Atypical Mycobacteria

The atypical mycobacteria are classified into four groups according to their rate of growth and whether they produce pigment under certain conditions

Learning objectives

- To recognize the Runyon classification of atypical Mycobacteria
- To know the diseases caused by Atypical bacteria
- To explain the pathogenesis , clinical features and types of diseases caused by Mycobacterium leprae

Atypical Mycobacteria

Classified by Runyon Classification on basis of

I. Growth rate

II. Pigment production-whether in dark or light

RUNYON CLASSIFICATION

- **Runyon I: Photochromogen**

  Produce a yellow-orange pigment when exposed to light. *M.kansasii, M.marinum, M.asiaticum, M. simiae*

- **Runyon II: Scotochromogen**

  Produce a yellow-orange pigment in the dark

  M.scrofulaceum, M. gordonae, M.szulgai, M. flavescens

RUNYON CLASSIFICATION

❖ **Runyon III: Nonchromogen**

Do not produce pigment. Some may produce very pale yellow, buff, or tan pigment but do not intensify upon light exposure. *M.avium-intracellulare, M. ulcerans, M. gastri, M.haemophilum, M. shimoidae,M.xenopi, M.nonchromogenicum*

❖ **Runyon IV: Rapid Growers**

Give colonies in 7 days. They do not produce pigment

M. fortuitum, M.phlei, M. abscessus, M. chelonae, M.smegmatis, M.vaccae

Atypical Mycobacteria

- Several species of mycobacteria are characterized as atypical, because they differ in certain respects from the prototype, *M. tuberculosis.* For example, atypical mycobacteria are widespread in the environment and are not pathogenic for guinea pigs, whereas *M. tuberculosis* is found only in humans and is highly pathogenic for guinea pigs. The atypical mycobacteria are sometimes called Mycobacteria Other Than Tuberculosis (MOTTS).

Atypical Mycobacteria

The atypical mycobacteria in groups I, II, and III grow slowly, at a rate similar to that of *M. tuberculosis,* whereas those in group IV are “rapid growers,” producing colonies in fewer than 7 days.

Atypical Mycobacteria

- **Group I** organisms produce a yellow-orange–pigmented colony only when exposed to light (**photochromogens),** whereas **Group II** organisms produce the pigment chiefly in the dark (**scotochromogens). Group III** mycobacteria produce little or no yellow-orange pigment, irrespective of the presence or absence of light (nonchromogens).

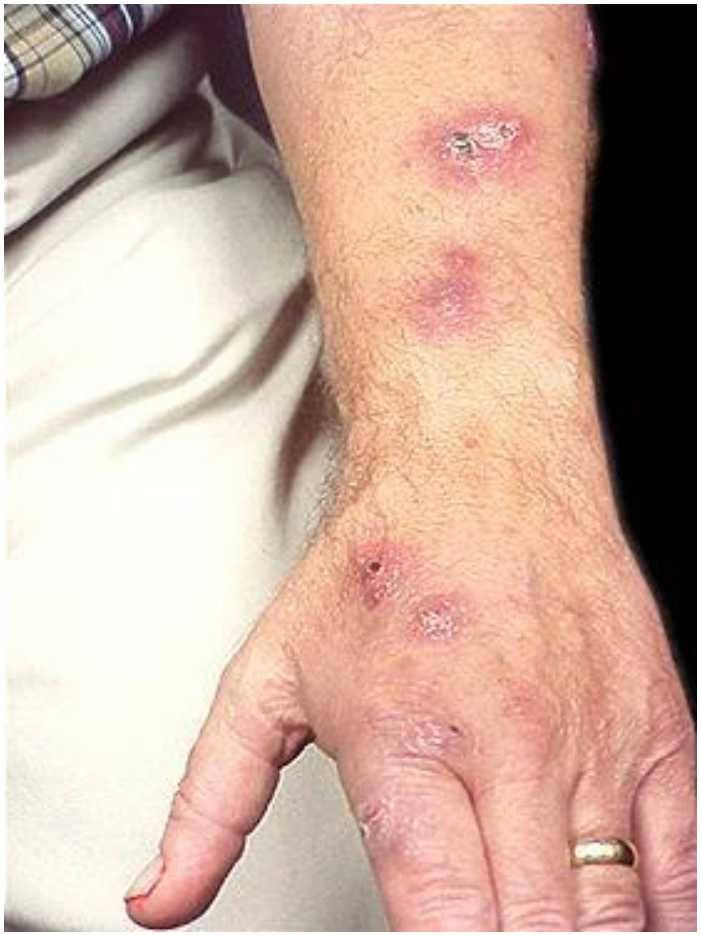
Group I (Photochromogens)

- *M. kansasii* causes lung disease clinically resembling tuberculosis. Because it is antigenically similar to *M. tuberculosis,* patients are frequently tuberculin skin test–positive. Its habitat in the environment is unknown. It is susceptible to the standard anti-tuberculosis drugs.

Group I (Photochromogens)

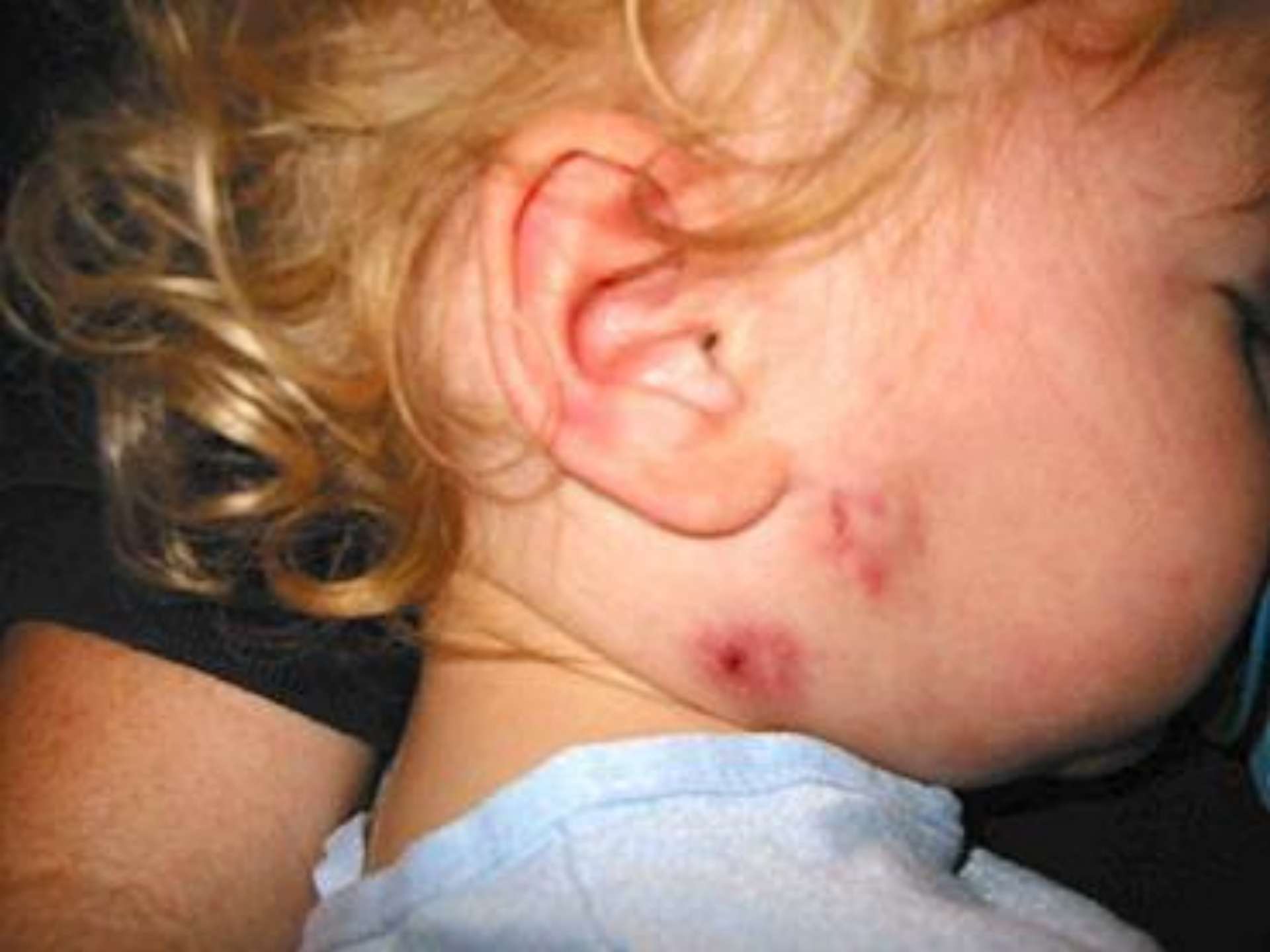
- *Mycobacterium marinum causes "swimming pool granuloma,"*also known as "fish tank granuloma." These granulomatous, ulcerating lesions occur in the skin at the site of abrasions, at swimming pools and aquariums. The natural habitat of the organism is both fresh and salt water. Treatment with a tetracycline such as minocycline is effective.

Fish tank granuloma/ *M.marinum*



Group II (Scotochromogens)

- *M. scrofulaceum* causes scrofula, a granulomatous cervical adenitis, usually in children. (*M. tuberculosis* also causes scrofula.) The organism enters through the oropharynx and infects the draining lymph nodes. Its natural habitat is environmental water sources, but it has also been isolated as a saprophyte from the human respiratory tract. Scrofula can often be cured by surgical excision.



Group III (Nonchromogens)

- *M. avium-intracellulare complex (MAI, MAC)* is composed of two species, *M. avium and M. intracellulare,* that are very difficult to distinguish from each other by standard laboratory tests. They cause pulmonary disease clinically indistinguishable from tuberculosis, primarily in immuno-compromised patients such as those with AIDS who have CD4 cell counts of less than 200/µL. MAI is the most common bacterial cause of disease in AIDS patients.

Group III (Nonchromogens)

- The organisms are widespread in the environment, including water and soil, particularly in the southeastern United States. They are highly resistant to antituberculosis drugs, and as many as six drugs in combination are frequently required for adequate treatment.

Group IV (Rapidly Growing Mycobacteria)

- *Mycobacterium fortuitum-chelonei* complex is composed of two similar species, *M. fortuitum* and *M. chelonei.* They are saprophytes, found chiefly in soil and water, and rarely cause human disease. Infections occur chiefly in two populations:

Group IV (Rapidly Growing Mycobacteria)

- (1)Immunocompromised patients and (2) Individuals with prosthetic hip joints and indwelling catheters. Skin and soft tissue infections occur at the site of puncture wounds. They are often resistant to anti-tuberculosis therapy, and therapy with multiple drugs in combination plus surgical excision may be required for effective treatment. Current drugs of choice are amikacin plus doxycycline.

Group IV (Rapidly Growing Mycobacteria)

- *Mycobacterium abscessus* is another rapidly growing mycobacteria acquired from the environment. It causes chronic lung infections, as well as infections of the skin, bone, and joints. It is highly antibiotic-resistant.
- *Mycobacterium smegmatis* is a rapidly growing mycobacterium that is not associated with human disease. It is part of the normal flora of smegma, the material that collects under the foreskin of the penis

Slow growing mycobacterial species	Disease caused
M.kansaii	Infection of previously damaged lungs or infection in HIV patients
M.malmoense	Infection of previously damaged lungs and cervical adenitis
M.marinum	Fish-tank granuloma and swimming pool granuloma Resistant to INH and PZA
M.ulcerans	Progressive ulcerating skin lesions
M.gordonae	Resistant to INH and PZA

Rapid growing mycobacterial species	
M.fortuitum (saprophytes)	Soil organism that causes prosthetic joint abscesses, injection site abscess, and secondary pulmonary infection
M.chelonei (saprophyte)	Wound infections
M.flavescens	Rarely pathogenic
M.smegmatis-phlei	Found in urine and smegma but have no clinical significance

MYCOBACTERIUM LEPRAE

This organism causes leprosy (Hansen's disease).

MYCOBACTERIUM LEPRAE

- *M. leprae has not been grown in the laboratory, either on* artificial media or in cell culture. It can be grown in experimental animals, such as mice and armadillos. Humans are the natural hosts.

MYCOBACTERIUM LEPRAE

- The optimal temperature for growth (30°C) is lower than body temperature; it therefore grows referentially in the skin and superficial nerves. It grows very slowly, with a doubling time of 14 days. This makes it the slowest-growing human bacterial pathogen. One consequence of this is that antibiotic therapy must be continued for a long time, usually several years.

Transmission

- Infection is acquired by prolonged contact with patients with lepromatous leprosy, who discharge *M. leprae in large* numbers in nasal secretions and from skin lesions. The disease occurs worldwide, with most cases in the tropical areas of Asia and Africa. The armadillo is unlikely to be an important reservoir because it is not found in many areas of the world where leprosy is endemic.

Pathogenesis

- The organism replicates intracellularly, typically within skin histiocytes, endothelial cells, and the Schwann cells of nerves. The nerve damage in leprosy is the result of two processes: damage caused by direct contact with the bacterium and damage caused by CMI attack on the nerves.

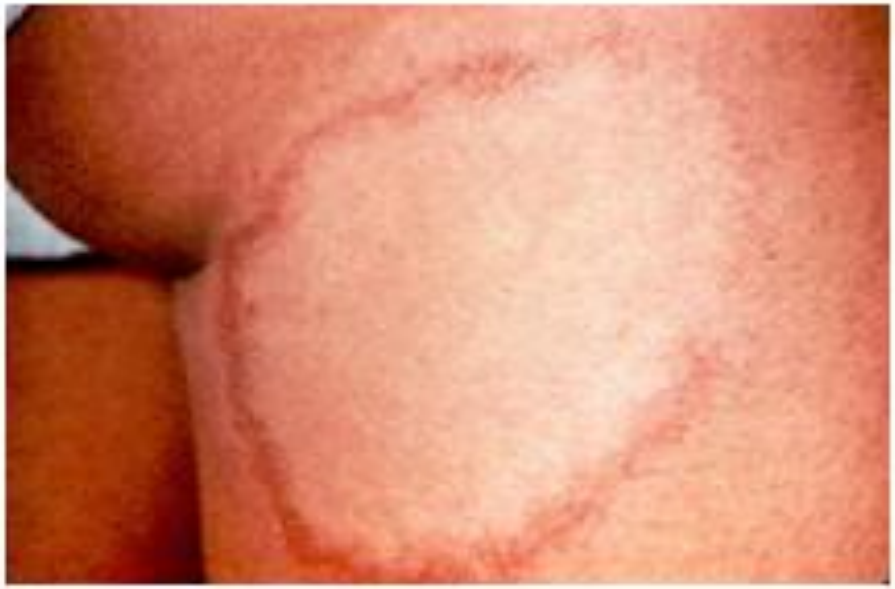
Pathogenesis

- **There are two distinct forms of leprosy-tuberculoid and lepromatous—with several intermediate forms between the two extremes**

Pathogenesis

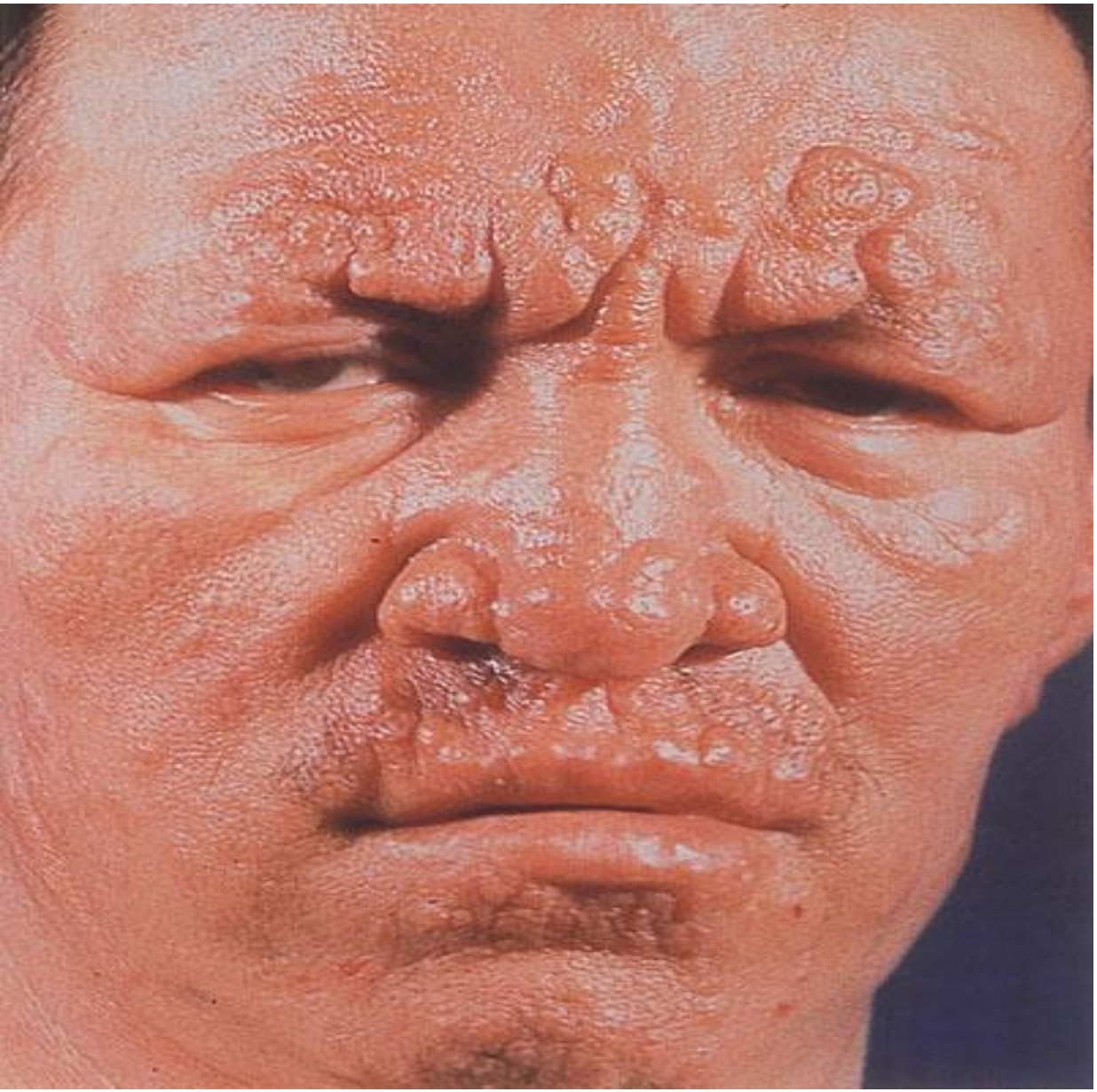
1) In tuberculoid leprosy, the CMI response to the organism limits its growth, very few acid-fast bacilli are seen, and granulomas containing giant cells form. The nerve damage seems likely to be caused by cell-mediated immunity as there are few organisms and the CMI response is strong.

TUBERCULOID



Pathogenesis

(2) In lepromatous leprosy, the cell-mediated response to the organism is poor, the skin and mucous membrane lesions contain large numbers of organisms, foamy histiocytes rather than granulomas are found, and the lepromin skin test result is negative. The nerve damage seems likely to be caused by direct contact as there are many organisms and the CMI response is poor.



Lepromatous leprosy

Clinical Findings

- The incubation period averages several years, and the onset of the disease is gradual. In tuberculoid leprosy, hypopigmented macular or plaque-like skin lesions, thickened superficial nerves, and significant anesthesia of the skin lesions occur

Clinical Findings

- In lepromatous leprosy, multiple nodular skin lesions occur, resulting in the typical leonine (lion-like) facies . After the onset of therapy, patients with lepromatous leprosy often develop erythema nodosum leprosum (ENL), which is interpreted as a sign that cell-mediated immunity is being restored. ENL is characterized by painful nodules, especially along the extensor surfaces of the tibia and ulna.

Clinical Findings

The disfiguring appearance of the disease results from several factors:

- (1) The skin anesthesia results in burns and other traumas, which often become infected;
- (2) Resorption of bone leads to loss of features such as the nose and fingertips;
- (3) Infiltration of the skin and nerves leads to thickening and folding of the skin. In most patients with a single skin lesion, the disease resolves spontaneously.

Clinical Findings

- Patients with forms of the disease intermediate between tuberculoid and lepromatous can progress to either extreme.

Laboratory Diagnosis

- In lepromatous leprosy, the bacilli are easily demonstrated by performing an acid-fast stain of skin lesions or nasal scrapings. Lipid-laden macrophages called “foam cells” containing many acid-fast bacilli are seen in the skin. In the tuberculoid form, very few organisms are seen, and the appearance of typical granulomas is sufficient for diagnosis.

Laboratory Diagnosis

- Cultures are negative because the organism does not grow on artificial media. No serologic tests are useful. The diagnosis can be confirmed by using the polymerase chain reaction (PCR) test

Treatment

- The mainstay of therapy is **dapsone (diamino-diphenylsulfone),** but because sufficient resistance to the drug has emerged, combination therapy is now recommended (e.g., dapsone, rifampin, and clofazimine for lepromatous leprosy and dapsone and rifampin for the tuberculoid form). Treatment is given for at least 2 years or until the lesions are free of organisms. Thalidomide is the treatment of choice for severe ENL reactions.

Prevention

- Isolation of all lepromatous patients, coupled with chemoprophylaxis with dapsone for exposed children, is required.
- There is no vaccine.