Corynebacterium diphtheriae

C. diphtheriae grows best under strict aerobic conditions. It is Gram positive and pleomorphic.

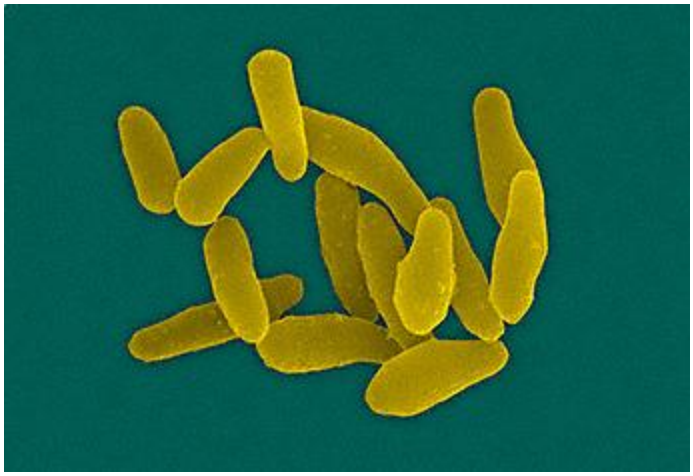

Figure : Corynebacterium diphtheriae. Rod,clubed-shaped Bacterium (SEM x24,000)

Colonization of the upper respiratory tract (pharynx and nose) and less commonly skin with *C. diphtheriae* can lead to diphtheria. The organism does not produce a systemic infection. However, in addition to a pseudomembrane being formed locally, systemic and fatal injury results primarily from circulation of the potent exotoxin (diphtheria toxin).

The latter begins over a period of a week. Thus treatment involves rapid therapy with anti-toxin. The gene for toxin synthesis is encoded on a bacteriophage (the tox gene). Corynebacteria that are not infected with phage, thus do not generally cause diphtheria. Diphtheria is now a disease of almost historic importance in the U.S. due to effective immunization of infants (in conjunction with pertussis and tetanus, DPT vaccine) with a toxoid (inactive toxin) which causes production of neutralizing antibodies. However, colonization is not inhibited and thus *C. diphtheriae* is still found in the normal flora (i.e. a carrier state exists). Immunity can be monitored with the Schick skin test. Treatment in non-immune individuals primarily involves injection of anti-toxin. Antibiotics are also administered at this time.

C. diphtheriae are identified by growth on **Loeffler's** medium followed by staining for **metachromatic bodies** (polyphosphate granules, Babes-Ernst bodies). The term

"metachromatic" refers to the color difference of the intracellular polyphosphate granules (pink) compared to the rest of the cell (blue). Characteristic **black colonies** are seen on **tellurite** agar from precipitation of tellurium on reduction by the bacteria. Production of exotoxin can be determined by *in vivo* or *in vitro* tests.

Other organisms which morphologically resemble *C. diphtheriae* ("diphtheroids" which include other corynebacteria and also propionibacteria) are found in the normal flora. Isolates should not be confused with these organisms.

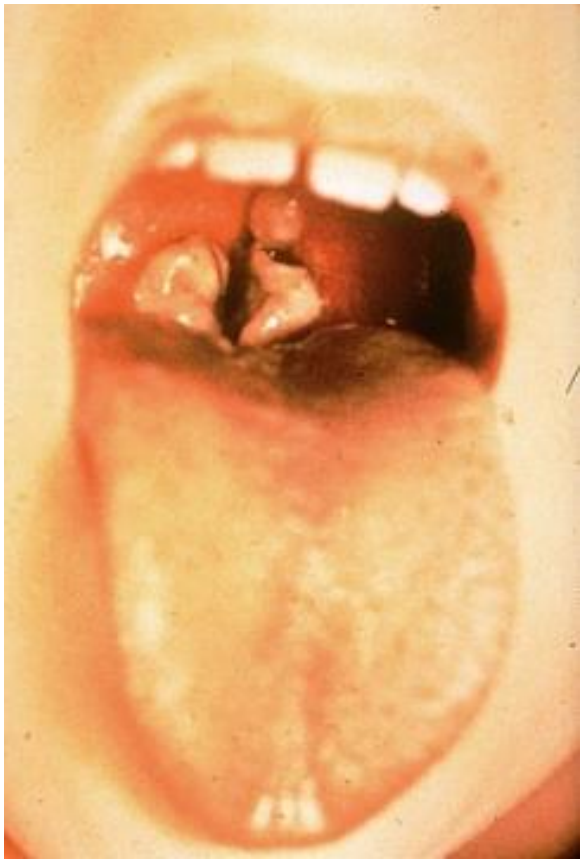

Figure : This child has diphtheria resulting in a thick gray coating over back of throat. This coating can eventually expand down through airway and, if not treated, the child could die from suffocation.

MYCOBACTERIA

Mycobacterium tuberculosis

Mycobacteria are obligate aerobic, acid-fast rods, spread via aerosols when an infected person coughs or sneezes; however, many people who become infected do not show any symptoms of the disease. This is a latent tuberculosis infection and these people are not infectious. The bacteria are kept under control by the immune system. In contrast, other people's immune system cannot control the bacteria and they show overt tuberculosis disease. Some, about 5 to 10%, people with latent tuberculosis may develop active disease many years after infection when their immune system weakens for a variety of reasons. Especially prone to activation of overt disease are people whose immune system has been weakened by HIV infection.

Figure: Computer-generated image of a cluster of rod-shaped drug-resistantMycobacterium tuberculosis. Image based on scanning electron microscopy.

M. tuberculosis bacteria infect the lungs (pulmonary tuberculosis) and are distributed systemically within macrophages where they survive **intracellularly**. Inhibition of phagosome-lysosome fusion and resistance to lysosomal enzymes have both been suggested to play a role. Cell-mediated immunity develops which causes infiltration of macrophages and

lymphocytes with development of granulomas (tubercles). The disease can be diagnosed by skin testing for delayed hypersensitivity with tuberculin (also known as protein purified from *Mycobacterium tuberculosis*. A positive test does not indicate active disease; merely exposure to the organism.

Symptoms of tuberculosis

These depend on the site of infection. In pulmonary tuberculosis, symptoms include:

- a cough that lasts 3 weeks or longer
- chest pain
- blood or sputum (phlegm from deep inside the lungs)
- weakness/fatigue
- weight loss
- appetite loss
- chills
- fever
- night sweats

Diagnosis and identification

A positive skin (Mantoux) test shows whether a person has been infected by the bacteria but people who have been inoculated against tuberculosis using the BCG vaccine can also give a positive test. X-ray imaging is also often used.

The presence of acid fast bacteria in sputum is a rapid presumptive test for tuberculosis. Subsequently, when cultured, *M. tuberculosis* will grow very slowly producing distinct non-pigmented colonies after several weeks. *M. tuberculosis* can be differentiated from most other mycobacteria by the

production of niacin. A rapid alternative to culture is polymerase chain amplification (PCR).

There are also blood tests called interferon-gamma release assays (IGRAs) which are done on blood samples. These are not affected by prior BCG vaccination.

Treatment

Tuberculosis is usually treated for extensive time periods (9 months or longer) since the organism grows slowly and may become dormant. By using two or more antibiotics (including rifampin, rifapentine and isoniazid), the possibility of resistance developing during this extended time is minimized.

Recommended treatment for overt tuberculosis includes some of ten approved drugs taken over a period of six to nine months. These drugs include, as a first line of attack:

- isoniazid
- rifampin
- ethambutol
- pyrazinamide

Vaccination

The BCG vaccine (*Bacillus de Calmette et Guerin*, an attenuated strain of *M. bovis*) has not been shown to be effective in many studies, yet in others a protective effect has been seen. In the United Kingdom, a protective effect of 60 to 80% has been reported. It is not known why the efficacy of BCG is so different in different studies.

Atypicals

The "atypicals" generally infect the immunocompromised host and are thus not transmitted man-man. With the AIDS epidemic, the atypical mycobacteria have taken on new importance with the recognition that the *M. avium* complex (MAC) results in the most commonly associated systemic bacterial infection. Atypical mycobacteria can cause tuberculosis-like or leprosy-like, diseases, and are not susceptible to certain common anti-tuberculous antibiotics.

Mycobacterium leprae

M. leprae is the causative agent of leprosy (Hansen's Disease), a chronic disease often leading to disfigurement.

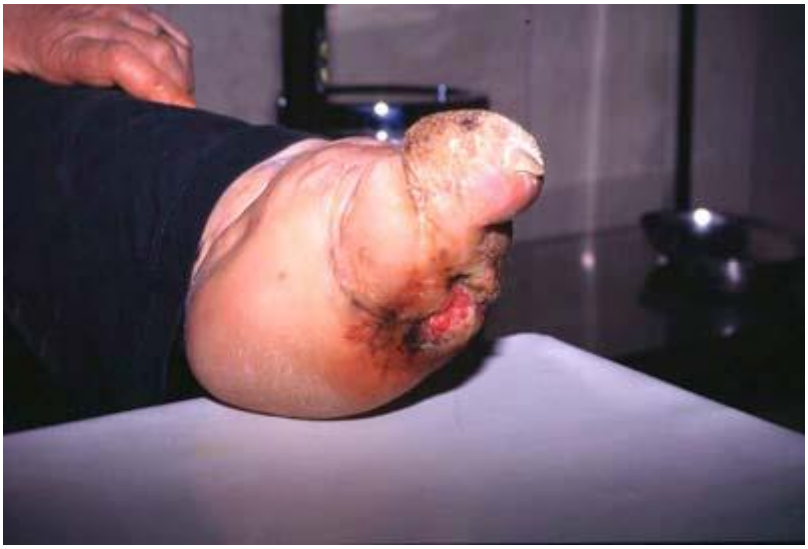

Figure: Azadegan Clinic, Teheran: The foot of a woman that has been grossly disfigured through leprosy infection.

Figure: patient with leprosy

It is rarely seen in the U.S. but common in the third world. The organism infects the skin, because of its growth at low temperature. It also has a **strong affinity for nerves**. In "tuberculoid" leprosy, there are few organisms due to control by active cell-mediated immunity. Treatment with antibiotics (initially dapsone and now multi-drug) is effective and the overall disease incidence worldwide is down. The organism does not grow in culture media. However, it grows well in the armadillo (which has a low body temperature), allowing production of *M. leprae* antigens and pathogenesis studies. *M. leprae* has traditionally been identified on the basis of acid-fast stains of skin biopsies and clinical picture. Lepromin is used in skin testing.

figure : the armadillo.