

# Leprosy (Hansen's Disease)

Mycobacterium leprae Infection | Medical Microbiology 3rd  
Year MBBS

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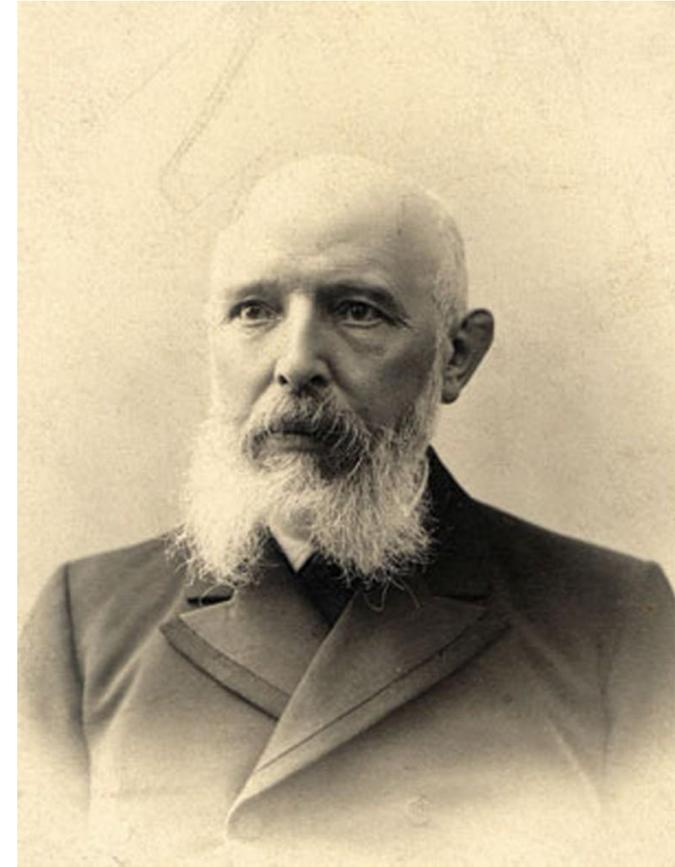
MBBS, Mutah university

MSC Medical Microbiology – University of Manchester

PhD Medical Virology - University of Manchester



- What is the oldest bacterial disease ever documented in human history?
- **Answer:** Leprosy / Gerhard Armauer Hansen (1873)  
— the first bacterium ever linked to human disease.



## Leonine facies



Coarse facial appearance with redundant skin & furrowed creases, resembling features of a lion\*

\*Due to diffuse skin infiltration (eg, lepromatous leprosy, cutaneous T-cell lymphoma).

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# Leprosy

- Leprosy (Hansen disease) is a chronic destructive infection of peripheral nerves caused by the *Mycobacterium leprae* complex.
- 5% lifetime risk even when living with an infected person (natural innate immunity is protective in most of the cases)
- Long-standing cases of leprosy classically develop deformities as a result of contractures following motor nerve palsies and/or repeated injury due to sensory loss.



# Mycobacterium leprae

## Introduction

- The M. leprae Complex — Two Subspecies:
  - Mycobacterium leprae — classical species (Hansen, 1873)
  - Mycobacterium lepromatosis — discovered 2008; produces clinically identical disease



# Mycobacterium leprae

## Introduction - Key Characteristics:

Property	Detail
Type	Obligate intracellular bacillus
Staining	<b>Acid-fast bacillus (AFB)</b> (Ziehl Neelsen)
Experimental model	<b>armadillo</b>
Generation time	<b>12–14 days</b> (slowest dividing bacterium)
Optimal temperature	<b>27–30°C</b> (cooler than core body temp)
Cell wall	Rich in <b>mycolic acids</b>
Shape	Rod-shaped (bacillus), aerobic



# Mycobacterium leprae

## Transmission

- **Primary Route:** Human-to-human via respiratory droplets (nasal secretions of lepromatous patients)
- **Secondary Route:** Prolonged direct skin-to-skin contact with infected lesions
- **Key Transmission Facts:**
  - Requires prolonged, close exposure — not easily transmitted by casual contact
  - 5% lifetime risk even when living with an infected person (natural innate immunity is protective in most of the cases)
  - Incubation period: 3–5 years (can be up to 5–10 years in some cases)
  - Only lepromatous form is highly infectious (high bacterial load)
  - Tuberculoid leprosy = very low infectivity



# Mycobacterium leprae

## Risk factors

- Poverty, overcrowding, poor sanitation
- Living in endemic regions (India, Brazil, Indonesia, Nepal, Myanmar, Nigeria)
- Close household contact with lepromatous patient
- Armadillo contact
- Poor innate immunity
- Genetic susceptibility
- Immunosuppression
- Age: children + middle-aged adults



# Mycobacterium leprae

## Leprosy main forms



Tuberculoid leprosy

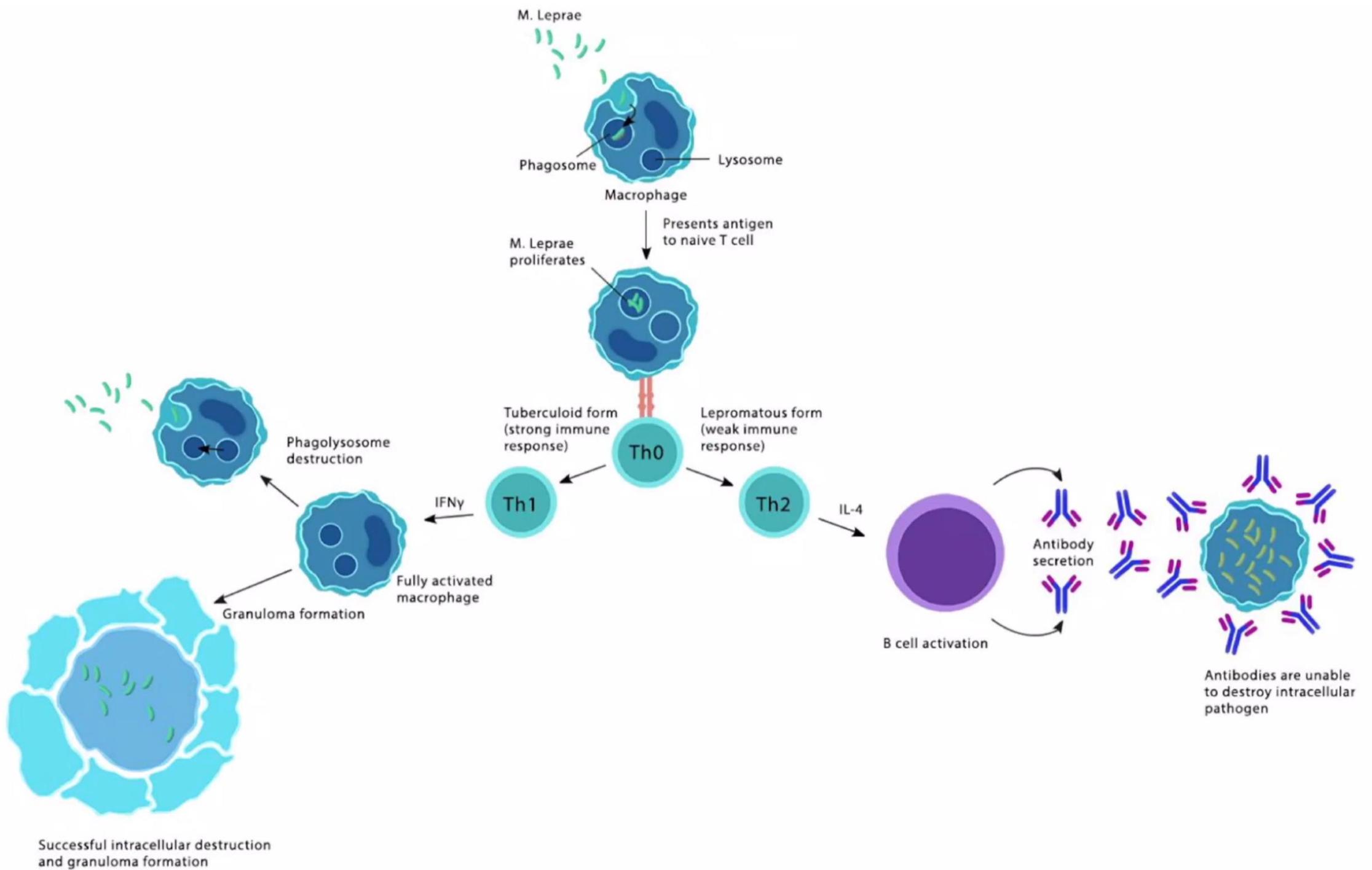
- Patients with an **effective** Th1 CMI response develop tuberculoid leprosy
- Low bacterial burden (paucibacillary) due to successful immune control.



Lepromatous leprosy (Leonine facies )

- Patients with an **ineffective** Th1 CMI response develop lepromatous leprosy, a more severe and diffuse form
- High bacterial burden (multibacillary) due to poor immune control





# Mycobacterium leprae

## Virulence Factors

- **Phenolic Glycolipid-1 (PGL-1):** Surface glycolipid; binds laminin-2 in Schwann cell basement membrane; detected serologically (95% sensitivity in LL)
- **Cord factor:** Resists phagolysosomal digestion
- **Lipoarabinomannan (LAM):** Inhibits phagosome-lysosome fusion → enables intracellular survival
- **Lipoarabinomannan** also detectable serologically



# Mycobacterium leprae

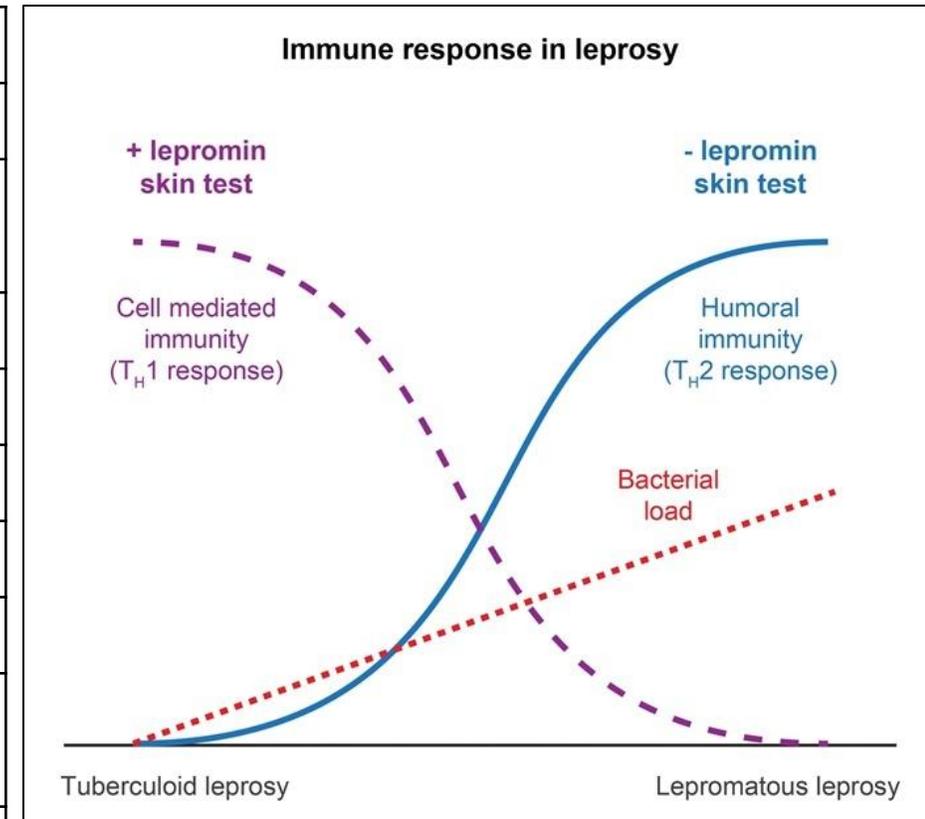
## Pathogenesis

- **Entry:** M. leprae inhaled as respiratory droplets → taken up by alveolar macrophages → disseminated via blood
- **Spread:** Reaches skin and peripheral nerves → specifically invades Schwann cells via PGL-1 binding to laminin-2
- **Intracellular survival:** Uses cord factor + LAM to resist phagolysosomal killing → survives inside macrophages
- **Temperature tropism:** Grows optimally at 27–30°C → thrives in: Skin, superficial peripheral nerves, anterior chamber of the eye, upper respiratory tract
- **Nerve damage:**
  - **Lepromatous:** Direct invasion and proliferation within Schwann cells
  - **Tuberculoid:** T-cell mediated immune response
- **Outcome determined by host immunity:** → See next slide



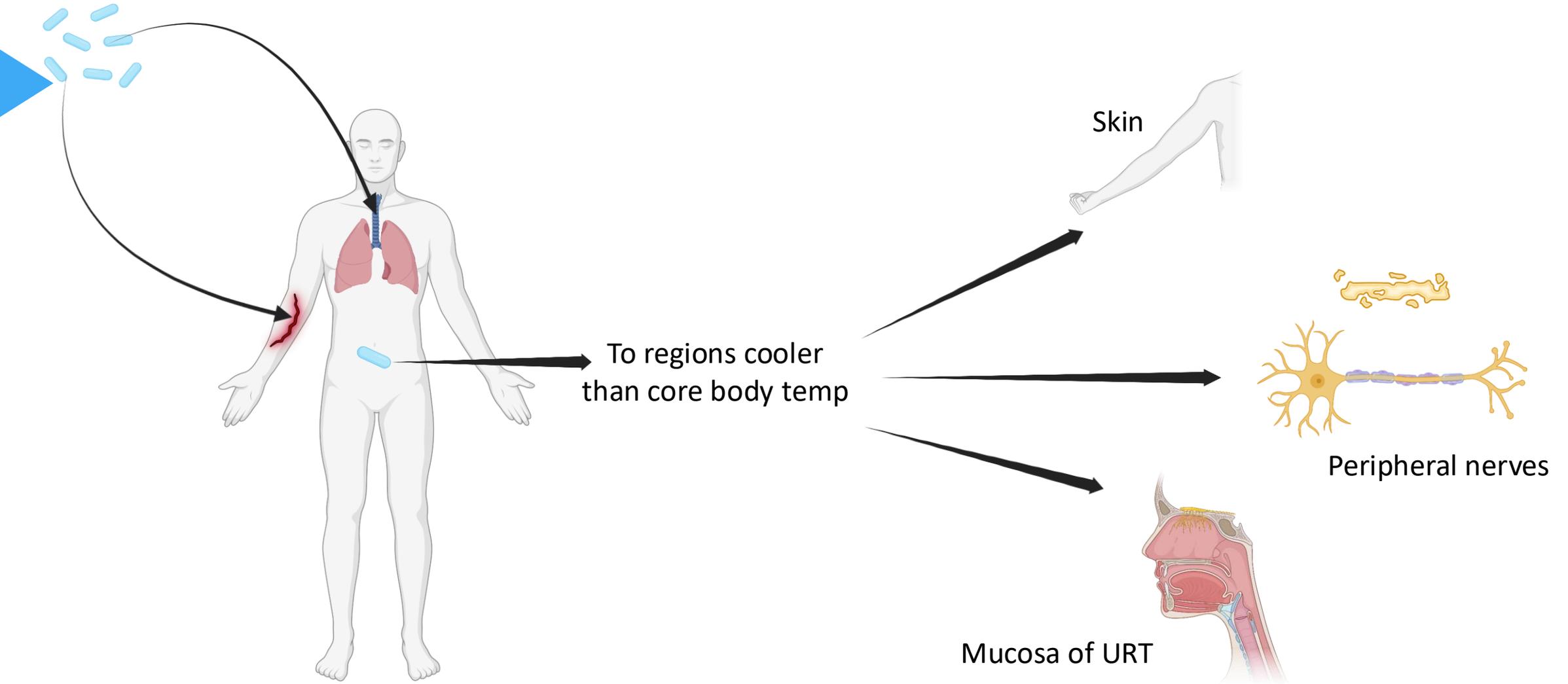
# Immunity: The key determinant

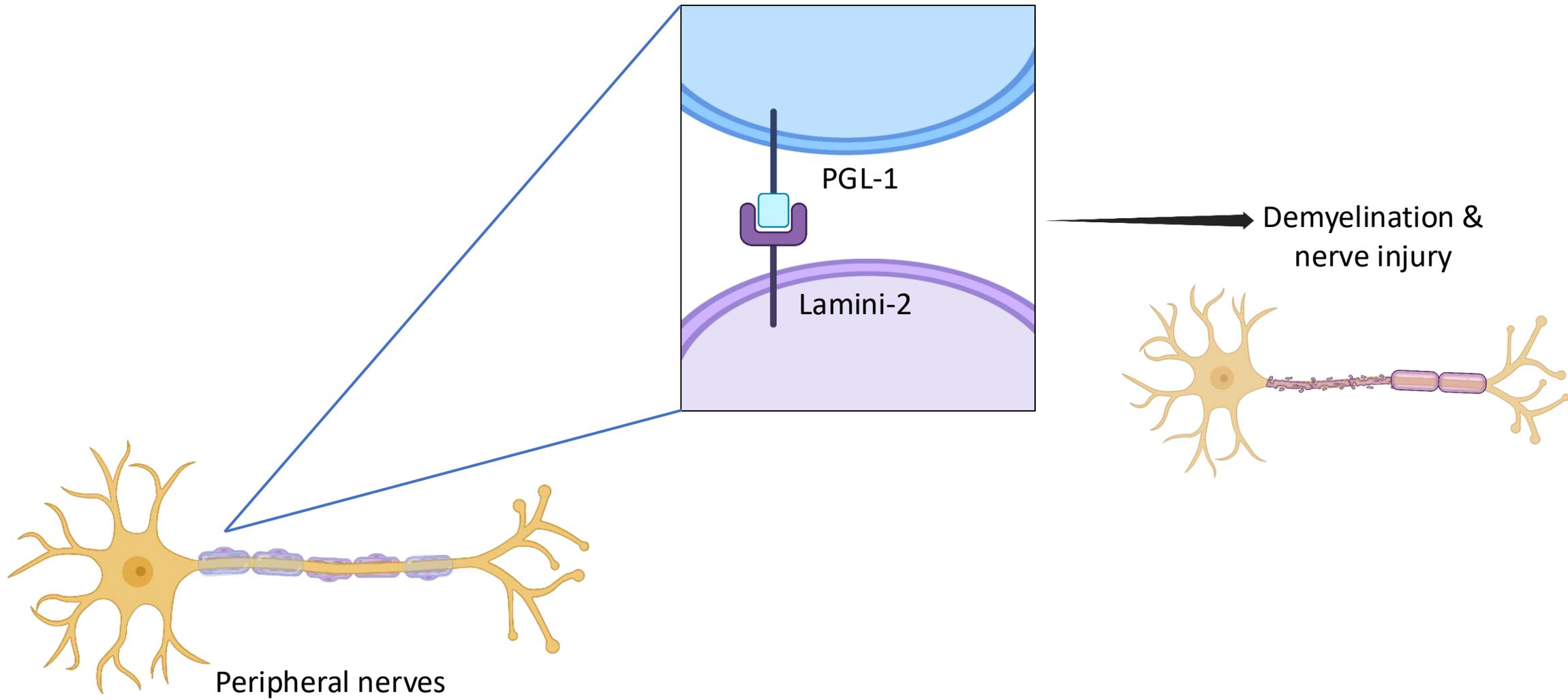
Feature	Tuberculoid	Lepromatous
Immune response	<b>Th1-dominant (CMI)</b>	<b>Th2-dominant (Humoral)</b>
Key cytokine	IFN- $\gamma$ $\rightarrow$ macrophage activation	IL-4, IL-10 $\rightarrow$ B-cell activation
Granuloma formation	<b>Yes</b> — tight, epithelioid	<b>No</b>
Bacterial load	<b>Low (paucibacillary)</b>	<b>Very High (multibacillary)</b>
Antibody production	Normal	<b>Hypergammaglobulinemia</b>
Lepromin test	<b>Positive</b>	<b>Negative</b>
Infectivity	<b>Low</b>	<b>Higher</b>
Nerve damage mechanism	T-cell mediated	Direct bacterial invasion
Prognosis	Milder, may self-limit	Severe, progressive



The Th1 component of CMI, where CD4<sup>+</sup> T cells produce IFN- $\gamma$  to stimulate granuloma formation, is particularly critical. For poorly understood reasons, some patients have an effective Th1 CMI response to *M leprae*, whereas others do not. The effectiveness of the Th1 CMI determines whether patients develop limited lesions (tuberculoid leprosy) or extensive lesions (lepromatous leprosy).



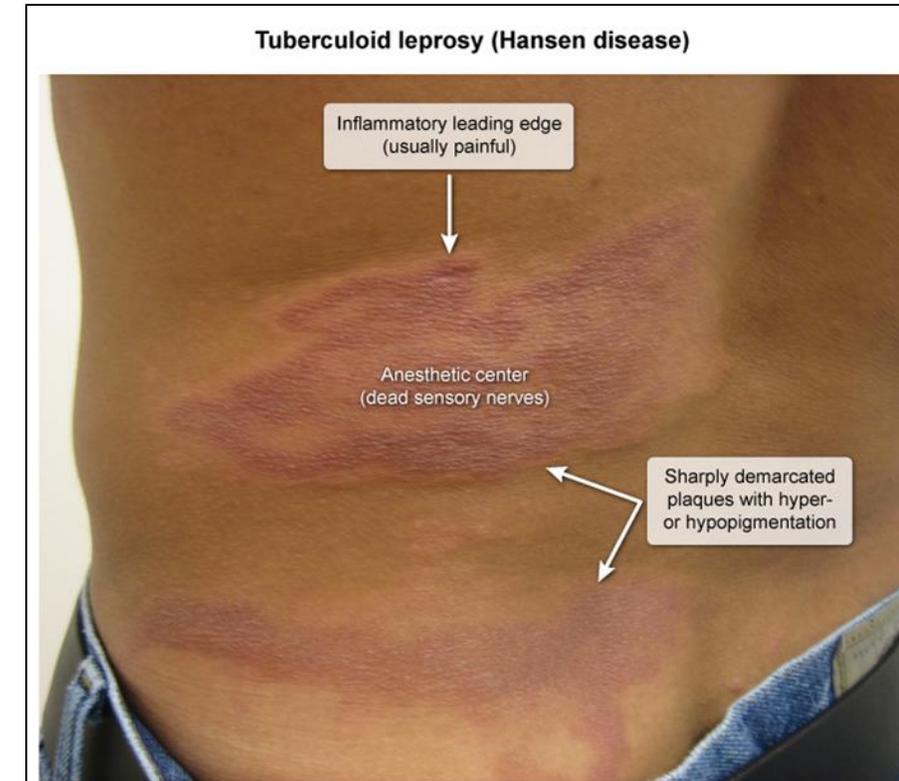




# Mycobacterium leprae

## Clinical presentation - Tuberculoid leprosy

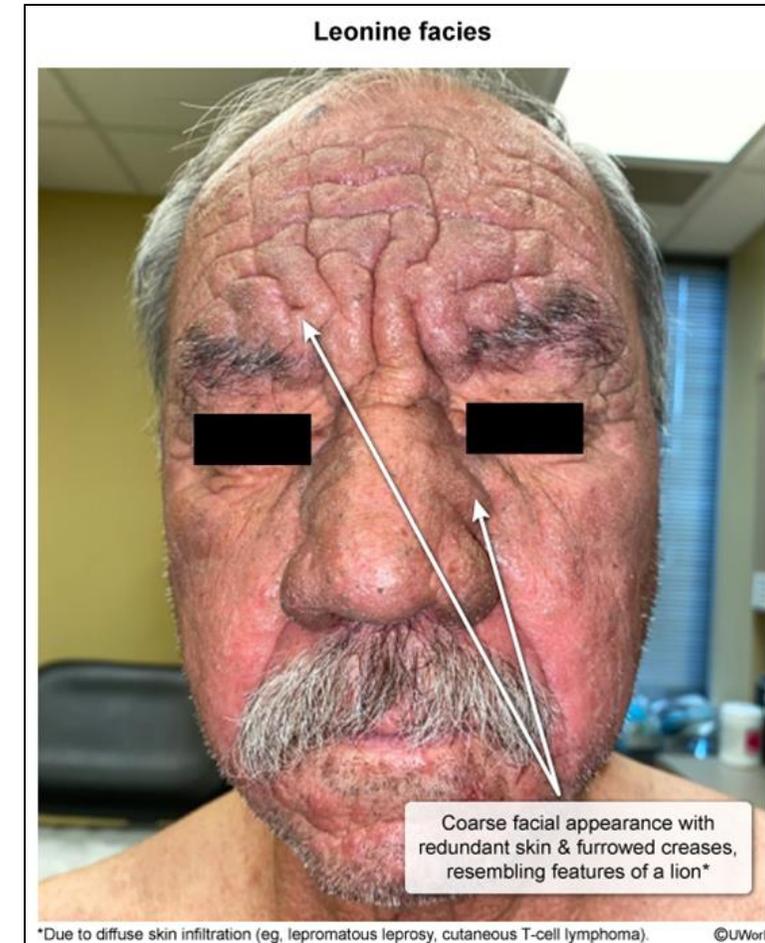
- Patients with an **effective Th1 CMI** response develop **tuberculoid leprosy**, a milder form of disease with:
  - Low bacterial burden (**paucibacillary**) due to successful immune control.
  - A **small number of sharply demarcated** skin lesions, reflecting a strong CMI response that limits infection to single or few superficial nerve branches.
- Patients with tuberculoid leprosy may experience negative cosmetic effects from skin lesions but typically do not have significant peripheral nerve damage.



# Mycobacterium leprae

## Clinical presentation - Lepromatous leprosy

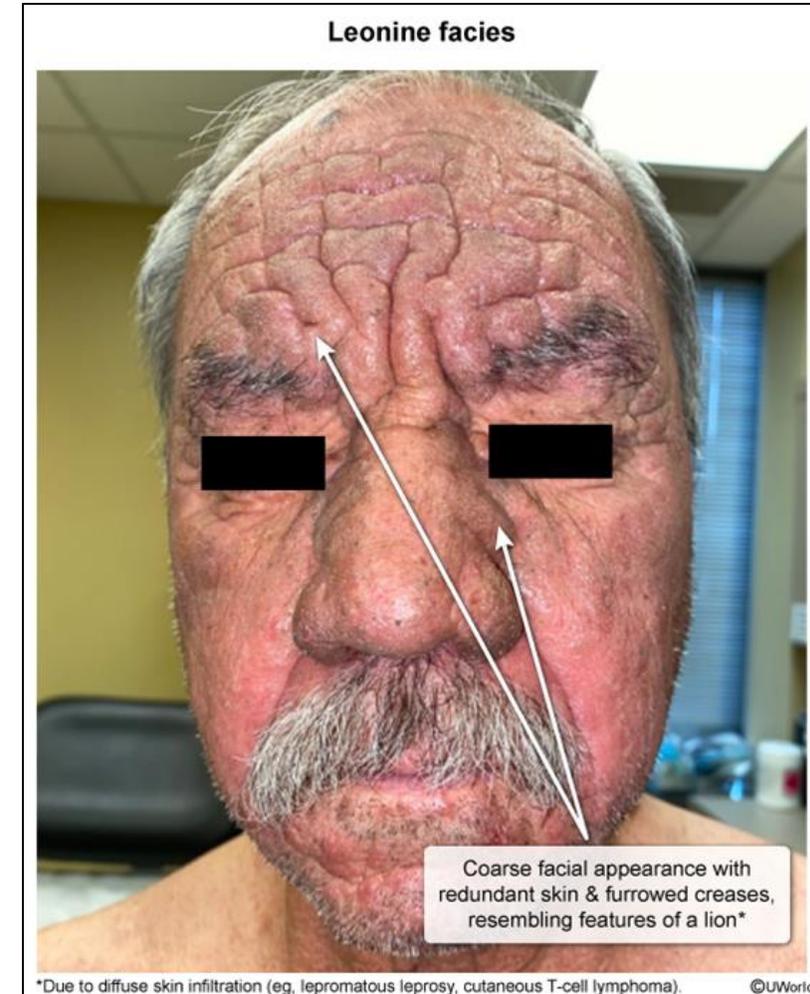
- Extensive nerve destruction leads to polyneuropathy affecting multiple body regions (eg, extremities, trunk, face).
- In late stages, sensory neuropathy produces anesthetic patches of skin. With diminished pain and temperature sensation, relatively minor injuries can go unnoticed, leading to nonhealing ulcers and bacterial superinfection (necessitating amputation in severe cases).
- Corneal anesthesia can eventually lead to undetected abrasions, scarring, and blindness.
- Facial nerve involvement produces thickened, corrugated skin (eg, leonine facies ) frequently with destruction of the ears and nose.
- Less commonly, motor neuropathy can produce muscle atrophy and weakness (eg, foot drop) and autonomic neuropathy can produce alopecia and anhidrosis.



# Mycobacterium leprae

## Clinical presentation - Lepromatous leprosy (cont.)

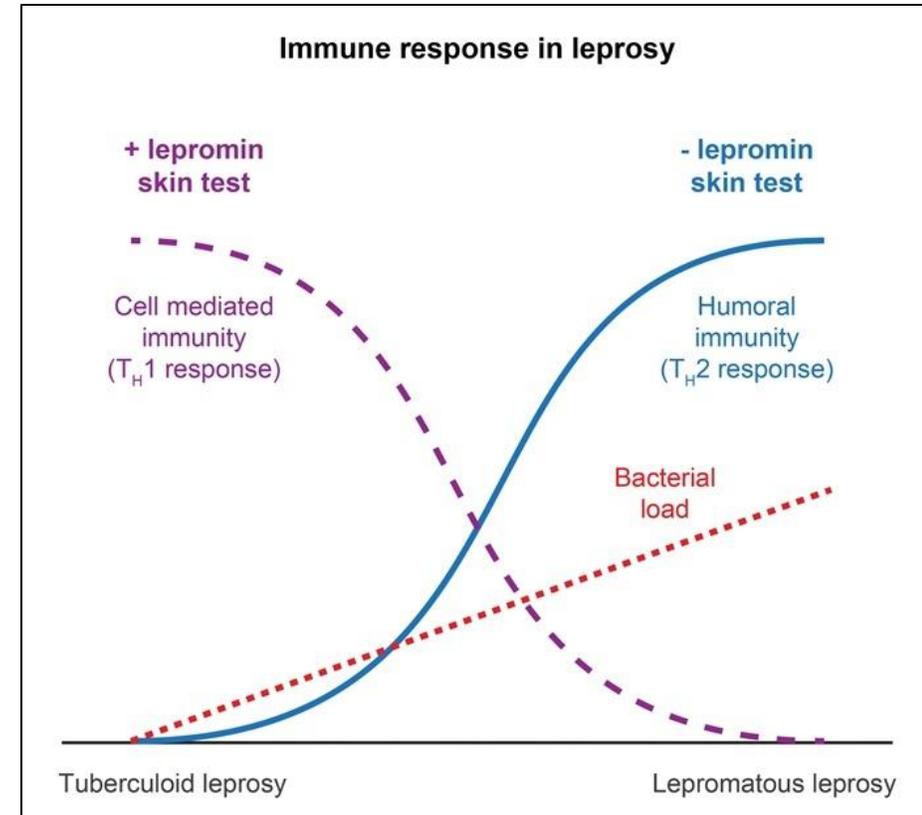
- Patients with an **ineffective Th1** CMI response develop **lepromatous leprosy**, a more **severe** and **diffuse** form of disease with:
  - High bacterial burden (multibacillary) due to poor immune control. Rather than a strong Th1 response, patients instead exhibit a humoral (Th2) response, producing antibodies that are ineffective against intracellular organisms such as *M leprae*. Therefore, the bacilli continue to proliferate within lesions.
  - Numerous widespread skin lesions with ill-defined borders, reflecting free bacterial spread across adjacent peripheral nerve territories.



# Mycobacterium leprae

## Clinical presentation - Borderline leprosy

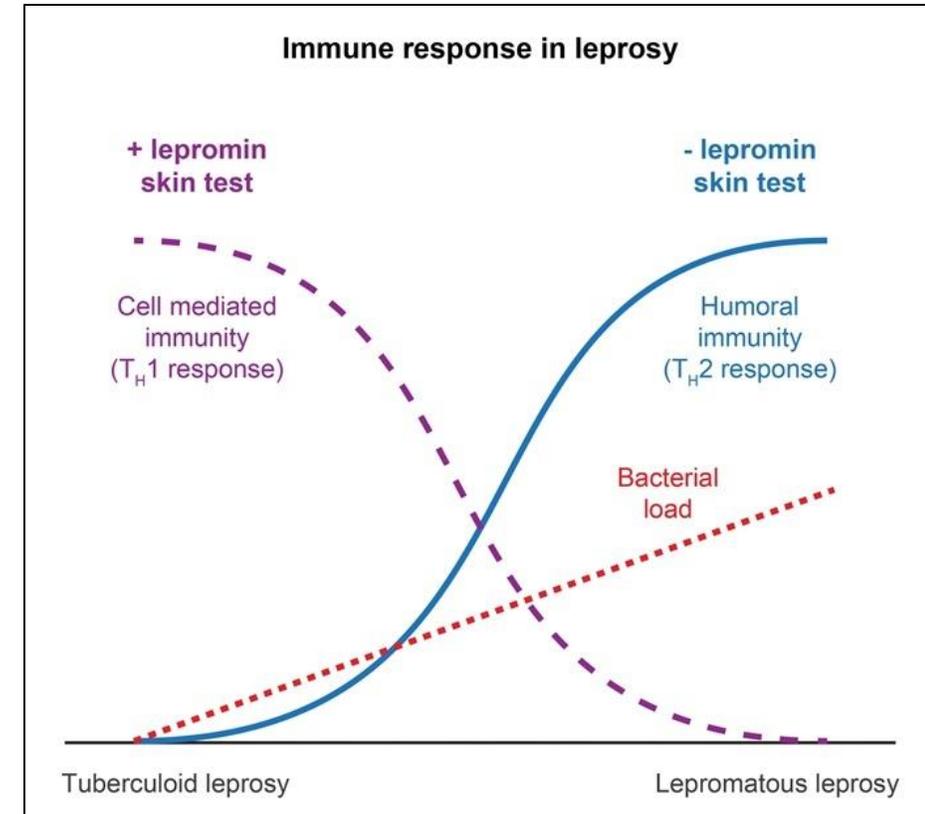
- Borderline leprosy represents an intermediate state between tuberculoid and lepromatous disease, with:
  - Moderate bacillary burden.
  - Mixed skin findings, such as few lesions (a tuberculoid feature) with ill-defined edges (a lepromatous feature) or numerous widespread lesions (a lepromatous feature) with sharply demarcated edges (a tuberculoid feature).



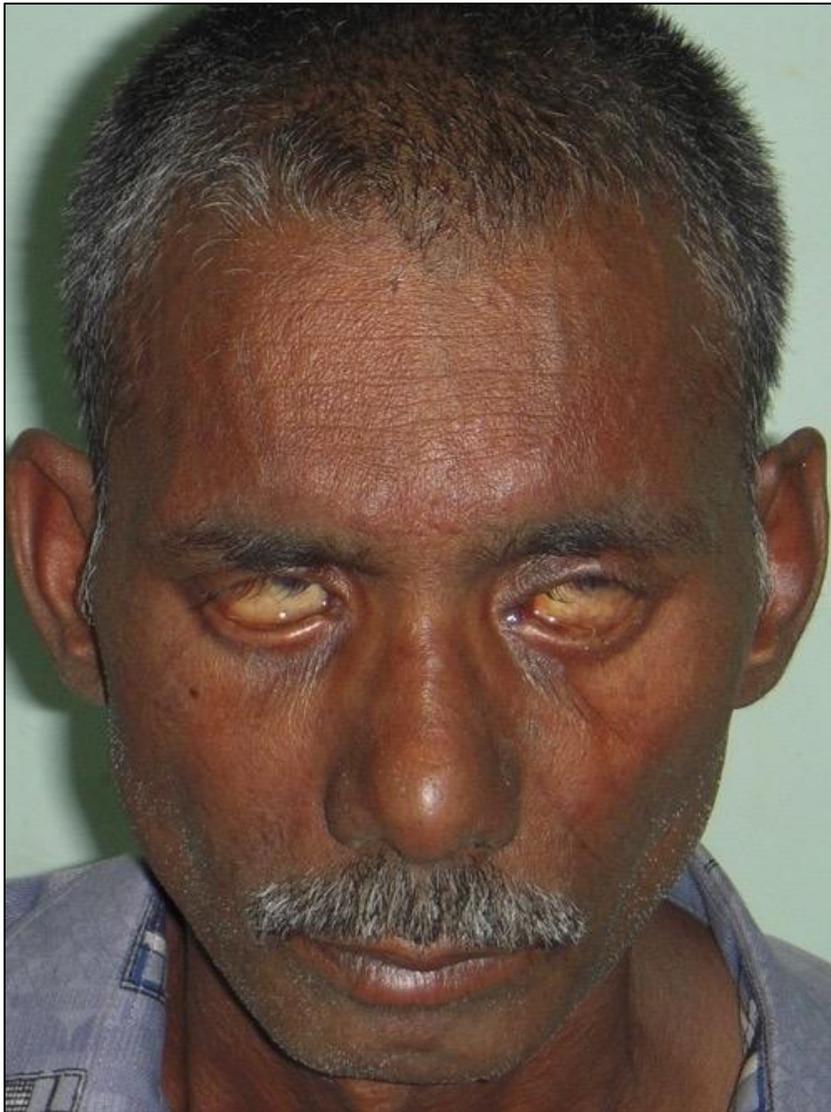
# Mycobacterium leprae

## Clinical presentation - Borderline leprosy (cont.)

- Borderline leprosy can shift between forms. The lepromin skin test evaluates CMI and can help identify patients with borderline leprosy who are at risk for progression to lepromatous leprosy. The test involves subdermal injection of heat-killed *M leprae* extract followed by assessment for induration over 24-72 hours:
  - Positive: Induration ( $\geq 5$  mm) indicates robust CMI response (lower risk).
  - Negative: Lack of induration indicates poor CMI with inability to form granulomas (higher risk).







Lagophthalmos in a patient with lepromatous leprosy:  
Patient is attempting to close his eyelids, but he is unable to do so.



Hand deformities in a patient with leprosy



# Diagnostic Tests

Test	Method	TT Result	LL Result
<b>Slit-Skin Smear (SSS)</b>	Scraping from earlobe/active lesion → Modified ZN stain	<b>Negative</b> (paucibacillary)	<b>Positive</b>
<b>Skin/Nerve Biopsy</b>	Full-thickness; from <b>leading edge</b> of lesion → modified ZN stain	Epithelioid granulomas, Langhans cells, many lymphocytes, <b>NO bacilli</b>	Foamy histiocytes (lepra cells), <b>numerous AFB</b>
<b>PCR</b>	<i>M. leprae</i> -specific gene sequences; from biopsy/smear/blood	Definitive — detects 40-50% of cases missed histologically	Definitive
<b>Lepromin Test</b>	Intradermal killed <i>M. leprae</i>	<b>Positive</b> (≥5mm induration)	<b>Negative</b>
<b>Serology (PGL-1, LAM)</b>	Antibody detection	30% sensitivity	<b>95% sensitivity</b>

*M. leprae* **CANNOT** be cultured — so regular bacteriological culture is useless here



# Management & prevention

- **Management**

- Multidrug treatment
- First-line treatment of leprosy involves multidrug treatment (MDT):
  - **Tuberculoid:** rifampicin + dapsone ( $\pm$  clofazimine) for 6 months.
  - **Borderline or lepromatous:** rifampicin + dapsone + clofazimine for 12 months.

- **Prevention**

- There is currently no vaccine for primary prevention.
- Close contacts of patients with leprosy can receive postexposure prophylaxis with a single dose of rifampicin.





Thank You

