Chapter 19 - The Gram-Positive Bacilli of Medical Importance*

*Lecture notes are to be used as a study guide only and *do not* represent the comprehensive information you will need to know for the exams.

19.1 Medically Important Gram-Positive Bacilli[1]

The gram-positive bacilli are differentiated in Table 19.1 and **System Profile 19.1.**

19.2 Gram-Positive Spore-Forming Bacilli

Bacillus and *Clostridium* species are endospore forming, gram positive, motile, rod shaped cells. The fact that these bacteria can form spores contributes to their pathogenicity.

General Characteristics of the Genus *Bacillus*

Members of the genus *Bacillus* are Gram positive heterotrophic, aerobic or facultative anaerobic, endospore forming bacteria widely distributed in soils (saprobic) and occasionally animals (fig 19.1a). The *Bacillus* genus is also known for producing antibiotics. The two species of medical importance are *B. anthracis* and *B. cereus*.

Bacillus anthracis *and Anthrax*

B. anthracis is the agent that causes **anthrax** disease. The human form of the disease can be of two forms, depending on the portal of entry. **Cutaneous anthrax** is the most common and least dangerous form and is caused by spores entering the skin through small cuts. The disease causes flu-like symptoms (cough, malaise, fever, achy muscles) and the formation of a malignant pustule at the infection site (fig 19.2). The pustule develops into a black necrotic lesion (**eschar**).

Inhalation of the spores, which then germinate in the lungs, causes a severe and often fatal pulmonary infection called **pulmonary anthrax**. Bacilli growing in the lungs release exotoxins that produce toxemia with a broad pathology including: capillary thrombosis and cardiovascular shock. Virulent strains produce a capsule composed of polyglutamic acid (polypeptide) and three different components as exotoxins. One exotoxin, LF = lethal factor and affects the CNS leading to respiratory failure and death, another promotes growth of the bacteria in the host (PA = protective factor), and the third toxin (EF = edema factor) produces edema.

Livestock contract the disease through abrasions in the mouth while grazing in contaminated pastures. Humans contract the disease from infected animals or their products. Higher reported cases among those associated with animals: vets, farmers, textile mill workers for felt and wool.

Given the lethal nature of pulmonary anthrax, and the fact that the spores can survive extremely harsh conditions (high heat, salt, dehydration, etc.), *B. anthracis* is a threat as a potential biological weapon. The U.S. military even designed a bomb containing *B. anthracis* spores for use during WWII, but apparently never used it (**19.1 MAKING CONNECTIONS**).

Methods of Anthrax Control A vaccination with *Bacillus anthracis* from an unencapsulated strain provides protection in humans and animals. Effective vaccination requires 6 inoculations over 1½ years with yearly boosters. Locally, vaccinations are not given to animals, but it is given throughout the state and can be ordered

Treatment: penicillin as drug of choice; tetracycline as an alternative.
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/anthrax_g.htm

[1] See Table 19.1 for spore-forming species.

See also **Pathogen Profile #1** *Bacillus anthracis*

Other* Bacillus *Species Involved in Human Disease

Bacillus cereus spores very abundant & bacteria is a common contaminant of cooked rice, potato, and meat dishes. Common cause of bacterial food poisoning. Fried rice is a typical source: spores survive boiling; if rice is not refrigerated, the spores germinate and vegetative cells produce an enterotoxin that is stable even if the rice is then fried. **Enterotoxin** causes nausea, vomiting, abdominal cramps, and diarrhea – onset 1-16 hours. No specific treatment – usually self-correcting within 24 hours.

The Genus Clostridium

Clostridium species are gram-positive spore forming rods. The clostridia are anaerobic and catalase negative, Table 19.2. They are found in soil, sewage and organic debris, and some species are commensals that inhabit the human body. They are not normally communicable, but occur when spores are introduced into the body by cuts in the skin. They produce **exotoxins** that play a role in their disease manifestation, such as botulism and tetanus.

The Role of Clostridia in Infection and Disease

Clostridial diseases are of two (2) types:

1. wound and tissue infections: myonecrosis, antibiotic-associated colitis, tetanus
2. food intoxication: perfringens and botulism

The diseases caused by Clostridial species relies on toxin production that act on specific cellular targets.

Gas Gangrene/Myonecrosis

Gas gangrene/myonecrosis results from a mixed bacterial infection. The primary etiologic agent is ***Clostridium perfringens*** (also *C. septicum* and *C. novii*), streptococci and peptococci are also involved.

Clostridium perfringens is an encapsulated nonmotile, spore-forming G+ rod. Since it is an anaerobe, it requires low oxygen concentrations, and so they do not often reproduce in the blood, but in tissues with low oxygen concentrations: for example, gastrointestinal tract pinched off by hernia and regions with poor circulation (diabetes, severe peripheral arteriosclerosis, amputations, deep wounds). Spores and organisms inhabit soil, water, mammalian intestinal tract and sewage, raw meats, fish and poultry. Isolated from the skin of 45% of uninfected persons, and in gastrointestinal tract of 35% of the population.

The disease is characterized by lymph and blood invasion, necrosis of tissue (fig. 19.4, ulcerating lesions and the formation of gas bubbles beneath the skin and within muscles (fig 19.3). *Clostridium perfringens* produces several exoenzymes including lecithinase, hyaluronidase and hemolysin. Lecithinase dissolves cell membranes and releases toxic cellular enzymes. Hyaluronidase destroys hyaluronic acid of connective tissue. Hemolysin destroys red blood cells. These enzymes contribute to the spread of the disease. The gas is produced as the organism ferments cellular polysaccharides. **Butyric acid** is another product of *C. perfringens* fermentation and gives gas gangrene its characteristic **stench**.

Extent and symptoms of Infection Two forms of gas gangrene – 1) anaerobic cellulitis, the bacteria resides in dead muscle tissue; 2) true myonecrosis, more destructive, toxins produced in one muscle tissue moves to other locations of muscle in the body. It is characterized by blackened necrotic tissue filled with bubbles of gas. Gangrenous infections can also occur as a result of septic abortions.

Treatment and Prevention of Gangrene Cephalosporin and hyperbaric or high oxygen tension therapy (fig 19.5).**Debridement** of dead tissue.

Tetanus, or Lockjaw

Clostridium tetani, an anaerobic, spore-forming, G+ rod, produces a neurotoxin called **tetanospasmin** (fig. 19.6), causing the neuromuscular disease **tetanus**, or lock jaw. It is introduced to the body by accidental puncture wounds, burns, and crushed body parts. Tetanus is most common among geriatric patients and IV drug users. It is a major cause of death for infants world-wide (fig. 19.7).

The Course of Infection and Disease This neurotoxin is taken up by motor neutrons and retrogradely transported to the spinal cord; there the toxin blocks the release of the neurotransmitters glycine and gamma-aminobutyric acid (GABA) from inhibitory interneurons. The absence of this inhibition permits the simultaneous spasms of both agonist and antagonist muscles, producing **muscle rigidity** and convulsions. Characterized by painful cramps, convulsions, labored breathing and spastic paralysis, tetanus occurs when opposing muscles are constantly stimulated to contract (fig 19.6b). Over stimulation of sympathetic nerves causes changes in blood pressure and heart rate. Exhaustion (ATP depletion), shock and death can occur.

As the result of a deep puncture wound, endospores of *Clostridium tetani* commonly found in the soil, germinate into vegetative cells. The damaged tissue provides the anaerobic environment needed. As the vegetative cells multiply, they release exoenzymes causing necrosis. Multiplication rate is slow, requiring 7-14 days for symptoms to appear. (Less than $2.5x10^{-9}$g/kg of body weight is required to kill a human. Therefore, 1.75×10^{-7}g or 0.175 μg of neurotoxin is all that is required to kill a 150-lb. person).

Treatment and Prevention of Tetanus Tetanus is preventable through a vaccination of **tetanus toxoid** – a denatured form of the neurotoxin. It is given in combination with diphtheria and pertussis (**DTaP**). Immunization schedule: 2, 4, 6 and 18 months with a booster at 5 years and additional boosters every 10 years thereafter. Boosters (**Td**) should also be given after persons acquire a deep puncture wound or serious compound fracture.

Treatment:
Antitoxin therapy with **human tetanus immune globulin (TIG)** or **heterologous tetanus antitoxin (TAT)**[2] should be started immediately should signs of tetanus develop. The antiserum contains antibodies against tetanus neurotoxin (passive immunity). However, antibodies in antiserum cannot bind to the neurotoxin which has already bound to neurons. Cleansing the wound and cephalosporin treatment can halt the synthesis of more organisms and more neurotoxin.

See also **Pathogen profile #2** *Clostridium perfringens, Clostridium tetani*

Clostridium difficile-*Associated Disease (CDAD)*

Clostridium difficile, an anaerobic spore-forming rod with fermentative metabolism, is associated with **antibiotic-associated pseudomembranous enterocolitis** (**AAPE**). The bacteria produce two toxins: toxin A (an enterotoxin) and toxin B (a cytotoxin) that are responsible for the pathology. Lab tests are available to test for the presence of these two toxins.

C. difficile is a normal resident of the intestine, but in very low numbers compared to G- flora such as *E. coli*. *C. difficile* is able to superinfect the large intestine when antibiotics have disrupted the balance of other normal flora.

Characterized by diarrhea and ulcerative lesions (fig. 19.8) AAPE is a **major cause of diarrhea in hospitals** and is the second most common intestinal infection after salmonellosis in industrialized countries. Spores are shed in the stool and are VERY EASILY spread to patients and staff. The symptoms are associated with administration of the antibiotics: clindamycin, ampicillin and cephalosporins. Mild cases respond to the withdrawal of antibiotics and replacement therapy for lost fluids. Interestingly, the antiprotozoal drug **metronidazole** (Flagyl™) is effective.

[2] A serum derived from horses; has a much higher incidence of side-effects, especially allergic reaction.

See also **Pathogen Profile #3** *Clostridium difficile*

Clostridial Food Poisoning

Two *Clostridium* species are involved in food poisoning – ***Clostridium botulinum***, which is associated with improper home food canning, and ***Clostridium perfringens,*** most common form of food poisoning.

Epidemiology of Botulinum Food Poisoning *Clostridium botulinum*, is also a G+ motile, strictly anaerobic spore-forming rod. Found in soils, on plants, animals and in water. It also produces a neurotoxin called **botulin**. This toxin is the causative agent of **botulism** poisoning. The bacteria often contaminate foods and under anaerobic conditions (e.g. home canning, canned mushrooms), the vegetative cells produce the neurotoxin, making it a food borne disease. *C. botulinum* and toxin presence are both odorless and tasteless. Besides being commonly found in canned and bottled foods that have not been properly sterilized, it can be found in sausages, fish and hams that do not contain bacterial inhibitors. The neurotoxin can be heat inactivated at 100ºC for 10 minutes.

Pathogenesis of Botulism The ingested toxin (botulin) travels from the intestines to the circulatory system and throughout the body. It prevents the release of acetylcholine at the neuromuscular junction (fig 19.9). In this way, muscle cells are not stimulated to contract, resulting in progressive **flaccid paralysis**. There is medical use for the botulinum toxin, a.k.a. "BOTOX" **19.2 MAKING CONNECTIONS.**

Symptoms appear 12-48 hours after ingestion of the toxin: Blurred vision, progressive weakness, difficulty in chewing or swallowing with eventual death due to cardiac or respiratory paralysis (20-50% of the cases).

Infant and wound Botulism Infants up to 1 year old are susceptible to **infant botulism**. This is a case of bacterial infection. Apparently, the spores can germinate in infants' intestines and the vegetative cells produce the neurotoxin. One of the first symptoms is the inability of the baby to hold its head erect (sometimes called "floppy baby syndrome"). It has trouble suckling and swallowing; the child's limbs become paralyzed; death can result from respiratory paralysis.

In wound botulism the spores enter the same way as tetanus, but instead symptoms are similar to food-borne botulism. Wound botulism is seen more in black tar heroin users.

Treatment and Prevention of Botulism Antibiotics are unnecessary because there is no active infection – only the toxin. There is no vaccine, but there is an antiserum. The antiserum (i.e., antitoxin) contains antibodies that can bind to the botulinum toxin. It is only partially effective once the symptoms appear.

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/botulism_g.htm

Prevention: avoid foods containing spores (honey, corn syrup) and those that promote the germination of spores (spinach). Boil home canned food items for at least 10 minutes. Raw honey should never be fed to infants.

Treatment: antiserum (for the toxin), penicillin for vegetative cells, and respiratory support.

Clostridial gastroenteritis is also caused by *Clostridium perfringens*. Characterized by cramps, abdominal pain, diarrhea, and nausea. This live infection usually has an onset 10-20 hours after ingestion and generally lasts 10-20 hours. A typical source would be food (especially beans) cooked in bulk and stored at improper temperatures.

Differential Diagnosis of Clostridial Species

Includes a variety of lab tests such as stains, growth characteristics on media and biochemical tests. ELISA and PCR are also used.

19.3 Gram-Positive Regular Non-Spore-Forming Bacilli

This group is divided based on morphology and staining characteristics. They are called **regular** because they stain uniformly. The predominant pathogens are *Listeria monocytogenes* and *Erysipelothrix rhusiopathiae*.

An Emerging Food-Borne Pathogen: *Listeria monocytogenes*

Listeria monocytogenes is a G+ unencapsulated, non spore-forming rod. It is not fastidious and is resistant to cold, heat, salt, pH extremes and bile. It is commonly found in soil and animals (dairy cattle, household pets).

Epidemiology and Pathology of Listeriosis

L. monocytogenes is the etiologic agent of **listeriosis**. Listeriosis is associated with consumption of contaminated milk, cheeses, ice cream and meat. A number of recent epidemics have resulted in huge recalls of meat products. *Listeria* readily survives through long storage and can grow during refrigeration.

Listeriosis occurs in many forms. One form, listeric **meningitis**, is characterized by headaches, stiff neck, delirium and coma. Another form is a blood disease accompanied by a large number of WBC (monocytes) (fig. 19.10). A third form is an infection of the uterus with vague flu-like symptoms.

L. monocytogenes can cross the placenta. If contracted during pregnancy, it may result in miscarriage of the fetus or brain damage in the newborn. It does not appear to be transmissible among humans.

Diagnosis and Control of Listeriosis

It is difficult to isolate the pathogen, must use a cold enrichment, but it can take 4 weeks. Other identification techniques are a positive CAMP test, ELISA and DNA analysis.

Treatment:
Ampicillin and trimethoprim-sulfamethoxazole are first choice drugs for treatment followed by erythromycin. The disease seems to be related to a suppressed immune system, occurring most often in the very young and elderly.
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/listeriosis_g.htm

See also **Pathogen Profile #4** *Listeria monocytogenes*

2. *Erysipelothrix rhusiopathiae* – ***FYI!!!!***

Erysipelothrix rhusiopathiae is a G+ rod widely distributed in animals and the environment. Primary reservoir seems to be the tonsils of pigs. Common portal of entry for human infection is through skin cuts. **Erysipeloid disease** is characterized by swollen, inflamed, dark red skin lesions that burn and itch (fig. 19.11). Rare cases of septicemia and endocarditis do occur. Animal handlers are at highest risk.
Treatment: Penicillin or erythromycin.

19.4 Gram-Positive Irregular Non-spore-forming Bacilli

These bacteria are **irregular** because they stain unevenly, they are pleomorphic. The genus of bacteria with this characteristic are: *Corynebacterium, Mycobacterium,* and *Nocardia*. They all have similar morphological and biochemical traits.

Corynebacterium diphtheriae

Corynebacterium diphtheriae is a aerobic G+, nonmotile, non-spore-forming pleomorphic rod. The cells are club-shaped and occur in palisades (fig. 19.12).

Epidemiology of Diphtheria

Diphtheria is an infectious disease caused by ***C. diphtheriae***. The number of cases have decreased over the years. Many cases occur in non-immunized children living in crowded, unsanitary conditions.

Pathology of Diphtheria

Symptoms are fever, headache, malaise, sore throat and the formation of a pseudomembrane on the mucous membranes of the nose and throat (fig. 19.13). The airway can become obstructed due to growth of bacteria in the pseudomembrane.

Diphtherotoxin and Toxemia Death can result from the exotoxin **diphtherotoxin** acting on the heart (myocarditis) and peripheral nerves. Diphtherotoxin inhibits proteins synthesis and causes the signs and symptoms characteristic of the disease. It is produced by bacteria in the throat, absorbed by mucous membranes and distributed to other organs by the circulatory system, which causes **toxemia**.

Diagnostic Methods for Corynebacterium

Since it can be fatal, the physician must make a preliminary diagnosis and begin treatment if it is suspected. Staining is done to view the cells, test for the presence of antibodies and PCR. It is important to differentiate *C. diphtheriae* from other "diphtheroids" such as *C. xerosis* and *C. pseudodiphtheriticum.*

Treatment and Prevention of Diphtheria

The combination **DTaP vaccine** protects against the disease. It is prepared from a modified non-toxic diphtherotoxin (i.e. a toxoid & is the "D" in DTaP).

Treatment: antitoxin against the diphtherotoxin and the antibiotic erythromycin.

The Genus *Propionibacterium*

Resembles *Corynebacterium* in morphology and arrangement, but can survive anaerobic conditions. ***Proprionibacterium acnes*** is a common resident of pilosebaceous glands of human skin and is involved in the etiology of **acne vulgaris** (severe acne). Acne is also influenced by genetic and hormonal factors. *P. acnes* release lipases which digest excess sebum (oil secretions); the fatty acids produced and bacterial antigens stimulates intense local inflammations which can burst hair follicles.

19.5 Mycobacteria: Acid-Fast Bacilli

Mycobacteria are distinguished by mycolic acids and waxes in their cell wall, and their staining characteristic, **acid fast**. They are resistant to a lot of chemicals used to disinfect microbes. They have a long, slender, almost filamentous morphology (fig. 19.14). Most are strict aerobes. Many people world wide are infected with tuberculosis and leprosy. The NTM (**n**on **t**uberculosis **m**ycobacteria) tend to infect those who are immunocompromised.

Mycobacterium tuberculosis: The Tubercle Bacillus

The **tubercle** bacillus is rod shapes that grow in long strands called cords (fig. 19.15). They do not produce exotoxins or exoenzymes, however, their cord factor makes it difficult to neutralize the bacteria via phagocytosis in a phagolysosome.

Tuberculosis is a chronic infection of the lower respiratory tract. It is characterized by chronic cough, low-grade fever and malaise. The disease is caused by ***Mycobacterium tuberculosis***. *M. tuberculosis* is a slender, acid-fast rod (fig. 19.14) with a high lipid content in the cell wall. It is an obligate aerobe and intracellular parasite. Some strains tend to stick together demonstrating **serpentine growth** (fig. 19.15).

Epidemiology and Transmission of Tuberculosis

Although an ancient disease, there are currently over 8 million people infected each year with approximately 1.6 million deaths. It is transmitted by fine droplets of respiratory mucous suspended in the air. Transmission is through aerosols of patients with the active disease and dairy cattle (unpasteurized milk). The minimum infectious dose for lung infection is around 10 cells. It can survive up to 8 months in this tiny droplet of mucous. People become infected when they breathe in these mucous droplets with the bacterium. If left untreated, the disease can progress very slowly over the lifetime of the patient. Countries with a high standard of living generally have a low incidence.

The Course of Infection and Disease

Clinical tuberculosis is divided into primary, secondary and extrapulmonary tuberculosis.

Initial Infection and Primary Tuberculosis **Primary tuberculosis** is the period during which the patient may be asymptomatic or run a mild fever. After 3 to 4 weeks, the immune system mounts a complex, cell-mediated response. Mononuclear cells infiltrate the lungs and play a role in the formation of specific infection sites called **tubercles**. Tubercles are granulomas with a central core of TB bacilli and enlarged macrophages surrounded by an outer wall of fibroblasts, lymphocytes, and neutrophils (fig. 19.16). This process can arrest the disease however, the centers of the cores can break down and become necrotic, caseous lesions that gradually heal by calcification of normal lung tissue. The patient would test positive to a tuberculin reaction. Many patients recover more or less completely from the primary episode of TB.

Latent and Recurrent Tuberculosis **Secondary tuberculosis** is when the bacilli become dormant but are reactivated weeks, months, or even years later, especially in persons with weakened immune systems. In persons with chronic TB, the tubercles fill with masses of bacilli, expand and drain into the bronchial tubes and upper respiratory tract. The patient experiences more severe symptoms: violent coughing, greenish or bloody sputum, low-grade fever, anorexia, weight loss, extreme fatigue, night sweats, and chest pain. The old name for the disease was *consumption*. Untreated secondary tuberculosis has about a 60% mortality rate.

Extrapulmonary tuberculosis is when the disease spreads to areas other than the lungs. Organs involved include the regional lymph nodes, kidneys, long bones, genital tract, brain and meninges. Untreated tubercular meningitis is invariably fatal, and even treated cases can have a 30% to 50% mortality rate.

Clinical Methods of Detecting Tuberculosis

Testing for recent or past infection or disease uses the **Mantoux test**[3] which gives three reactions: negative, indeterminate, and positive (fig. 19.17). Chest x-rays help verify TB when other tests have given indeterminate results (fig. 19.18). Acid-fast staining of sputum uses the Ziehl-Neelsen method. Cultivation methods are done under strict federal guidelines in approved labs. Rapid tests are also available.

Management and Prevention of Tuberculosis

Active cases are treated with a combination of drugs: INH (isoniazid), ethambutol, rifampin, streptomycin and para-aminosalycylic acid (PAS) for 6-24 months. Prolonged bed rest and wholesome nutrition speed up recovery. Unfortunately, drug resistant strains of *M. tuberculosis* are now present world-wide. Misuse of antibiotics and the rise in HIV cases has lead to the emergence of many resistant strains. Recently, strains called **extensively drug-resistant TB** (**XDR-TB)**[4] have emerged that have resistance to nearly all the traditional drugs.
http://www.cdc.gov/tb/faqs/default.htm

Vaccination with **BCG (Bacillus Calmette-Guerin) vaccine**, derived from a strain of *M. bovis*, has reduced the incidence of TB in developing countries. Although the BCG vaccine is safe, it is generally not recommended in the U.S. due to the low incidence of tuberculosis. However, it is recommended for certain health professionals, military personnel, government workers and missionaries. The vaccination is more effective in children than in adults.

See also **Pathogen Profile #5** *Mycobacterium tuberculosis*

Mycobacterium leprae: The Leprosy Bacillus

Hansen's disease or **leprosy** is caused by ***Mycobacterium leprae***. It is an aerobic, slightly curved rod that is a strict parasite (does not grow on artificial media). The cell walls contain mycolic acid (responsible for acid-fast staining).

The disease itself is characterized by the development of multiple lesions on the skin, often with a loss of sensory perception. This leads to secondary infections and mutilating injuries.

Epidemiology and Transmission of Leprosy

The incidence of leprosy is decreasing world wide, but it is still endemic in some places in the world like Asia, Africa, Korea, and South America. The mechanism of transmission among humans is yet to be verified. Although, in some cases zoonotic infection is suspected in the US. Living conditions seem to be a major factor in contracting the disease.

Leprosy occurs in two major forms (Table 19.3):

1. **Tuberculoid leprosy** (the healing form) consists of discolored lesions which develops (5-20 cm in diameter). The skin is lighter than normal in dark-skinned persons and with reddish patches appearing on the skin of light-skinned individuals (fig 19.20). The lesions are actually the result of cell-mediated immune responses, and this causes tissue damage. Relatively few bacilli and lepra cells are seen. Lepra cells are the infected epithelial cells. This form has fewer complications and is more easily treated than other types of leprosy.

[3] A small amount of purified protein derivative (PPD) obtained from culture filtrates of *M. tuberculosis* is injected intradermally into the forearm.
[4] also called “extremely drug resistant TB”.

2. **Lepromatous leprosy** is the severe and extensive form (fig 19.21). Many lepra cells occur in the multiple lesions. The prognosis is poor. The bacteria prefers less than body temperature (30ºC). Hence, the lesions occur on hands, ears, nose, face and unclothed regions. Nerve involvement also occurs. Advanced lepromatous leprosy causes a loss of sensitivity that predisposes the patient to trauma, mutilation, secondary infections, blindness, and kidney or respiratory failure.

3. A third form known as **intermediate** or **borderline leprosy** can progress in either direction, depending upon treatment and immunological competence. The bacilli are found in areas of necrosis, but rarely elsewhere. The prognosis is fair. The most severe effect of this form is early damage to nerves that control muscles of the hands and feet. Sensory nerve damage can lead to loss of fingers and toes (fig 19.22). Shifts in phases can occur, including remission.

Diagnosing Leprosy

Little is known about the physiology of the cell because it cannot be cultured *in vitro*. Studies in lab animals suggest it is a slow grower with a generation of 12-14 days. The incubation period averages 2 years, but can range from 12 weeks to more than 40 years.

The disease is not highly contagious, although children appear to acquire the disease on briefer contact than adults. The bacteria enter the skin through cuts and abrasions and divide slowly within epithelial and nervous tissue. The disease is prevalent in Africa, Southeast Asia and South America. In the U.S., it occurs in a few isolated pockets (Texas and Louisiana).

Treatment and Prevention of Leprosy

Tuberculoid leprosy requires rifampin and dapsone for six months. Lepromatous leprosy requires rifampin, dapsone, and clofazimine until the number of skin lesions has been substantially reduced (requiring up to 2 years). Then dapsone can be taken alone from 10 years up to life-long treatment.
http://www.cdc.gov/nczved/dfbmd/disease_listing/leprosy_ti.html

Infections by Nontuberculous Mycobacteria (NTM)

There has been a recent rise in opportunistic and nosocomial mycobacterial infections.

Disseminated Mycobacterial Infection in AIDS *Mycobacterium avium* (MAC) cause secondary infection in people with AIDS with a low T-cell count. It enters via the respiratory tract, and can multiply rapidly in body tissues and fluids. Drug treatment includes rifabutin, azrithromycin, and rifampin.

Miscellaneous Mycobacterial Infections *M. marinum* causes swimming pool granuloma (fig. 19.23). *M. paratuberculosis* has been shown to be present in people with Crohn's disease.

19.6 Actinomycetes: Filamentous Bacilli

Actinomycetes are non motile, filamentous rods that may be acid-fast. They are closely related to *Mycobacteria*. The actinomycetes can grow like fungi.

Actinomycosis

Actinomycosis is caused by *Actinomyces* normally living the human oral cavity, tonsil, and intestine, the cervicofacial region of the body. The disease is caused by *A. israelii* (fig. 19.24). Poor oral hygiene is usually the cause.

Nocardiosis

Nocardia brasiliensis is a primary pulmonary pathogen, and *N. asteroids* and *N. caviae* are opportunistic pathogens. Pulmonary nocardiosis is a form of bacterial pneumonia with pathology and symptoms similar to tuberculosis. It can extend from inside the body to outside the body (fig. 19.25).