Spirochaetes

spirochaete derived from Greek word for coiled hair

- bacterial cells which are
  - extremely narrow
  - elongated
  - cylindrical in shape
  - spiral with tight coils with tapered ends
- possess endo- or internal flagella
  - number varies according to the species
- actively motile also exhibit rotational movement

- spirochaetes possess some bacterial cell structural characteristics which are
  1. similar to typical Gram negative organisms
     - several characteristics
  2. different from Gram negative organisms including
     a. lack of cell wall lipopolysaccharide
     b. inability to stain readily by commonly used stains
        - few specific species are stainable by
          a. modified Gram's stain
             - as Gram negative cells
          b. Wright's stain

Genera of spirochaetes associated with human infections

- are
  1. Treponema
  2. Borrelia
  3. Leptospira

Treponema

- composed of pathogenic and non-pathogenic organisms

Non-pathogenic species consist of

1. human bacterial normal flora detectable in the mouth and genital tract

2. saprophytic species

- consist of laboratory strains of pathogenic species
  - used in laboratory studies
    a. Reiter's strain of *Treponema pallidum*
       - antigenically related to pathogenic *T. pallidum*
       - can be grown in artificial media
         - requires anaerobic incubation
    b. Nichol's strain of *T. pallidum*

Pathogenic species of Treponema

- previously 1. *Treponema pallidum*
  2. *T. pertenue* 3. *T. carateum*
- re-classified as sub-species of *T. pallidum*
- other species associated with human disease include *T. denticola* as causative agent of infections in the mouth
- all Treponema species or sub-species are similar in morphology and antigenic composition
  - cause cross reactions in serological tests
- differentiated by a. geographical location
  b. clinical manifestations c. genetic characteristics

Treponema pallidum pallidum

- not stainable by Gram's stain
  - not detectable in specimens by Gram's staining and microscopy
- may be visualized by special staining methods and microscopes including
  1. dark field microscope
  2. fluorescence staining and microscopy
  3. special staining in infected tissues and microscopy
  4. electron microscope

Growth of *T. pallidum pallidum* in the laboratory

- does not grow in artificial culture media
- live organisms can be inoculated in various parts of laboratory animals for propagation
  - spectrum of manifestations of disease observed in infected humans rarely develops in the animal

Physical properties

- delicate organism
  - loses viability rapidly when exposed to
    a. dry conditions
    b. heat
    c. low temperatures including 0° to 4° c for more than 2 days

Antigenic properties and antibodies of *T. pallidum pallidum*

- immune system is stimulated during infection
- exact antigenic components are not clearly identified
- detectable distinct antibodies are produced in response to infection including

1. antibody which reacts with **cardiolipin**
   - cardiolipin is a lipid compound in beef heart muscle
   - antibody is referred to as
     a. Wasserman's
     b. reagin
     c. lipoidophil
     d. anticardiolipin antibody
2. **antitreponemal antibody** which is antibody formed in response to a specific treponemal antigen

Some characteristics of *T. pallidum pallidum* associated with pathogenicity

- does not possess common virulence factors found in other pathogenic bacteria
- specific virulence factors are not identified
- can survive for a long time in patients without treatment
  - possibly through various protective mechanisms against detection and clearance by cells of the host's immune system
- antibodies produced in response to infection are not efficient in elimination of *T. pallidum pallidum*

Clinical implications of *T. pallidum pallidum*

- natural infection is limited to humans
- causative agent of syphilis
  - in the absence of adequate treatment syphilis
    - is a chronic illness
    - produces a wide range of severe manifestations
    - is associated with severe long term complications

Transmission of *T. pallidum pallidum* depends on the presence of organisms in the blood and syphilitic lesions

1. **sexual** transmission
   - as venereal disease or STD or STI
   - transmission rate depends on the stage of the illness
2. **vertical** transmission from infected pregnant female to the expected baby
3. **blood transfusion**
   - can occur through transfusion of donated blood containing the organism into a susceptible recipient

Sexually transmitted *T. pallidum pallidum*

- infectious lesion in the majority is on the skin or mucosal surface of the external genital organs
- entry into a susceptible person is through broken skin or mucous membrane
- multiplication occurs at the site of entry
- incubation period follows during which the person is not infectious

manifestations

- change as the disease progresses
- basis for classification of syphilis into
  1. primary 2. secondary 3. tertiary
  4. late syphilis

Primary syphilis

- characterized by
  a. localized invasion of mucus membranes
  b. relatively rapid multiplication of the organism
  c. initial dissemination through lymphatics and blood circulation
- manifestations occur within 10 to 90 days after exposure
- main lesion is an ulcer referred to as the primary sore or chancre or hard chancre
  - exudate contains *T. pallidum pallidum*

chancre

- starts as a papule
  - commonest site is on the surface of external genital parts
  - ulcerates and forms a painless ulcer with clearly defined margin
- single lesion occasionally multiple
- associated with painless enlarged inguinal lymph nodes in most cases
- heals spontaneously in 3 to 8 weeks without treatment
  - the organisms are not necessarily eliminated

Secondary syphilis

- a large number of spirochaetes characterized by resulting in
  - widespread dissemination of infection causing marked invasion of
    - the blood circulatory system
    - other tissues and various organs
- varied manifestations including
  1. skin rash
  2. lesions on the mucous membranes and ulcers in the mouth
  3. generalized lymph node enlargement
  4. small swellings described as plaques on various parts including the skin and mucosal surfaces
     - can develop into wart-like lesions referred to as *condylomata lata*

- uncommon manifestations including inflammatory processes involving bones joints possibly eyes
- lesions of secondary syphilis contain numerous *T. pallidum pallidum*
- possible outcome
    a. healing in the absence of treatment
    b. development of asymptomatic illness referred to as **latent syphilis**
    c. progression to tertiary syphilis

Tertiary syphilis

- develops approximately 3 to10 years after the primary lesion
- *T. pallidum pallidum* is rarely detected in lesions
- manifestations include small chronic inflammatory swellings on various tissues and organs
  - commonly observable on the
    a. skin b. mucous membranes c. bones
    - swellings referred to as **gummas**
    - skin gummatous lesions may ulcerate

Late syphilis

- manifests 10 to 20 years after primary disease
- involve mainly

1. **cardiovascular system** majority as
   - inflammation and other abnormalities
   - aorta including the aortic valve is more commonly affected
2. **central nervous system**
   - generally referred to as **neurosyphilis**
   - associated with abnormalities related to the function of affected parts
   - manifestations include
     a. abnormal gait
     b. trophic changes of joints
     c. abnormal mental capacity
     d. those due to involvement of meninges and blood vessels

Latent syphilis

- dormant disease without clinical manifestations
- detectable by serological tests
- capable of progression to cardiovascular disease or neurosyphilis in the absence of treatment

Congenital syphilis

- transmission can take place any time throughout the pregnancy
  - may be as early as the 10th week or at the time of delivery
  - associated with septicaemia in the foetus and widespread dissemination

manifestations of congenital syphilis

- include
  - a. death of fetus
    - may be associated with a miscarriage
  - b. developmental abnormalities
  - c. baby born with latent infection or manifestations which develop anytime within the first two years including
    - failure to thrive
    - skin rash
    - nasal and other abnormalities

Laboratory investigation of syphilis

specimens according to manifestations include

1. exudate from infected tissues
2. blood
3. cerebrospinal fluid
4. infected tissue

examination procedures

- applied to detect the organism or antibodies formed in response infection
  1. **detection of *T. pallidum pallidum***
     a. in unstained freshly collected fluid or scrapings from a chancre or ulcerated lesions of secondary syphilis
        - examined by **dark field microscope**

- dark field microscopy
  - performed promptly and repeatedly if necessary
  - *T. pallidum pallidum* is observable as spiral organism with characteristic motility

b. **fluorescence staining** in exudates with antibody attached to fluorescent stain and examination by fluorescence microscope
   - **immunofluorescence staining** technique

c. specific staining techniques for *T. pallidum* in infected tissues and microscopic examination

2. serological tests for syphilis involve

- detection of antibodies in patient's serum generally and cerebrospinal fluid in suspected neurosyphilis
- do not distinguish syphilis from infections by other pathogenic Treponema species or sub-species

types of tests

a. non-treponemal tests

- detect the anticardiolipin antibody include
  1. Venereal Disease Research Laboratory (VDRL)
  2. Kahn test
  3. Rapid Plasma Reagin (RPR)
- most sera become positive approximately 10 to 14 days after appearance of the chancre

associated with

a. false negative results
   - may occur in early primary and late stages of syphilis

b. false positive results
   - may be due to other infectious and non infectious diseases

positive in all patients with secondary syphilis

used as screening tests
- positive results are subjected to confirmatory tests

sera of patients testing positive and are confirmed positive become negative after successful treatment
- may be used to monitor response to treatment

b. **Treponemal tests for syphilis**

- detect the specific antibody to treponemal antigen
- associated with fewer false positive reactions
- most patients with sera which test positive tend to remain positive after completion of successful treatment

tests include

1. *T. pallidum* haemagglutination assay (TPHA)
2. Fluorescent Treponemal antibody absorption test (FTA-ABS)
3. ELISA
4. *T. pallidum* immobilization test or TPI
   - has several disadvantages including use of live treponemes

other tests include gene detection tests

Antimicrobial susceptibility of *T. pallidum pallidum*

- susceptible to a wide range of antimicrobial agents
- more commonly used for treatment
  - **penicillin** various preparations
    - mostly used is **benzathine penicillin**
  - others tetracycline erythromycin
    - a. choice b. dose c. duration
    - d. routes of administration

      all depend on patient factors and stage of syphilis

Prevention of *T. pallidum pallidum* infection

1. **sexually transmitted infection**
   - methods of prevention of STI and STD in general are applied
   - screening clients with other STDs for syphilis and giving appropriate treatment if infected
2. **congenital syphilis**
   - antenatal screening of expectant females
   - prompt diagnosis
   - adequate treatment of infected expectant females
3. **blood transfusion**
   - screening all donated blood for *T. pallidum* before use and discarding if infected