🦠 "Mycobacterium leprae – Leprosy (Hansen's Disease)"

📌 Disease Overview

- Causative Agent: *Mycobacterium leprae*
- Disease: Leprosy (Hansen's disease) – chronic granulomatous infection
- Primary Targets: Skin, superficial nerves, eyes, upper respiratory mucosa

📌 Exam Tip: Nerve involvement → hallmark of leprosy; differentiates from other skin infections.

🔬 Important Properties

Property	Description
Cultivation	Cannot grow on artificial media or cell culture

Experimental Growth	Can be propagated in mice footpads & armadillos 🐭🐢
Natural Host	Humans (main); armadillos = regional reservoir (southern USA)
Type of Disease	Zoonotic in some southern US regions
Optimal Growth Temperature	~30°C → explains predilection for cooler sites: skin, superficial nerves
Growth Rate	Very slow → doubling ≈ 14 days
Therapeutic Implication	Requires long-term antibiotics (years)
Related Species	*M. lepromatosis* → Lepromatous leprosy in Mexico & Caribbean; infects red squirrels 🐿️

🧭 Transmission

🦠 Source

- Lepromatous patients: shed large numbers of bacilli via:
  - Nasal secretions 🤧
  - Exudates from skin lesions

🧍 Mode of Transmission

- Prolonged close contact with untreated lepromatous patients
- Entry via:
  - Respiratory route (droplets)
  - Skin abrasions

🌎 Epidemiology

Region	Remarks
USA	Texas, Louisiana, California, Hawaii 🇺🇸
Global	Endemic in tropical Asia & Africa 🌍

- Reservoir: Armadillos in certain US regions (does not explain global endemicity)

🔁 Flowchart – Transmission

Leprosy Patient (Lepromatous)

↓ (Shedding bacilli in nasal secretions & skin lesions)

Prolonged Close Contact → Entry via Respiratory Tract /

Skin Abrasions

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Infection of Skin & Superficial Nerves (cool body areas)

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Chronic Granulomatous Disease → Leprosy (Hansen's Disease)

⚙️ Pathogenesis

🧫 Site of Multiplication

- Intracellular replication in:
  - Skin histiocytes
  - Endothelial cells
  - Schwann cells of peripheral nerves

🧠 Nerve Damage

1. Direct invasion of Schwann cells by bacilli
2. Cell-mediated immune response attacking infected nerves

🔄 Flowchart – Pathogenesis

Inhalation / Skin Entry

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Phagocytosis by Macrophages & Schwann Cells

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Intracellular Replication of *M. leprae*

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Depending on Host CMI:

→ Strong CMI → Tuberculoid Leprosy (Localized)

→ Weak CMI → Lepromatous Leprosy (Disseminated)

🌓 Types of Leprosy

🔳 Tuberculoid (Paucibacillary)

- Immune Response: Strong CMI (Th1 dominant)
  - Cytokines: IFN-γ, IL-2, IL-12
- Microscopy: Few acid-fast bacilli

- Granulomas: Present, Langhans giant cells 🧱
- Lepromin Test: Positive ✅

Nerve Damage: Immune-mediated inflammation

Clinical Features:

- Few hypopigmented macules or plaques
- Loss of sensation (anesthesia)
- Thickened superficial nerves
- Lesions localized, often self-healing

2️⃣ Lepromatous (Multibacillary)

- Immune Response: Weak/absent CMI (Th2 dominant)
- Microscopy: Numerous bacilli in foamy macrophages 🫧 ("lepra cells")
- Granulomas: Absent
- Lepromin Test: Negative ❌

Nerve Damage: Direct bacterial invasion of Schwann cells

Cytokine Profile:

Form	Interferon	Effect
Tuberculoid	IFN-γ	Activates macrophages → kills bacteria
Lepromatous	IFN-β	Inhibits IFN-γ → poor CMI response

📌 Exam Tip: Lepromatous = high bacillary load, high infectivity, anergic to M. leprae.

⚖️ Comparison Table – Tuberculoid vs Lepromatous

Feature	Tuberculoid (Paucibacillary)	Lepromatous (Multibacillary)
Lesions	Few, localized, minimal tissue destruction	Many, diffuse, marked tissue destruction
Acid-Fast Bacilli	Few / none	Numerous
Granulomas	Prominent	Absent; foamy histiocytes
CMI	Strong (Th1)	Weak / absent (Th2)
Lepromin Test	Positive ✅	Negative ❌
Infectivity	Low	High
Nerve Damage	Immune-mediated	Direct bacterial invasion

Transmission Potential	Minimal	Highly contagious

📝 Key Points

- Cool body sites are preferentially infected due to M. leprae's growth temperature
- Tuberculoid: Strong immunity, few lesions, self-limited, low transmission
- Lepromatous: Poor immunity, widespread lesions, high infectivity
- Armadillos → important zoonotic reservoir in southern USA
- Diagnosis: Clinical + skin smears / histopathology (acid-fast bacilli)

💥 Erythema Nodosum Leprosum (ENL)

- Occurs after starting therapy in lepromatous leprosy

- Represents restoration of CMI ("immune reconstitution")
- Clinical Features:
  - Painful erythematous nodules (esp. tibia & ulna) 🌡️
  - Neuritis (nerve pain)
  - Uveitis (eye inflammation) 👁️

📌 Exam Tip: ENL is a type 2 leprosy reaction; indicates immune system awakening.

👁️ Clinical Findings – Summary

Feature	Tuberculoid	Lepromatous
Incubation Period	Several years	Several years
Onset	Gradual	Gradual

Skin Lesions	Few hypopigmented macules or plaques	Multiple nodular lesions → leonine facies 😐
Anesthesia	Marked in lesions	Less prominent early
Prognosis	Often self-limited	Progressive, deforming

🧭 Flowchart – Clinical Progression

M. leprae Infection

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Host CMI Response → Strong → Tuberculoid → Localized → Few Lesions → Positive Lepromin Test ✅

– OR –

→ Weak → Lepromatous → Disseminated → Many Lesions → Negative Lepromin Test ❌

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(After Therapy) → ENL → Signs of Immune Recovery

😔 Causes of Disfigurement in Lepromatous Leprosy

1. Loss of sensation → repeated burns & trauma 🔥
2. Secondary skin infections
3. Bone resorption → loss of nose tip, fingers, etc.
4. Skin infiltration → thickened, folded skin (leonine facies) 🦁

🧩 Intermediate (Borderline) Forms

- Exhibit features between tuberculoid & lepromatous
- Can progress toward either pole depending on host immune status

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🔬 Laboratory Diagnosis

🧫 1) Direct Microscopy

- Specimens: Skin smears, biopsies, nasal scrapings (esp. lepromatous)

- Stain: Ziehl-Neelsen acid-fast or Fite-Faraco
- Findings:
  - Lepromatous → Numerous acid-fast bacilli in foam cells 🫧
  - Tuberculoid → Few/no bacilli; granulomas diagnostic

🧬 2) Culture

- ❌ Cannot be grown on artificial media → differentiates from *M. tuberculosis*

🧪 3) Serologic Test

Test	Principle	Usefulness
IgM anti-Phenolic Glycolipid-I (PGL-I)	Detects antibodies to M. leprae glycolipid	Positive in lepromatous; negative in tuberculoid

💡 4) Molecular Test

- PCR on skin biopsies → detects M. leprae DNA

- Highly sensitive & specific, especially in paucibacillary cases

🚫 5) False-Positive Serology

- Lepromatous patients may show false-positive VDRL / RPR
- Due to nonspecific antibodies cross-reacting

🧭 Flowchart – Laboratory Diagnosis

Skin Lesion / Nasal Scraping

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🔹 Acid-Fast Stain → Bacilli seen (many in lepromatous; few in tuberculoid)

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🔹 Histopathology → Foam cells (lepromatous) / Granulomas (tuberculoid)

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🔹 Serology → +ve in lepromatous

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🔹 PCR → Confirms diagnosis

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🔹 Culture → Not possible ❌

💊 Treatment of Leprosy

🩹 Principles

- Prolonged MDT required due to:
  - Slow growth of bacillus
  - Prevention of drug resistance

💊 Drug Regimens

Type	Drugs	Duration
Tuberculoid (Paucibacillary)	Dapsone + Rifampin	6–12 months

Lepromatous (Multibacillary)	Dapsone + Rifampin + Clofazimine	12–24 months
Alternative (resistant cases)	Ofloxacin + Clarithromycin	As needed

Drug Mechanisms:

- Dapsone: Inhibits dihydropteroate synthase (like sulfonamides)
- Rifampin: Inhibits DNA-dependent RNA polymerase
- Clofazimine: Binds bacterial DNA; also anti-inflammatory

🌡️ Management of ENL

- Severe ENL: Thalidomide 💊 (teratogenic → contraindicated in pregnancy)
- Mild ENL: Corticosteroids or Clofazimine

🧭 Flowchart – Treatment Overview

Diagnosis Established

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Determine Clinical Type

→ Tuberculoid → Dapsone + Rifampin (6–12 mo)

– OR –

→ Lepromatous → Dapsone + Rifampin + Clofazimine (12–24 mo)

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If ENL → Add Thalidomide / Corticosteroid

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Long-Term Follow-Up 🔄

🛡️ Prevention

Measure	Description
Isolation	Lepromatous patients to prevent spread 🧍

Chemoprophylaxis	Dapsone for children & household contacts
Vaccination	❌ No specific vaccine; BCG offers partial protection
Public Health	Early detection & free MDT programs under WHO 🌍

💭 Quick Revision – Tuberculoid vs Lepromatous

Aspect	Tuberculoid	Lepromatous
AFB Seen	Few	Many
Lepromin Test	Positive	Negative
CMI Response	Strong	Weak
Treatment Duration	6–12 mo	12–24 mo
Infectivity	Low	High

🧩 Mnemonic – Drugs in Leprosy

"Real Doctors Cure Leprosy"

- R = Rifampin
- D = Dapsone
- C = Clofazimine
- L = Leprosy

-> The End <-