

Mycobacterium Tuberculosis

- Are rod shaped, obligate aerobic bacteria.
- They are difficult to stain, but once stained resist decolourization with acid and are therefore called **acid- fast bacilli**.
- The **acid fastness** of the organism is due to the **high lipid** content of their thick cell wall (up to 60% of the cell wall content).
- They **can't be stained by Gram's stain**.
- It can be stained by a special stain; **Ziehl Neelsen (Z.N.) stain**.

Mycobacteria that cause disease in man are:

Mycobacterium tuberculosis complex (MTB), it includes:

1. ***Mycobacterium tuberculosis***: causes tuberculosis (TB) in man. Human is the only reservoir. Transmitted by air borne particles from patients with open pulmonary tuberculosis.
2. ***Mycobacterium bovis***: is the principle cause of tuberculosis in cattle, may be transmitted to man by drinking contaminated milk from infected cattle (zoonosis).

Virulence factors:

The organism produces disease by its ability to **survive and multiply within the macrophages**.

Disease:

- **Primary tuberculosis** is usually acquired via the respiratory tract.
- It starts with inhalation of the organism into the alveoli.
- Initially, the organism is phagocytosed and removed to regional lymph nodes where it replicates and generally kills the phagocytes.

- *M. tuberculosis* circulates and replicates until an effective cell-mediated and tissue hypersensitivity response occurs. Outcome is dependent on the individuals' immune system.

The potential fates of engulfed bacilli:

1. Latent–Dormant tuberculosis:

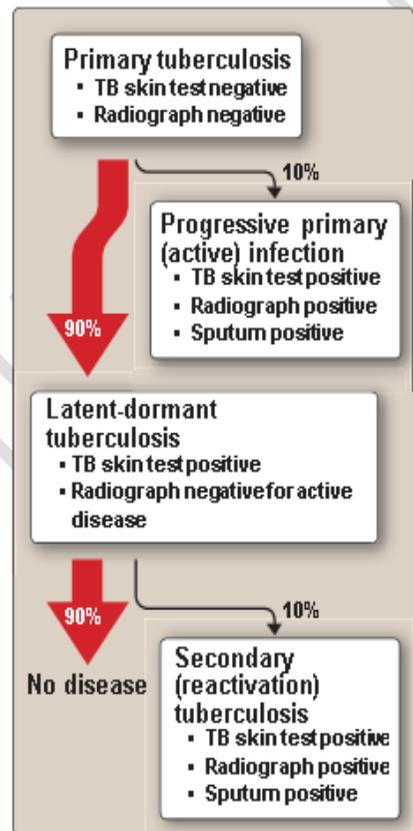
Most (90%) individuals with a primary infection are asymptomatic, and radiograph negative for active tuberculosis (latent infection) and are detected by a positive tuberculin skin test (TST).

2. Progressive primary (active) infection:

(10 % of infected adults). Immediate disease occurs in individuals who cannot mount a strong cell-mediated immune response.

3. Secondary tuberculosis

(**Reactivation**): Proliferate after a latency period. This occurs most commonly in previously sensitized individuals with a weakened immune response (e.g., malnutrition, immunotherapy for other diseases).



Clinical forms of tuberculosis:

- Pulmonary TB: it is the most common clinical form.
- Extra pulmonary TB: affecting other organs e.g. meninges, kidney or bone.

Oral manifestations of tuberculosis:

- Tuberculous lesions of the oral mucosa: include Oral ulceration, granulomas and fissures.
- Cervical lymphadenitis; with the formation of an abscess

and sinus (cold abscess).

- Periapical granuloma and bone infections: secondary tuberculous osteomyelitis may involve the maxilla or mandible.

Laboratory Diagnosis

1. Staining and microscopic examination of specimen according site of infection e.g. sputum, with: Acid fast stain (Z.N stain), and Auramine-rhodamine stain.
2. **Culture on selective media** e.g. Löwenstein-Jensen agar.
3. **Nucleic acid amplification:** for rapid & direct detection of DNA of mycobacteria in clinical samples.
4. **Tuberculin skin test (Mantoux):** is use for diagnosis of latent tuberculosis. Groups that should be screened with PPD skin test include people with HIV infection, close contacts of patients with active tuberculosis, healthcare workers and intravenous drug users.

Test interpretation: Purified protein derivative (PPD) was injected intradermally. It is read 48 to 72 hours later for the presence and size of an area of induration at the site of injection.

Positive skin test if:

- ≥ 5 mm: in HIV infected, immunosuppressed, or anyone who have had contact with infectious individuals.
- ≥ 10 mm: in high-risk population e.g. health care workers, IV drug users.
- ≥ 15 mm: in Persons with no risk factors.

Treatment

Multidrug therapy is used to prevent the emergence of drug-resistant mutants during the long (6- to 9-month) duration of treatment;

- **First-line drugs:** This includes four drugs, isoniazid, rifampin, pyrazinamide, and ethambutol.

- **2nd line drugs:** For the treatment of multidrug resistant (MDR) organisms usually involves the use of four or five drugs, including aminoglycosides, ciprofloxacin, amikacin, ethionamide, and cycloserine.

Prevention

A. Immunoprophylaxis (Vaccines)

1. **Bacille Calmette Guerin (BCG) vaccine:** is live attenuated vaccine prepared from **bovine strain** (*bovine strain is genetically identical to the human strain*). It is given to children I.D in **first year of life**.
2. **Recombinant vaccine:** By **recombinant DNA** technique.

B. Chemoprophylaxis:

For Latent (asymptomatic) tuberculosis infections with:

- INH for 6-9 month or
- INH and rifampicin for 3 month.

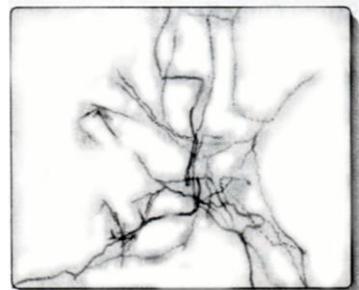
C. Pasteurization of milk: preventing *M. bovis* infection.

ACTINOMYCES

• Characteristics:

Gram positive bacilli, anaerobic, tend to form branching filaments *e.g. Actinomyces israelii*

- Epidemiology: are normal bacteria flora in oral cavity, upper respiratory tract, gastrointestinal tract and female genital tract.



Disease: Actinomycosis

- It is a chronic opportunistic infection.
- When the normal mucosal barrier is disrupted by local trauma, the organism may invade the deep tissues,

where it finds anaerobic condition, resulting in suppurative infection.

Site of infection:

- Face, neck abscess: near lower jaw following tooth extraction or oral surgery (majority of cases).

- **Clinical findings:** Actinomycosis appears as a hard multiple abscesses that drain pus through sinus tracts; which contain **microcolonies** of the organism **called sulphur granules** (yellow or orange granules). Sulfur granules are masses of filamentous organisms bound together by calcium phosphate.

- **Laboratory Diagnosis of Actinomycosis:**

1. **Macroscopic examination of purulent exudate:** sulfur granules can be seen macroscopically in the exudates.
2. **Gram's stain smear:** crushed sulfur granules between two glass slides shows Gram-positive branching bacilli.
3. **Culture:** Culture on **anaerobic** medium, Identification by: B.R

Treatment

- Surgical drainage of the abscess.
- penicillin is the antibiotic of choice.

ANAEROBIC GRAM NEGATIVE BACILLI

Classification:

The most important genera are:

- 1- Prevotella
- 2- Porphyromonas.

• **Epidemiology:**

Anaerobic Gram negative bacilli are found in the mouth, gastrointestinal tract, upper respiratory tract, and female genital tract of healthy individuals as a part of the normal commensals.

• **Diseases:**

These bacteria cause **opportunistic infections:**

- When they traslucate to sites other than their natural habitat .**Or**

- In a host with immunocompromised immune state e.g. surgery, trauma, or chronic disease.

*Foul smelling exudate is characteristic for anaerobic infections.

Features of anaerobic Gram negative bacilli

	Natural habitat	Disease
Prevotella	- Mouth - Respiratory tract	- Dental infection - Lung abscess. - Brain abscess
Porphyromonas	Mouth	- Dental infection e.g. gingival and periapical tooth infection

• **Laboratory Diagnosis of Gram negative anaerobic infections:**

1. **Gram's stain Smear of exudates for lesion.:** Gram negative bacilli and pus cell.

4. **Culture:** on **anaerobic** medium, Identification of culture by: B.R.

• **Treatment:**

Clindamycin and metronidazole are the drugs of choice for treatment of anaerobic infections.

Fusobacterium (Fusiform bacilli)

- **Characteristics** Pleomorphic Gram -ve bacilli. They are normal flora of the mouth.
- **Disease:**
 1. **Trench mouth** (ulcerative gingivostomatitis): together with normal spirochaetes of the mouth (Borrelia. vementi).
 2. **Vincent's angina:** when tonsils involved.

ANAEROBIC GRAM POSITIVE BACILLI **Lactobacilli**

- Lactobacilli are major members of normal flora of the vagina, mouth, stomach and small intestine.
- Play a role in pathogenesis of dental caries.

ANAEROBIC GRAM NEGATIVE COCCI **Veillonella**

It is the earliest anaerobes that colonize the mouth and found principally in dental plaque.

SPIROCHAETES

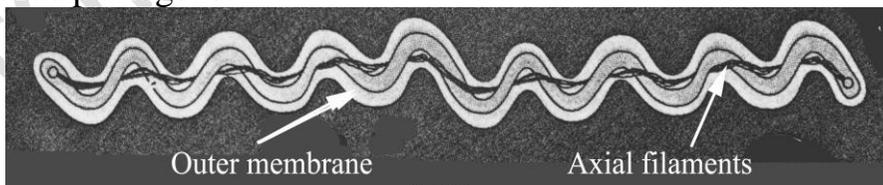
Treponema, Borreliae

• Characteristics:

- Are Gram negative spiral shaped motile organisms.
- The characteristic **shape** and **movement** of the organism is due to internal flagellae, immediately under the outer membrane called **axial filaments**, which are attached to each end, and are intertwined along the length of the spirochaete, producing characteristic motility that consists of rapid rotation about its longitudinal axis and bending.
- **Treponema**, are too thin that they **don't stain** by ordinary stains, and difficult to be seen by ordinary light microscope.

They can be seen only by:

- ▶ Silver impregnation methods (Fontana stain).
 - ▶ Dark-field microscopy.
 - ▶ Immunofluorescent stain.
- **Borreliae** are larger, can be stained with Gram's and Giemsa stains and can be seen by the ordinary light microscope.
 - Some spirochetes are free living; some are part of the normal flora of mouth, intestinal tract, or genital tract. Others are true pathogens.



two genera are of medical importance:

- 1- **Treponema e.g** : *Treponema pallidum*: causes syphilis.
2. **Borrelia e.g** : *Borrelia vincenti*: cause ulcerative gingivostomatitis (vincen't angina).

Treponema pallidum

Disease caused by T.pallidum: Syphilis

Mode of transmission:

- a. T pallidum is transmitted by **sexual contact** with lesions of skin and mucous membrane (genitalia, mouth, and rectum) containing spirochaetes.
- b. It is also transmitted **transplacentally** from pregnant mothers to their fetuses.
- c. Rarely, through **blood transfusion**

Congenital syphilis

T. pallidum can be transmitted through the placenta to a fetus
Infection can cause:

- a. Abortion.
- b. still birth, or
- c. Congenital syphilis:
 - Early congenital syphilis: manifestations appear before the age of 2 years which are similar to secondary syphilis; including mucocutaneous lesions.
 - Late congenital syphilis: the disease manifested by Hutchinson's triad: notched teeth, interstitial keratitis, and eighth-nerve deafness.

Treatment: Penicillin: is the drug of choice.

BORRELIA

Borreliae are irregular wide spirals , highly flexible, and motile.

Borrelia vincentii

- **Natural habitat**: *B. vincentii* is commensal of the mouth.
- **Pathogenesis**: Under certain conditions, particularly injury to mucous membrane, nutritional deficiency, or infection e.g. Herpes simplex *B. vincentii* together with anaerobic fusiform bacilli (fusobacteria) will flourish and increase in number.
- **Disease**: **ulcerative gingivostomatitis (trench mouth or Vincent's angina)**
- **C/P**: Mouth ulcers are formed on the tonsils and the gum with pseudomembrane containing pus cell and necrotic tissues.
- **Laboratory Diagnosis of Vincent's angina**:
 1. **Specimen**: swab from pseudomembrane.
 2. **Gram's stain**: Gram-negative spiral rods, with 3-10 spirals (***B. vincentii***), Gram negative pleomorphic bacilli (**fusobacteria**), and large number of pus cells.
 3. **Culture**: deep column of broth enriched with ascitic fluid, incubated anaerobically.
- **Treatment**: penicillins

Candida albicans.

□ **Characteristics:** Gram positive oval budding yeast cells.

- **Natural habitat:** It is one of the normal flora of skin, mouth, gastrointestinal tract and female genital tract.

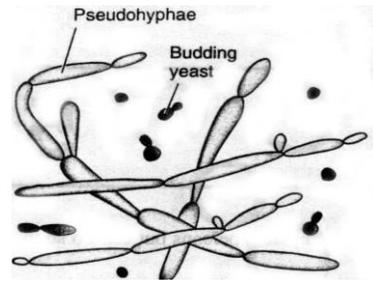


Fig .34. *Candida albicans.*

• **Pathogenesis:**

Infections with candida usually occur in the following conditions:

- **Patients with impaired immunity** e.g. AIDS, diabetes, extreme of age, pregnancy, use of corticosteroids or immunosuppressive drugs, cancer, burns, and skin truma.
- **Prolonged antibiotic therapy:** destroy the balance of normal flora, allowing candida to overgrow and disseminate to bloodstream causing systemic infection.

• **Diseases caused by candida albicans :**

1. **Oral thrush:** whitish pseudomembrane lesion composed of epithelial cells, yeast on tongue, lips, palate, gums. Spread of infection to G.I.T, lungs, skin, or other areas can occur.
2. **Skin & nail , systemic infections:**

Laboratory Diagnosis of *C. albicans* Infection

1. **Gram's stained film:** Gram'+ve budding yeast cells & pseudohyphae
2. **Culture:** Sabouraud's dextrose agar,.
3. **Antigen detection in specimen:** by latex agglutination, ELISA

Treatment

1. **Oral thrush, skin, mucocutaneous infections:** topical nystatin + oral ketoconazole, or fluconazole.
2. **Systemic candidiasis :** Amphotericin B and Flucytosine.

Dental Plaque

- Dental plaque biofilm is a microbial community which develops on soft and hard-tissue surfaces of the teeth.
- The microorganisms that form the biofilm are almost entirely bacteria (mainly streptococcus and anaerobes),
- The microorganisms present in dental plaque are all naturally present in the oral cavity, and are normally harmless.
- However, failure to remove plaque by regular tooth brushing allows building up in a thick layer.
- Plaque build up can also become hardened and calcified to form calculus.
- If plaque not removed regularly, it can lead to dental cavities (caries) or periodontal problems (such as gingivitis).

Dental caries

Dental caries is the localized destruction of the tissues of the tooth by acid produced from the bacterial degradation of fermentable sugars.

Microbial etiology of caries

- *Streptococcus mutans* is the first important colonizer on the surface of teeth, especially in people that eat a high sucrose (sugar) diet.

- These bacteria will break down the sugar and produce **extracellular polysaccharide** (glycocalyx) that enable the bacterial cells to stick onto the surface of the tooth.
- When this sugar is broken down, a lot of lactic acid will be produced.
- lactic acid increases the level of acidity in the mouth, which will aid in the growth of lactobacilli.
- The crevices between the teeth and gums are microenvironments with low levels or an absence of oxygen, thus favoring the growth of anaerobic microbes.
- Next in the microbial succession are the **actinomycetes**, *Veillonella* , *spirochaetes* and *fusobacteria*.

Gum disease (periodontal disease)

Gum disease (periodontal disease) means infection or inflammation of the tissues that surround the teeth.

Depending on the severity, gum disease is generally divided into two types - gingivitis and periodontitis:

1. Gingivitis means inflammation of the gums. most cases of gingivitis are caused by plaque.

2. Periodontitis occurs if gingivitis becomes worse and progresses to involve the tissue that joins the teeth to the gums (the periodontal membrane).