the mother is given adequate treatment before the fourth month of pregnancy. The obstetric history in an untreated syphilitic woman is typically one of abortions and stillbirths followed by live births of infants with stigmata of syphilis and finally of healthy infants.

Laboratory diagnosis

Laboratory diagnosis consists of demonstration of the spirochetes under the microscope and of antibodies in serum or CSF.

1. Specimen: Specimens should be collected with care as the lesions are highly infectious. The lesion is cleaned with gauze soaked in warm saline and the margins gently scraped so that the superficial epithelium is abraded. Gentle pressure is applied to the base of the lesion and the serum that exudes is collected, preventing admixture with blood. Serum is collected for serology. CSF can be collected for neurosyphilis.

2. Microscopy: Diagnosis by microscopy is applicable in the primary and secondary stages and in cases of congenital syphilis with superficial lesions. Wet films are prepared with the exudate and after applying thin coverslips, examined under the dark ground microscope. *T.pallidum* is identified by its slender spiral structure and slow movement. Differentiation from saprophytic spirochetes commonly present in the genital area can be done by morphology and motility.

- **Dark ground examination** is useful and has low sensitivity. A treponemal concentration of 10^4 per ml in the exudates is required for the test to be positive.

- **Direct fluorescent antibody test** for *T.pallidum* (DFA-TP) is a better and safer method for microscopic diagnosis. Smears of the exudate are fixed with acetone and sent to the laboratory,where the DFA-TP test is done using fluorescent tagged anti-*T.pallidum* antiserum. The use of a specific monoclonal antibody has made the test more reliable.
- **Silver impregnation** smears can be stained by methods. Fontana's method is useful for staining films and Levaditi's method for tissue sections.

3. Serological tests: These tests form the mainstay of laboratory diagnosis. A large number of tests have been described, of which only a few are now in use. Serological tests for syphilis may be classified as follows:

Reagin antibody tests: These tests use the lipoidal or cardiolipin antigens and are known as standard tests for syphilis (STS). (The antibody reacting with cardiolipin is known as reagin. This can be misleading, as the IgE antibody in atopy is also called reagin, though there is no connection between the two.)

The antigen is a purified lipid extract of beef heart (called cardiolipin), with added lecithin and cholesterol, as standardised by Pangborn (1945), and the test used is **VDRL (Venereal Disease Research Laboratory**, USPHS, New York, where the test was developed). The VDRL test is rapid and gives quantitative results. In this test, the inactivated serum (serum heated at 56°C for 30 minutes) is mixed with cardiolipin antigen on a special slide and rotated for four minutes. Cardiolipin remains as uniform crystals in normal serum but forms visible clumps on combining with the reagin antibody. The reaction is read under a low power microscope.

Antibody titre interpretation: By testing serial dilutions, the antibody titre can be determined. The results are reported qualitatively as 'reactive', 'weak by reactive' or 'not reactive'. For quantitative reporting, the reciprocal of the end point is given as the titre, for example 'reactive 4 dilution' or 'titre 4'.

The VDRL test can be used for testing CSF also, but not plasma. CSF need not be heated prior to the test.

A number of modifications to the VDRL test have been developed, of which **Rapid Plasma Reagin (RPR)** is the most popular. This test uses the VDRL antigen containing fine carbon particles, which make the result more clear-cut and evident to the naked eye. The RPR test can be done with unheated serum or plasma but is not suitable for testing CSF. Automated RPR test (ART) is available for large-scale testing.

Biological false positive (BFP) reactions: As the cardiolipin antigen is present both in *T.pallidum* and in mammalian tissues, reagin antibodies may be induced by treponemal or host tissue antigens. This accounts for the biological false positive (BFP) reactions, which constitute the major disadvantage of STS. BFP reactions are defined as positive reactions obtained in cardiolipin tests, within specific treponemal tests, in the absence of past or present treponemal infections—and not caused by technical faults. They represent non-treponemal cardiolipin antibody responses.

BFP reactions may occur in about one per cent of normal sera. BFP antibody is usually IgM, while reagin antibody in syphilis is mainly IgG. Clinically, BFP reactions may be classified as acute or chronic. Acute BFP reactions last only for a few weeks or months and are usually associated with acute infections, injuries or inflammatory conditions. Chronic BFP reactions persist for longer than six months and are typically seen in SLE and other collagen diseases. Leprosy, malaria, relapsing fever, infectious mononucleosis, hepatitis and tropical eosinophilia are examples of other conditions associated with BFP reactions.

The reagin antibody becomes detectable 7–10 days after the appearance of primary chancre (or 3–5 weeks after acquiring the infection). Sensitivity in the primary stage is 60–75 per cent, with the titres being low, up to eight. In the secondary stage, sensitivity is 100 per cent and titres range from 16 to 128 or more. The **prozone phenomenon** may be a problem in high titre sera and it is therefore essential to test sera in dilutions.

Another stage of syphilis in which such high titres are seen is congenital syphilis. After the secondary stage, titres diminish and about a third of patients with late syphilis are seronegative. The titres may rise in patients developing cardiovascular, neurological or gummatous lesions. In some cases of neurosyphilis, reagin tests may be negative with serum but positive with CSF. Reagin tests usually become negative 6–18 months after effective treatment of syphilis, depending on the stage at which treatment is given. However, if treatment is started late, the tests may remain positive in low titres.

Group-specific treponemal tests: To avoid BFP reactions, tests using cultivable treponemes as antigens were developed. These used the Reiter treponemes (origi-

nally believed to be an adapted strain of *T.pallidum*). The test most commonly employed in this group was the Reiter protein complement fixation **(RPCF) test**, using a lipopolysaccharide–protein complex antigen derived from the treponeme. Its sensitivity and specificity were lower than those of tests using *T.pallidum*. Though RPCF was generally free from BFP reactions, it still gave some false positive reactions. RPCF and other Reiter treponeme tests are now not in general use.

Specific *T.pallidum* tests: These tests use the virulent Nichol's strain of *T.pallidum* maintained by serial inoculation in rabbit testes.

- ***Treponema pallidum* immobilisation (TPI)** the first in this group is the test introduced in 1949. The test serum is incubated with complement and *T.pallidum* maintained in a complex medium anaerobically. If antibodies are present, the treponemes are immobilised, that is, rendered non-motile, when examined under dark ground illumination.
- In its time, TPI was the most specific test available for the diagnosis of syphilis and was considered the **gold standard** in syphilis serology. However, because of its extreme complexity, it was available only in a few laboratories. The TPI test has now been supplanted by others such as FTA-ABS and TPHA which are quite as specific and much simpler.
- **Fluorescent treponemal antibody (FTA)** test is an indirect immunofluorescence test using as antigen, smears prepared on slides with Nichol's strain of *T.pallidum*. The slides can be stored for several months in deep freeze. The currently used modification of the test is the FTA-absorption **(FTA-ABS)** test in which the test serum is preabsorbed with a sonicate of the Reiter treponemes (*sorbent*) to eliminate group-specific reactions. FTA-ABS is as specific as the TPI test and is now accepted as a standard reference test. However, as it can be done only in suitably equipped laboratories, it is not available for routine testing.
- ***T.pallidum* hemagglutination assay (TPHA)** uses tanned erythrocytes sensitised with a sonicated extract of *T.pallidum* as antigen. The procedure in use is a micro-hemagglutination test (MHA-TP), which is capable of being automated.
- The test sera for TPHA are absorbed with a diluent containing components of the Reiter treponeme, rabbit testis and sheep erythrocytes. Sera are screened at an initial dilution of 1:80 but titres of 5120 or more are common in the secondary stage. TPHA is just as specific as FTA-ABS and almost as sensitive, except in the primary stage. It is also much simpler and more economical. No special equipment is needed. Kits are available commercially. These advantages have made TPHA a standard confirmatory test. Table 41.1 shows the relative sensitivities of the serological tests in common use.
- **Enzyme immunoassays (EIA)** have been developed using *T.pallidum* antigens and are available commercially (Bio-Enza Bead test; Captia Syphilis-G test). A rapid agglutination test has been developed, using latex particles coated with three immunodominant proteins of *T.pallidum*, obtained by recombinant technology. It is claimed to be as specific as TPHA, and more sensitive.

Diagnostic utility of serological assays: The practice for serological screening for syphilis varies in different countries. In the UK, a combination of VDRL and TPHA tests is used. This is an efficient combination for the detection or exclusion of syphilis at all stages, except the early primary stage. A repeat test 1–3 months later will bring even this to light. In the USA, screening is by VDRL or RPR test alone. This may fail to detect about one per cent of secondary syphilis due to the prozone effect and about 30 per cent of latent or late syphilis.

Response to treatment: Quantitative tests are useful in monitoring the patient's response to treatment, indicating the stage of the disease and in detecting re-infection. **VDRL** or **RPR** is preferred because they usually become negative following treatment. If treatment is given very early, the serum may not become positive at all. Treatment in the primary stage leads to seroreversal in about four months; in the secondary and early latent stages, it takes 12–18 months; in later stages, it may take five years or more. In some cases, low titre reactivity may persist indefinitely in spite of effective treatment. Specific treponemal tests are of little value as indicators of clinical cure as they tend to remain positive in spite of treatment. TPHA titres may

Table 41.1 *Frequency of reactive serological tests in untreated syphilis (percentage)*

Stage	VDRL/RPR	FTA-ABS	TPHA
Primary	70–80	85–100	65–85
Secondary	100	100	100
Latent/late	60–70	95–100	95–100

fall rapidly following treatment in secondary syphilis but remain positive for life in low titres.

4. Diagnosis: **TPHA** and **FTA-ABS** are helpful in excluding or confirming the diagnosis of syphilis and for identifying BFP reactions. Though **false positive reactions** were believed to have been eliminated with the introduction of these specific tests, it is not truly so. Both TPHA and FTA-ABS can give false positive results, though very rarely. All serological tests for syphilis may be positive in non-venereal treponematoses, and some in a few other spirochetal infections as well. In Lyme disease, the VDRL test is negative, but FTA-ABS may be positive.

A **negative TPHA** virtually excludes the diagnosis of syphilis, past or present, except in the very early stages. In neurosyphilis, a negative CSF VDRL test may not be conclusive but a negative TPHA test eliminates the possibility of neurosyphilis. Detection of **specific IgM antibody** may be helpful in some situations. Being the initial type of antibody to appear, IgM is detectable by the second week of infection. IgM antibody production ceases soon after elimination of infection by treatment. Persistence of the antibody indicates continuing active disease and the need for treatment.

Diagnosis of congenital syphilis: As IgM does not cross the placenta, its presence in neonatal serum confirms congenital syphilis and helps differentiate it from seropositivity due to passively transferred maternal antibody (syphilotoxemia). Many techniques have been developed for the selective detection of IgM antibodies. These include modifications of the FTA-ABS, TPHA, EIA and VDRL tests, using whole sera or separated IgM fractions. When such tests are not available, parallel tests of maternal and neonatal sera may settle the diagnosis of congenital syphilis, in which the neonatal serum may show a higher titre of antibody than the maternal serum. Serial testing is also useful because the titre of passively transferred antibody decreases rapidly, the VDRL test becoming negative by three months.

Epidemiology

Venereal syphilis is worldwide in distribution. During the five centuries that it has been recorded and studied, the disease has undergone much variation in its natural history and clinical features. As originally described, it was a highly virulent disease with florid cutaneous manifestations. With the discovery of the dramatic therapeutic response to penicillin, it was hoped that it may even be possible to eradicate syphilis, as the disease has no extra human reservoir. However, not only has it not been possible to eliminate the disease but an increase has occurred in its incidence, due to the changing customs, habits and values in society.

HIV and syphilis: The advent of the AIDS pandemic has had an impact on syphilis. In most places, fear of AIDS and safer sex practices led to a fall in the incidence of syphilis and all STDs initially, but this trend did not continue everywhere. Concurrent infection with syphilis and HIV is common and may lead to earlier evolution of neurosyphilis.

Immunity

The immune mechanisms in syphilis are not adequately understood. Humoral immune response against the treponeme does not appear to be effective as the disease progresses even in the presence of a vigorous antibody response. Cell-mediated immunity may be more relevant. T lymphocytes and macrophages are predominant in early syphilitic lesions. Specifically sensitised Th1 cells secrete cytokines favouring the clearance of spirochetes by activated macrophages.

Re-infections do not appear to occur in a person already having active infection. Some degree of immunity to re-infection may occur in persons whose infection has been completely eliminated by treatment.

Prophylaxis

As transmission is by direct contact, it is possible to protect against syphilis by avoiding sexual contact with an infected individual. The use of physical barriers (such as condoms), antiseptics (potassium permanganate) or antibiotics may minimise the risk. The use of prophylactic penicillin carries the danger that it may suppress the primary lesion without eliminating the infection, so that recognition and treatment of the disease may become more difficult. No vaccine is available.

Treatment

Penicillin is uniformly effective in syphilis but it is necessary to give an adequate dose and maintain the drug level for a sufficiently long period to establish cure. A single injection of 2.4 million units of benzathine penicillin G is adequate in early cases. For late syphilis, this amount may be repeated weekly for three weeks. In patients allergic to penicillin, doxycycline may be used. Ceftriaxone is effective, particularly in neurosyphilis.

Penicillin treatment in syphilis sometimes induces the **Jarisch–Herxheimer reaction**, consisting of fever, malaise and exacerbation of symptoms. It is frequent, but harmless, in primary and secondary syphilis, and can be managed with bed rest and aspirin. It is rare in late syphilis but can be dangerous in some cases of gummatous, cardiovascular or neurosyphilis. It is believed to be due to the liberation of toxic products like tumour necrosis factors from the massive destruction of treponemes or due to hypersensitivity.

NON-VENEREAL TREPONEMATOSES

Non-venereal treponemal diseases occur in endemic foci in several parts of the world, in communities with poor standards of hygiene. The diseases have been given different names in different regions and vary somewhat in clinical manifestations, but the treponemes responsible are virtually indistinguishable from *T.pallidum* and are now considered as its subspecies. Infection is usually transmitted by direct body-to-body contact.

Three distinct forms of non-venereal treponematoses are recognised—endemic syphilis, yaws and pinta.

Endemic syphilis

Syphilis, transmitted non-venereally, was endemic in several foci. The causative agent is the *T.pallidum* subspecies *endemicum*.

With recognition of such foci and mass treatment with penicillin under the auspices of the WHO, endemic syphilis has become very rare. It has also been reported from India.

The disease is common in young children. The primary chancre is not usually seen, except sometimes on the nipples of mothers infected by their children. The disease is usually seen with manifestations of secondary syphilis, such as mucous patches and skin eruptions. The disease progresses to tertiary lesions, particularly gummatous lesions. Cardiovascular and neurological involvement is rare. Congenital syphilis is also not found. Laboratory diagnosis and treatment are as for venereal syphilis.

Yaws

Yaws, also known as frambesia, pian, parangi and by many other synonyms, is endemic in the tropical areas of Africa, Asia and America. Yaws eradication campaigns by mass penicillin injection in endemic areas led to the virtual eradication of the disease. However, it has subsequently reappeared in some areas. In India, cases have been identified in Andhra Pradesh, Orissa and Madhya Pradesh.

The causative agent is *T.pallidum* subspecies *pertenue* (*T.pertenue*) which is morphologically and antigenically indistinguishable from *T.pallidum*. The primary lesion (mother yaw) is an extragenital papule which enlarges and breaks down to form an ulcerating granuloma. As in syphilis, secondary and tertiary manifestations follow, but cardiovascular or neurological involvement is rare. Destructive gummatous lesions of the bones are common.

Infection is by direct contact. Flies may act as mechanical vectors. The small fly, *Hippolates pallippes,* has been found feeding on open sores but its epidemiological importance is not known. Laboratory diagnosis and treatment are as for syphilis. There appears to be some cross-immunity between yaws and syphilis, in that venereal syphilis is rare in communities where yaws is endemic.

Pinta

Pinta (carate, mal del pinto) is endemic in Central and South America and the neighbouring islands. The primary lesion is an extragenital papule, which does not ulcerate but develops into a lichenoid or psoriaform patch. Secondary skin lesions are characterised by hyperpigmentation or hypopigmentation. Tissues other than skin are seldom affected.

The causative agent is *T.carateum.* It is very closely related to *T.pallidum* but is not antigenically identical, so cross-immunity between pinta and syphilis is only partial.

NON-PATHOGENIC TREPONEMES

Several commensal treponemes occur on the buccal and genital mucosa and may cause confusion in the diagnosis of syphilis by dark field examination. They are a heterogeneous group and have not been adequately characterised. Best known among them is the oral spirochete, *T.denticole,* which can be readily cultivated. Treponemes also occur on the surface of gastric and colonic epithelium in human beings and animals.

BORRELIA

Borreliae are large, motile, refractile spirochetes with irregular, wide, open coils. They are usually 5–30 μm