

MYCOBACTERIA

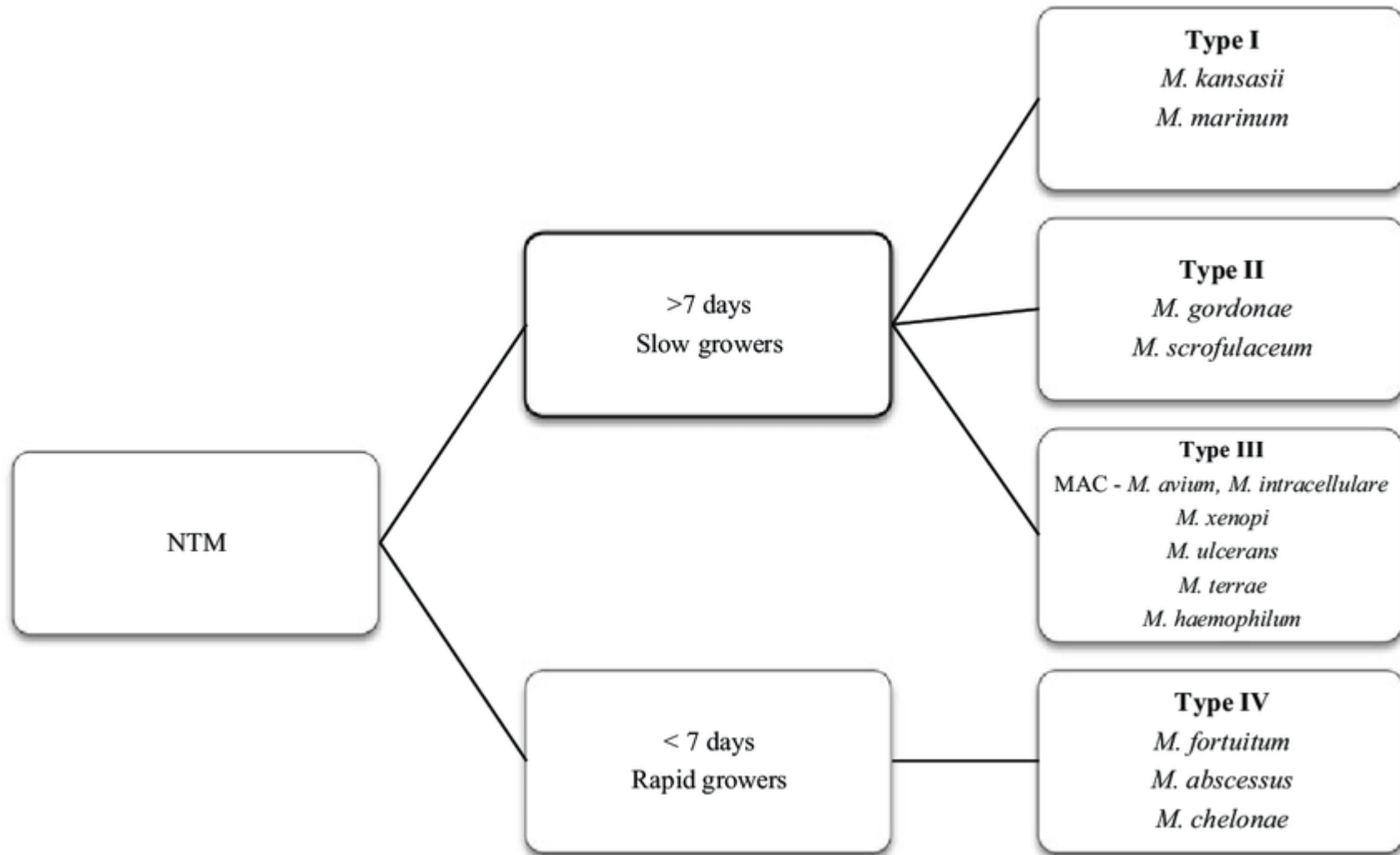
Properties

- Acid fastness
- Non- motile, non-sporing, non –capsulated
- Weekly gram+
- Straight or slightly curved rod shaped bacteria
- Obligate aerobes
- Sometimes show branching filamentous forms resembling fungal mycelium

Classification

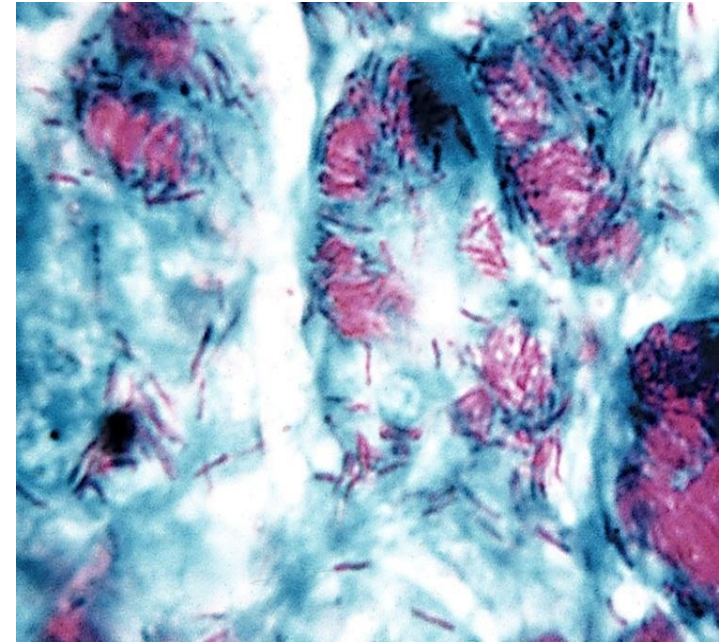
- *M. tuberculosis* complex
- *M. leprae*
- Nontuberculous mycobacteria (NTM)'
- Saprophytic mycobacteria

Nontuberculous mycobacteria (NTM)'



Morphology

- Straight rods 1 - 8 x 0.2 - 0.5 μ m
- Single / groups
- Intracellular
- Acid fast bacilli with 5% H₂ SO₄
- Bound together like cigar bundles by lipid- like substance: Glia
- Globi present in virchow's lepra cells or Foamy cells

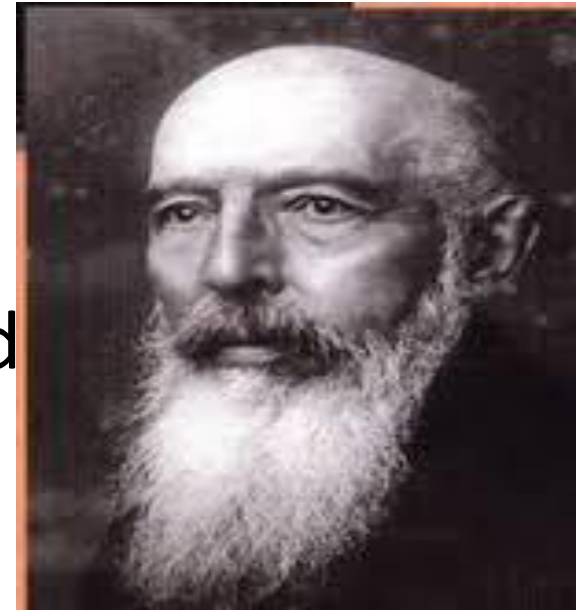


Cultivation

- Generation time: 12-13 days
- Methods:
 - ✓ Foot pad of mice
 - ✓ The nine banded armadillo

LEPROSY

- A disease of skin and nerves caused by the intracellular bacterium *Mycobacterium leprae*
- Discovered by Hansen in 1873, hence it is also known as **Hansen's disease**





Transmission

Source : Nasal or Skin discharges from lesion

Portal of entry:

- Damaged skin –Inoculation
- Nasal mucosa- Inhalation

Epidemiology

- **The South-East Asia Region accounts for 74% of new cases worldwide** - the major burden being from India, Bangladesh, Indonesia and Nepal
- **India and Nepal account for 62% of the world's leprosy**

Risk Factors

Genetic predisposition

HLA-DR 2 , 3 associated with tuberculoid form

HLA-DQ 1 associated with lepromatous form

other factors

- Poverty
- Living in an endemic area
- Living in the same house with a patient
- Other diseases that compromise immune function

Classification of leprosy

I. Madrid (1953)

1. Lepromatous leprosy
2. Tuberculoid leprosy
3. Dimorphous leprosy
4. Indeterminate leprosy



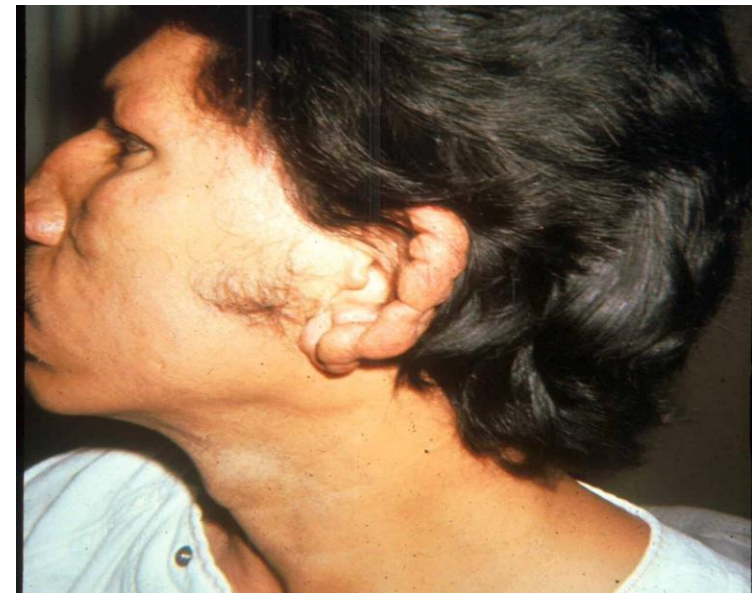
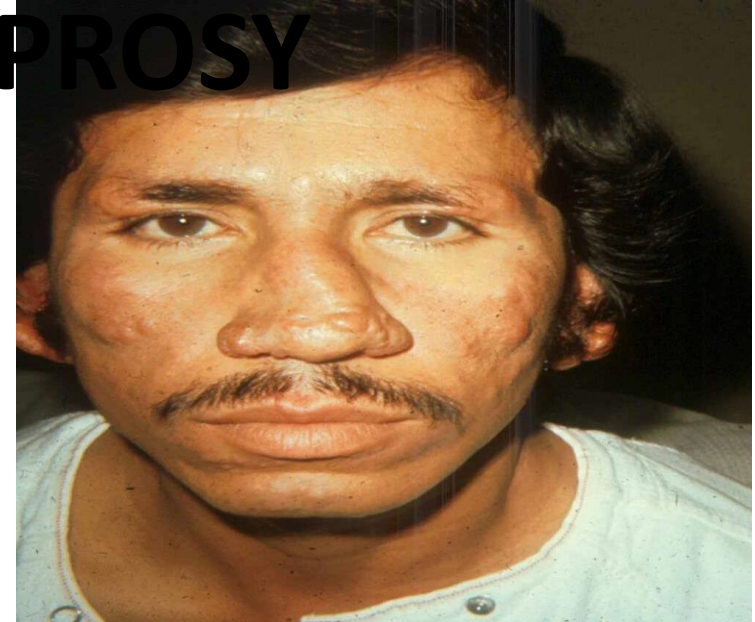
LEPROMATOUS LEPROSY

- Seen where host resistance is low
- Clinical
 - disseminated nodules
 - thickening of skin
 - face results in 'leonine facies'



LEPROMATOUS LEPROSY

- Histopathology
 - disorganized granulomas
 - foamy macrophages
 - few lymphocytes
 - many bacilli on acid fast stain
- Lepromin test is negative



TUBERCULOID LEPROSY

- Seen in patients with high degree of resistance
- Clinical
 - elevated, sharply marginated plaques
 - decreased sensitivity to stimulation
- Histopathology
 - organized granulomas
 - multi-nucleated giant cells
 - acid fast bacilli are absent or very few
- Lepromin test is positive



Classification of leprosy

II. Ridley–Jopling system

- Tuberculoid polar Leprosy (TT)
- Borderline Tuberculoid (BT)
- Midborderline (BB)
- Borderline Lepromatous (BL)
- Lepromatous polar Leprosy (LL)

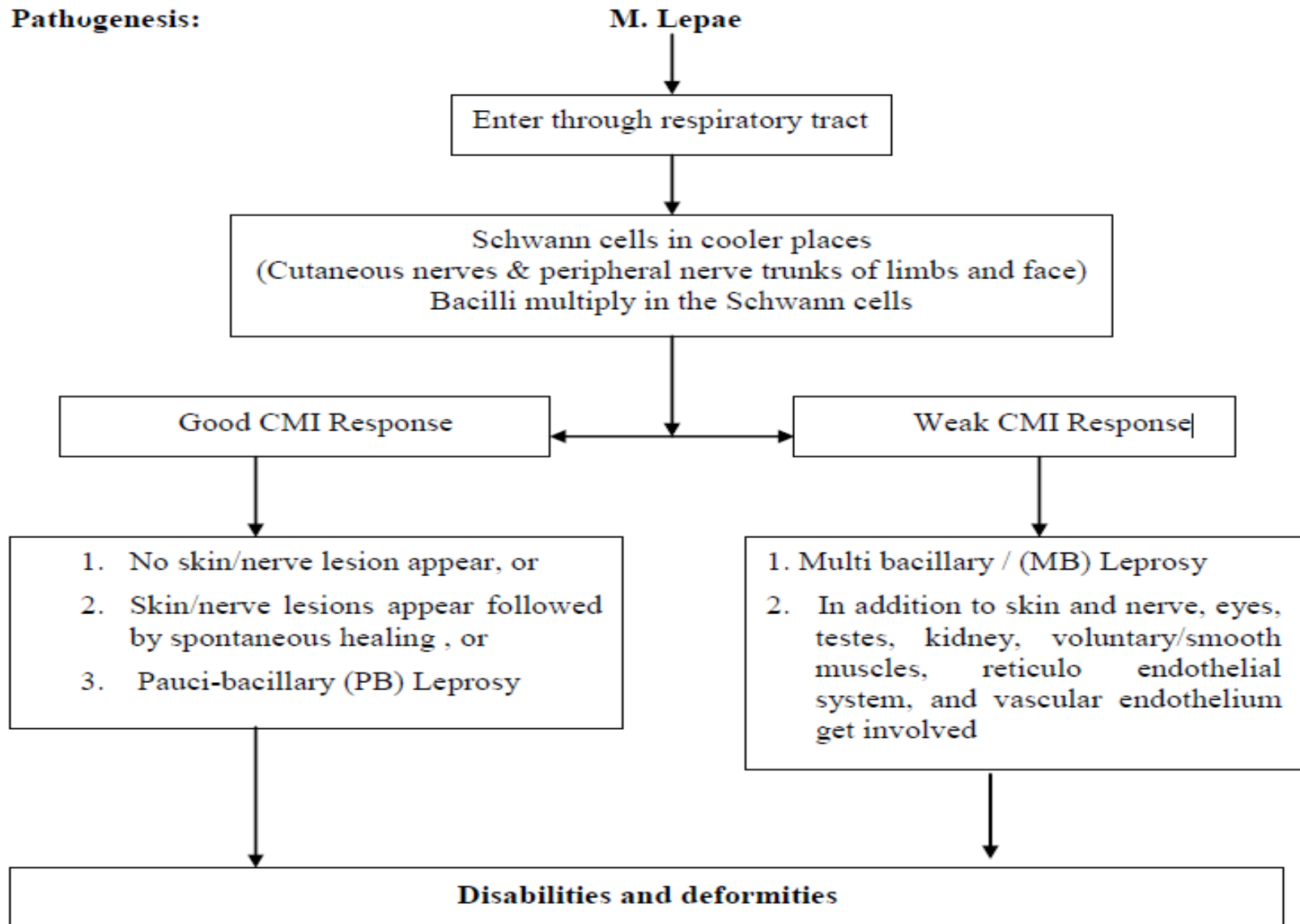
Classification of leprosy

III. WHO operational classification of leprosy

Leprosy type	Number of skin lesions
Paucibacillary	1–5
Multibacillary	6 or more

- **Paucibacillary (TT, BT)**
- **Multibacillary (midborderline (BB), BL, LL)**

Pathogenesis:

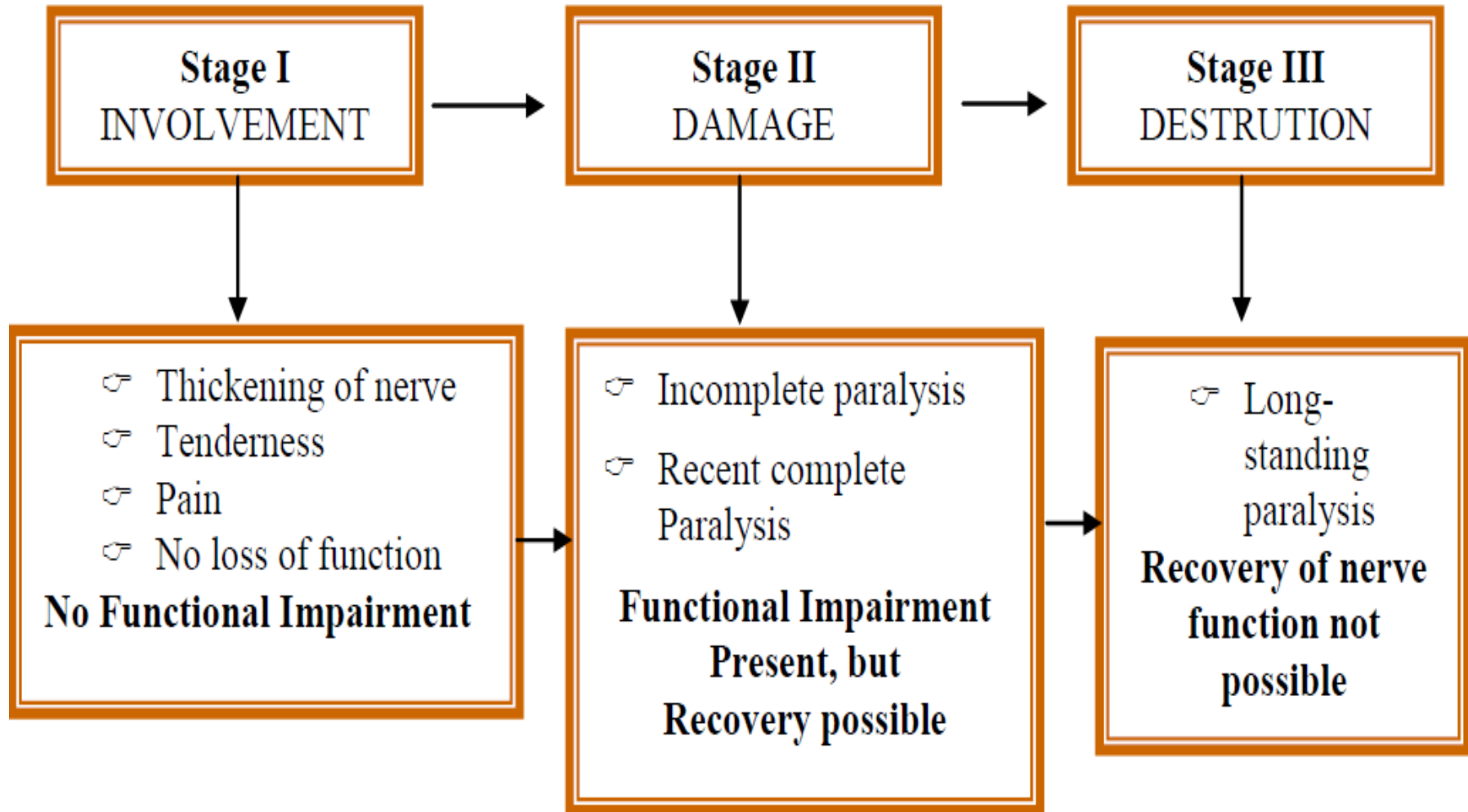


Clinical Features

TABLE 1: Clinical features of leprosy.

Characteristics	Tuberculoid	Borderline tuberculoid	Midborderline	Borderline lepromatous	Lepromatous leprosy
Number of lesions	Single or upto 3	A Few (up to 10)	Several (10–30)	Numerous, asymmetrical (>30)	Innumerable, symmetrical
Size	Variable, usually large	Variable, some are large	Variable	Small, some can be large	Small
Surface changes	Hypopigmented	Dry, scaly, look bright, and infiltrated	Dull or slightly shiny	Shiny	Shiny
Sensations	Absent	Markedly diminished	Moderately diminished	Slightly diminished	Minimally diminished
Hair growth	Nil	Markedly diminished	Moderately diminished	Slightly diminished	Not affected initially
Skin smear	Negative	Negative or 1+	1–3+	3–5+	Plenty, including globi (6+)
Lepromin test	Strongly positive	Weakly positive	Negative	Negative	Negative

Stages of involvement of nerves



Immunology

- Innate immunity
- Humoral antibodies
- Cell mediated Immunity

Immunology

- Tuberculous disease is the result of high cell-mediated immunity with a largely Th1 type immune response
- Lepromatous leprosy is characterized by low cell-mediated immunity with a humoral Th2 response

immunologic reactions or lepra reactions

REVERSAL REACTIONS

ERYTHEMA NODOSUM LEPROSUM

Reversal Reaction

- Occurs in borderline leprosy
- Characterized by edema and erythema of existing skin lesions, the formation of new skin lesions, neuritis
- The presence of an inflammatory infiltrate with a predominance of CD4+ T cells



ERYTHEMA NODOSUM LEPROSUM

- Occurs in lepromatous patients
- Characterized by,
 - Fever, chills, anorexia, malaise
 - Subcutaneous tender nodules
 - Lymphadenitis, arthritis, orchitis, iritis



- During the course of treatment a large number of leprosy bacilli are killed and antigen is released
- These antigens combine with the existing antibodies producing antibody antigen complexes
- Immune complexes get deposited in various tissues with resultant inflammation
- Characterized by neutrophil infiltration and IgG and complement deposition in lesions

Lepromin Skin Test

- only method to study immunity in leprosy
- An extract of *M.leprae* is injected intradermally and induration is observed 48 hours later

Lepromin Skin Test

- Fernandez reaction or early reading
 - Present within 48 hours.
 - Correspond with tuberculin test.
- Mitsuda reaction or late reading:
 - occurs at three weeks.
 - characterized by the presence of granulomas
 - positive in tuberculoid patients, negative in lepromatous patients.

Uses of Lepromin test

1. To classify the lesions of leprosy patients
2. To assess the prognosis and response to treatment
3. Assessing resistance to leprosy in individuals

LUCIO'S REACTION

- Diffuse lepromatosis
- Unusual reaction
- Some cases of Mexico and Caribbean
- Mitsuda test negative

Laboratory Diagnosis

Specimens :

Scrapings from

- Skin lesions
- Nasal mucosa
- Ear lobules (Slit skin smear)

Z-N staining : Acid fast bacilli

- Live bacilli : Solid, uniformly stained
- Dead bacilli : Fragmented and granular

Slit skin smear

- It is technique followed to collect the sample from skin and ear lobes.
- The preferred site is edge of lesion and lesion is cleaned with spirit, then it is pinched up tight to minimize bleeding.
- A 5 mm long incision is made with a scalpel, deep enough to get into the infiltrated layers.
- After wiping off lymph or blood that may have exuded, the scalpel blade is rotated transversely to scrap the sides and base of the incision so as to obtain a tissue pulp from below the epidermis
- which is smeared uniformly over an area of 8 mm diameter on a slide

Nasal specimen

- Nasal blow:
 - In this method, the early morning mucus sample is collected by blowing the patient's nose on a clean cellophane sheet.
- Nasal scraping:
 - In this method, by using a mucosal scraper to scrape the nasal septum sufficiently so as to remove a piece of mucous membrane, and which transferred onto a slide and teased out into a uniform smear.

Microscopy

- Under the oil immersion field, red acid fast bacilli arranged single or cigar like bundles (in groups), and bounded together by lipid-like substance, the globi to form globi.
- The globi are present inside the foamy macrophages which is called Virchow's lepra cells or foamy cells.

Load of bacilli

1. Bacteriological index:

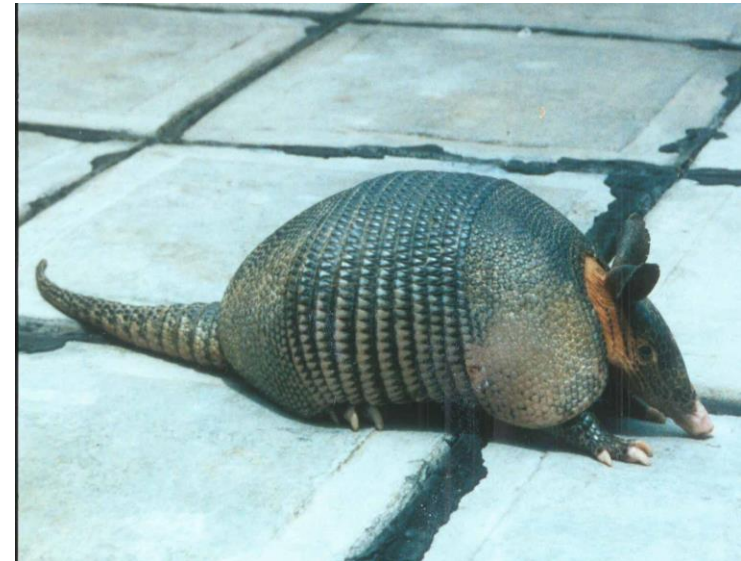
- 1-10 / 100 oil immersion fields : 1+
- 1 -10/10 “ “ : 2+
- 1 -10 / 1 “ “ : 3+
- 10-100/ field : 4+
- 100-1000 /field : 5+

2. Morphological index (% of uniformly stained bacilli)

$$= \frac{\text{Uniformly stained bacilli}}{\text{Total number of bacilli}} \times 100$$

Culture

- Mouse :
 - Intradermally into foot pads
 - Granulomatous lesions in 1- 6 months
 - Intact CMI : Limited replication
 - ↓CMI : Generalized leprosy
- Armadillo: Highly susceptible
- Chimpanzees, Mangabey monkey



- Lepromin test : To know prognosis. Not for diagnosis
- Serological test : ELISA
- Molecular diagnosis : PCR

MANAGEMENT

- Combination chemotherapy: dapsone, rifampin and clofazamine.
- Antiinflammatory for reactions: steroids, thalidomide
- Supportive care, eyes, hands, feet (to prevent tissue injury related to neurologic deficit)

WHO recommended Multi drug therapy

Paucibacillary case

- Rifampicin 600 mg/ month] 6 month
- Dapsone 100mg / day
- For patient with single lesion a single dose of Rifampicin (600mg), Ofloxacin (400mg) and Minocycline (100mg)

Multi bacillary case:

- Rifampicin 600mg / month
- Dapsone 100 mg / day
- Clofazimine 300 mg / month
+ 50 mg / day



2 or more years