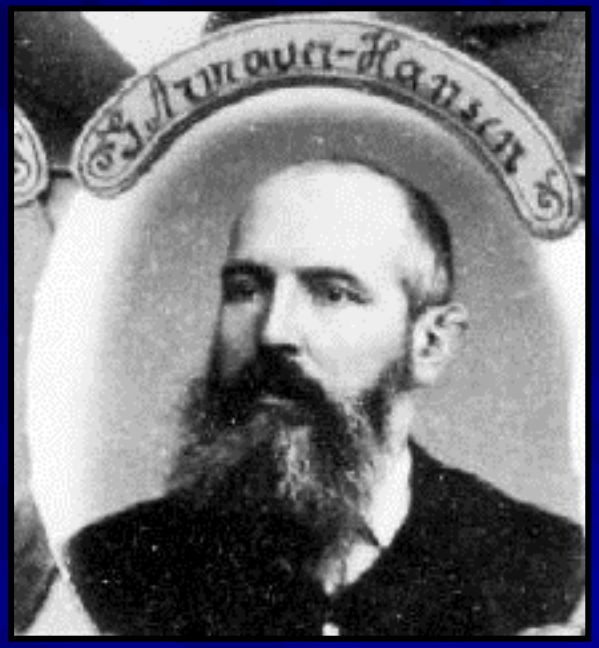
Mycobacterium leprae

Armauer Hansen in 1868



Morphology :

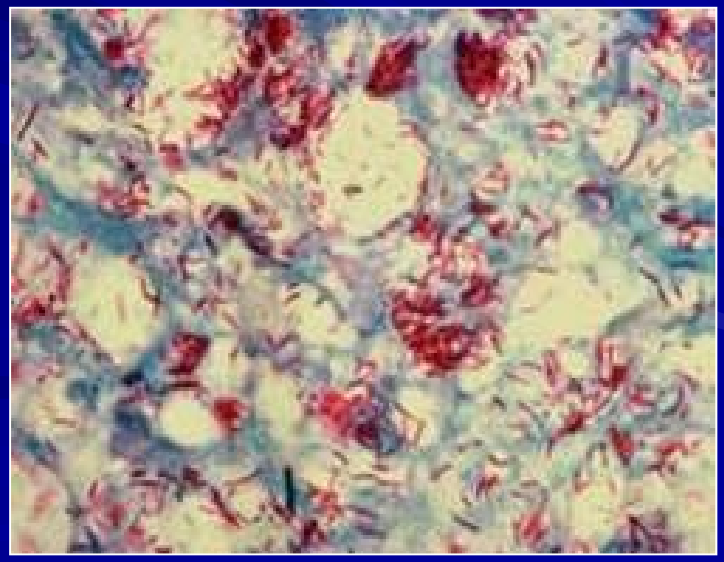
Straight rods. 1 - 8 x 0.2 - 0.5µm

Single / groups. Intracellular.

Acid fast bacilli with 5% H_2SO_4.

Bound together like cigar bundles by lipid- like substance: **Glia.**

Globi present in virchow's lepra cells or **Foamy cells .**



Cultivation

No artificial media / tissue culture available.

Mouse :

Intradermally into ***Foot pads.***

Granulomatous lesions in 1- 6 months.

Intact CMI : Limited replication.

↓CMI : Generalized leprosy.

Armadillo: Highly susceptible.

Chimpanzees, Manghabey monkey.

Resistance

Warm humid environment 9 - 16 days.

46 days in Moist soil

2 hours in Sunlight

30 minutes U V rays

Surface lipid – Peptidoglycolipid (PGL-I) A carbohydrate antigenic determinant.

Epidemiology

World wide (tropics).

Least infectious.

Transmission -Nasal secretions.

(Nasal blow releases 8 x 10^8 bacilli)

Incubation period is 3-5 years.

Continuous close contact.

Rare in children < 5 Years.

India : 12 million cases

estimated -- 1980

2 millions -- 1996

Classification of leprosy

I. Madrid (1953)

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

II. Ridley & Jopling

1. Tuberculoid (T T).
2. Borderline tuberculoid (BT).
3. Borderline (BB).
4. Borderline lepromatous (BL).
5. Lepromatous leprosy (LL).

III. WHO classification

Based on bacterial load.

1. Paucibacillary

   I, T T, BT

2. Multibacillary

   BB, BL, LL.

Leprosy

Slow, chronic & progressive Granulomatous disease of *Peripheral nerves,skin and Muco- cutaneous tissues (Nasal mucosa).*

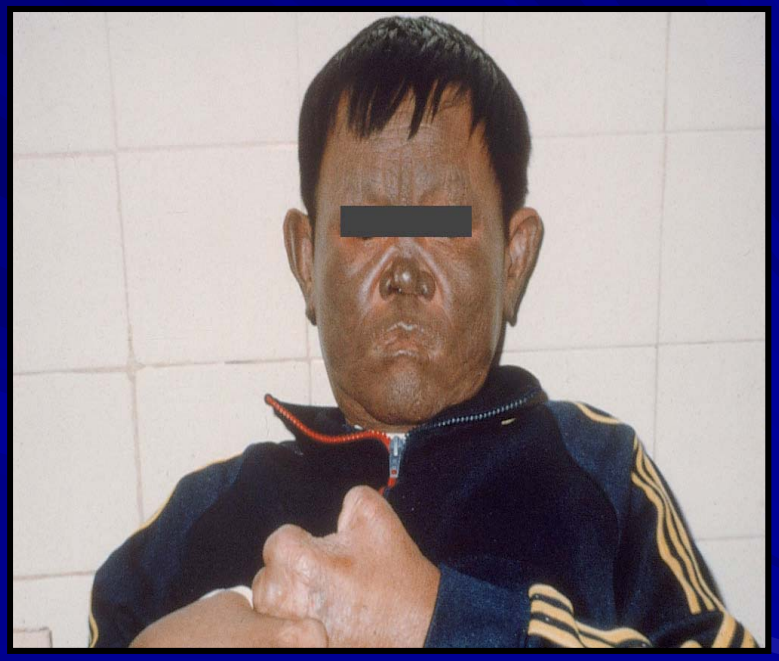
It affects Skin, Lungs, liver, testes ,bones.

Pathogenesis

Source : Nasal or Skin discharges from lesion.

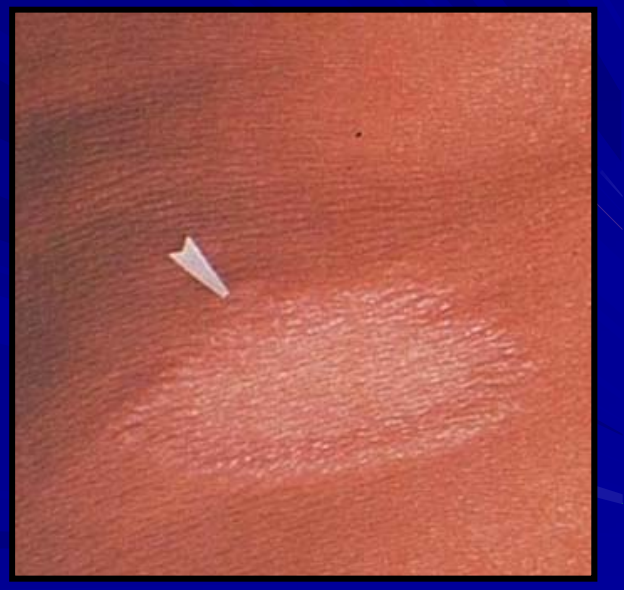
Portal of entry: Damaged skin -Inoculation.

Nasal mucosa- Inhalation



Pathogenesis contd....:

- Infiltration of bacilli in *cooler body tissues* like skin (nose, outer ear), testicles & superficial nerve endings→ (maculae) ***visible lesions.***



- A non-specific or Indeterminate skin lesion is the **First sign of disease.**

- **Schwann cell is target cell.**

  Neuritis leads to *Anesthesia & muscle paralysis.*

Tuberculoid leprosy

- Lesions are large maculae on skin, superficial nerve endings.
- CMI is intact.
- Low infectivity

Regression

Progression

Lepromatous leprosy

- Extensive maculae,

  papules or nodules;

  Extensive destruction of skin.
- CMI severely depressed
- High infectivity

Lepromatous leprosy

Generalized form with decreased CMI.

"Lepromata" : Granulation tissue with plenty of vacuolated cells, from MN cells to Lepra cells.

↓

Ulceration

↓

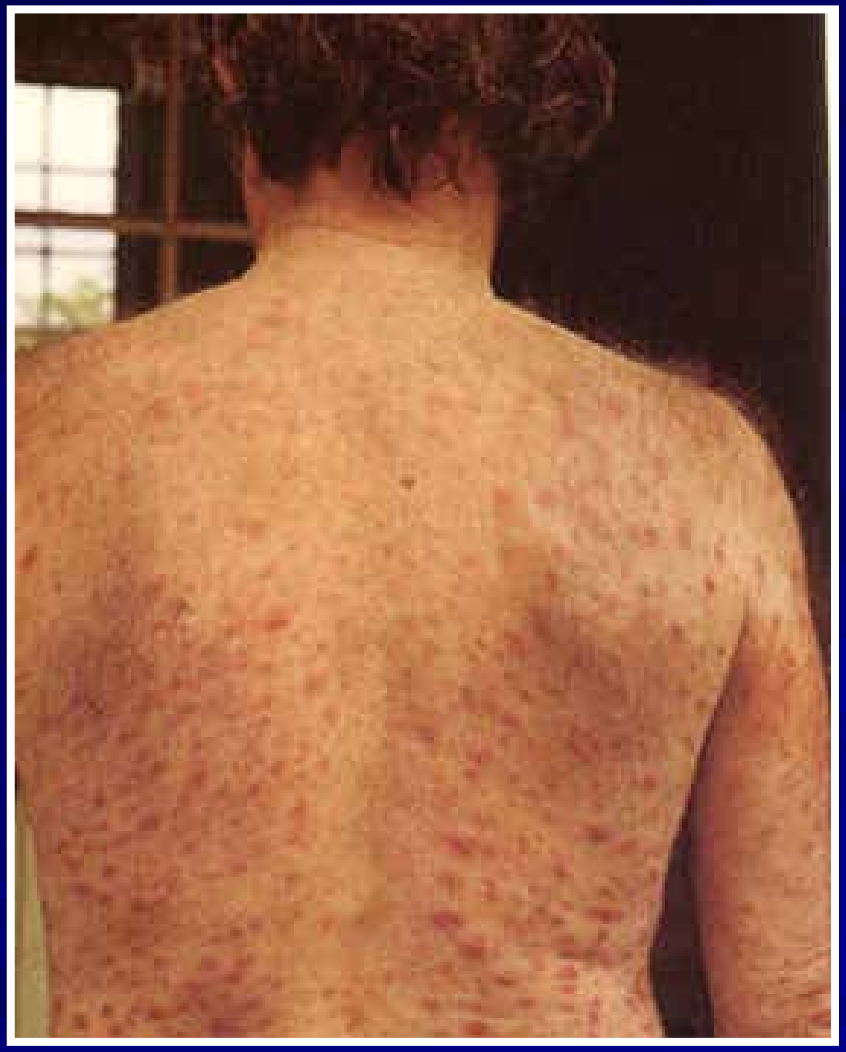
Secondary infection & Mutilation of limbs.

Skin lesions are extensive and bilaterally symmetrical.

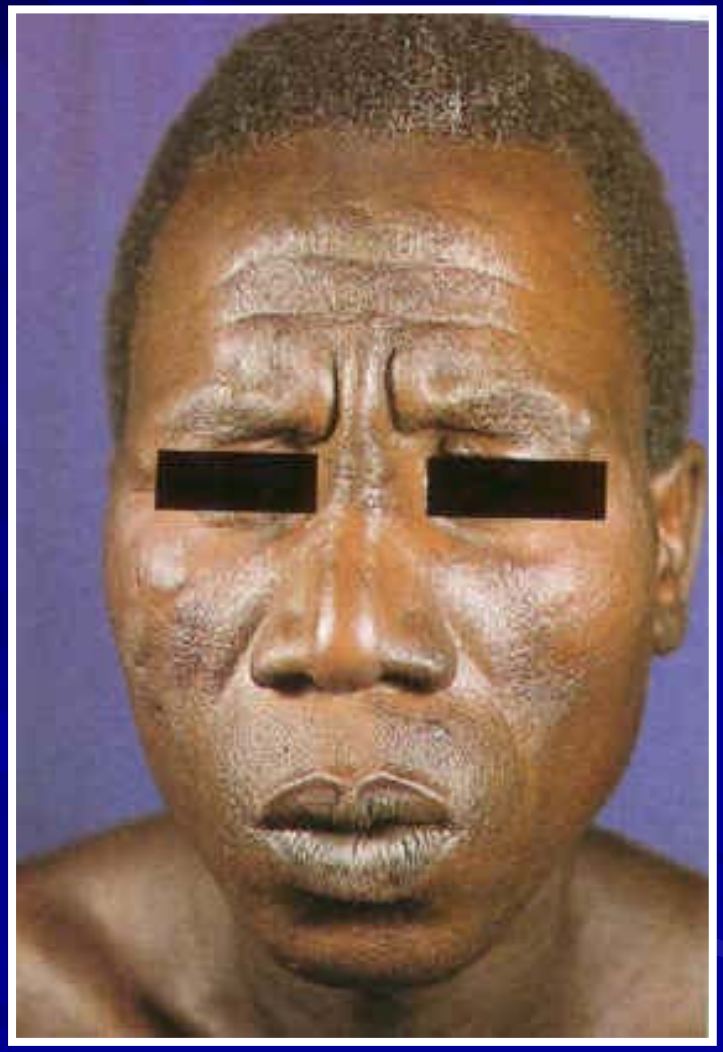
- Face,ear lobules,hands and feet.
- Symmetrical thickening of peripheral nerves & anesthesia.
- Bacilli invade mucosa of Nose , Mouth and
- Respiratory tract → shed in secretions.

  Bacteremia present.
- *Lepromin test* is negative. CD8+ cells in plenty
- Auto antibodies are produced.
- Lateral part of eyebrows are lost.

Lepromatous leprosy



Lepromatous leprosy



Complications :

- Acute exacerbations.
- Testicular atrophy, Gynaecomastia
- Diffuse thickening of face – ***(Leonine face).***

- Necrosis of nasal bones, cartilage with loss of upper incisors.
- Corneal ulcers.

Tuberculoid leprosy

Localized form in individuals with intact CMI.

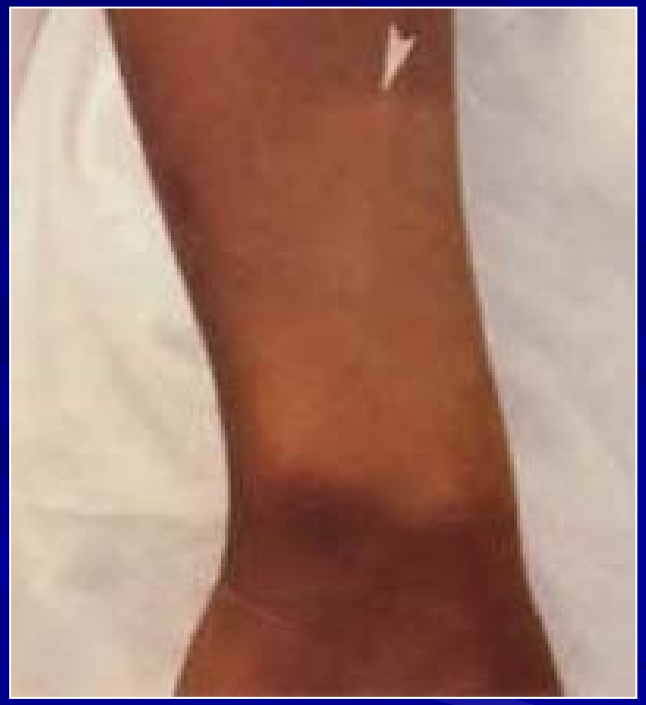
Skin lesions :

Few hypo or hyper pigmented macular patches.

Seen on Face, trunk and limbs.

Bacilli are scanty or absent.

Infectivity is low.

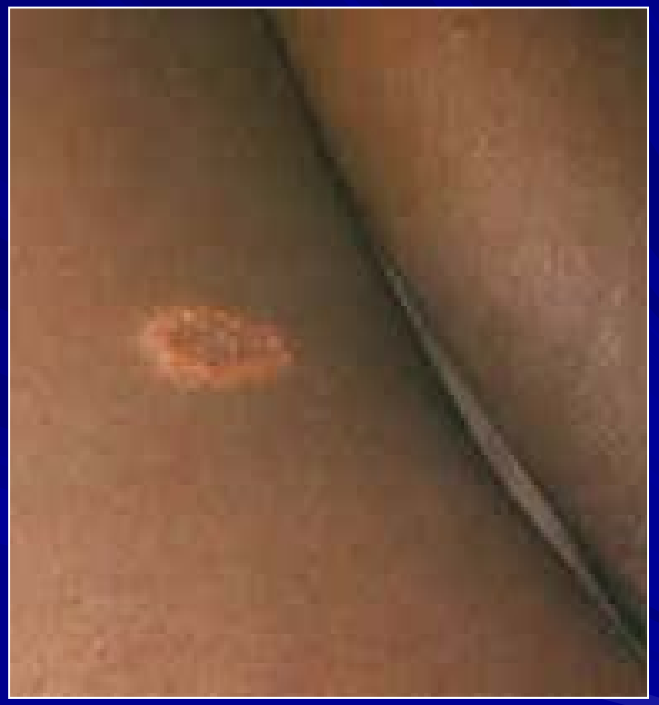


- Diagnosed with Clinical + Histological evidences.

Nerves : Peripheral Nerves to bigger nerves involved.

Thickened, hard and tender.

Lepromin test is positive. Auto antibodies production is rare. CD4+ cells.



Complications

- Peripheral neuropathy.
- V & VII th cranial nerve : Corneal ulcers.
- Ulnar nerve : Claw hand.
- Lateral popliteal nerve : Foot drop.
- Posterior tibial & medial nerve:
  Trophic ulcers,
  Loss of digits.

Dimorphous type :

Lesions resembles both LL (bacteriology) & T T (Clinically).

May turn to complete LL or T T type.

Indeterminate type:

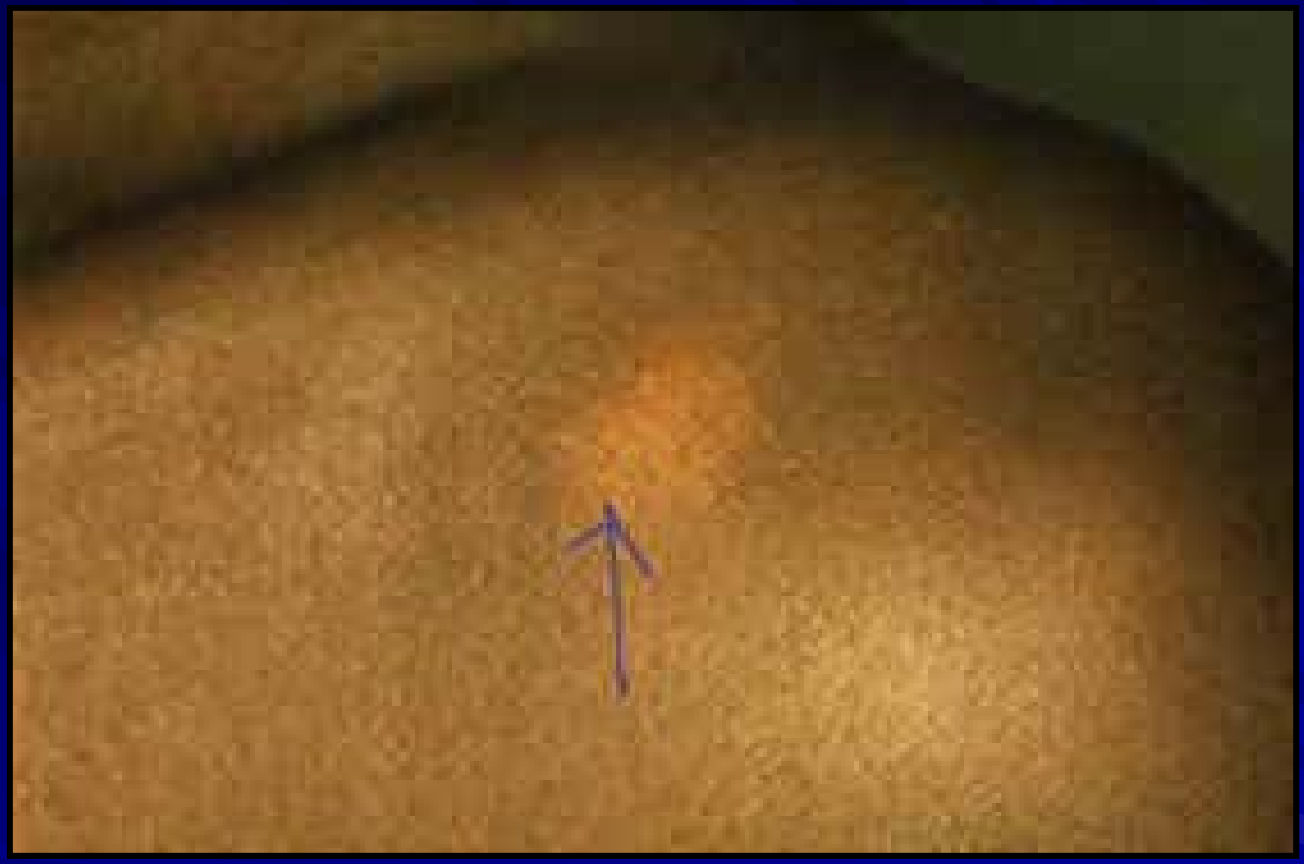
Early stages : Maculoanesthetic patches.

Lesions are not like T T or LL

Spontaneous healing.

Turn to either LL or T T type.

Indeterminate type



Immunity : High degree of innate immunity.

Induces both AMI & CMI.

Antibodies are not effective.

LL Pts : Large number of CD**8** cells.

TT Pts : Predominantly CD4 cells.

Genetic relation: T T : HLA – DR2

L L : HLA MTI

- **Lepra reactions:**

Acute inflammation of the disease

due to *Immunological reactions* against bacilli.

Medical emergency.

Two types:

Jopling type 1: CMI response against bacilli

Synonym: Reversal reaction

Occurrence: Spontaneous, Chemotherapy.

Seen in BT, BB, BL.

Due to influx of lymphocytes into lesions and changed to T T morphology.

Lesions are painful, tender,

Erythema and swelling.

Jopling type 2 : (Erythema nodosum leprosum)

Due to vasculitis (Antigen – Antibody complex).

Seen in LL & BL few months after starting the chemotherapy.

Characterised by:

Tender, inflamed subcutaneous nodules.

Fever.

Lymphadenopathy, arthralgia.

Lucio phenomenon:

Cutaneous hemorrhagic infarct in LL cases.

Main features of lepra reactions.

	Type 1	Type 2
1.Immunological basis :	CMI	Vasculitis with Ag – Ab deposits.
2. Type of patient :	BT,BB, BLBL, LL.	
3. Systemic disturbances :	Not seen .	Present.
4. Hematological disturbances:	Not present	Present
5. Proteinuria	Not seen.	Frequently present.
6.Relation to therapy	Seen in first 6 months.	Rare in first 6 months

Lepromin test :

Skin test for ***delayed hypersensitivity*** to lepra bacilli.

Antigens:

1. Boiled extract of Lepromatous tissue in isotonic saline.
2. Leprosins : Ultrasonicates of tissue – free bacilli from lesions.
   a). leprosins – H b). leprosins – A
3. Dharmender's antigen.
4. Soluble antigen.

Two types of reactions on Intradermal injection

1. Early reaction of ***Fernandez :***

   Erythema & Induration within 1 - 2 days

   Remains for 3 - 5 days.

   Poorly defined with little significance.

2. Late reaction of ***Mistuda***.

   Erythematous, indurated , granulomatous nodular skin lesion.

   Seen in 1 - 2 weeks reaches to peak in 4 weeks.

   Indicates CMI status in leprosy patients.

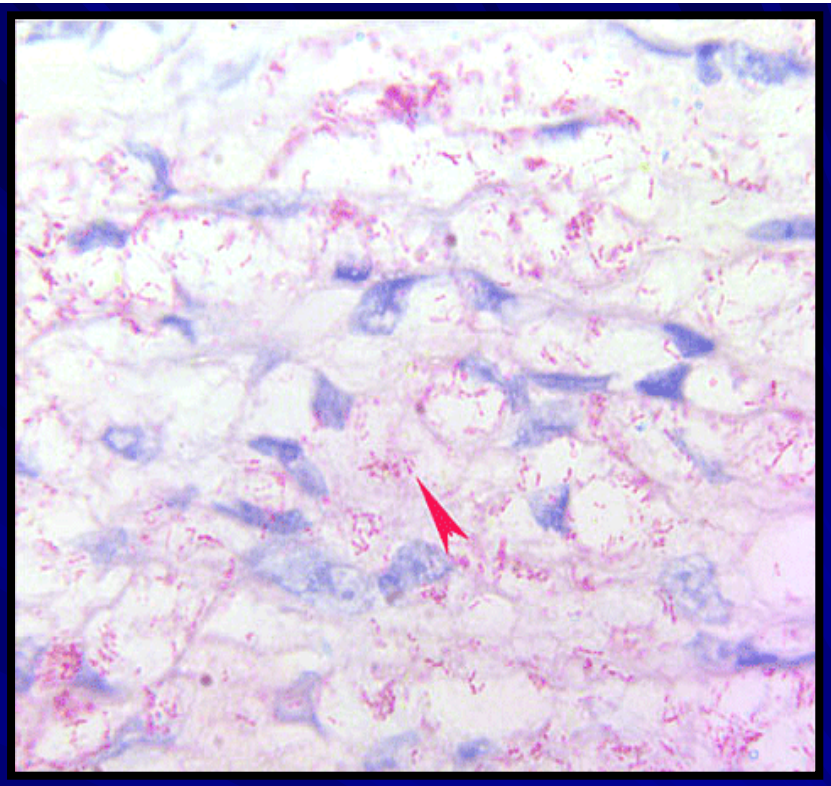
Significance :

1. To classify the lesions of leprosy.
   T T (+) L L (-) Borderline (+/-)

2. To assess prognosis & response to treatment.
   Positive: Good prognosis
   Negative: Bad prognosis

3. To assess the resistance of individuals to leprosy.

Lab. Diagnosis



Specimens :

1. Scrapings from

Lesion ,Nasal mucosa.

Z-N staining.

Acid fast bacilli within the undifferentiated macrophages: L L

Live bacilli : Solid, uniformly stained.

Dead bacilli :Fragmented and granular.

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)

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

2. Skin & Nerve biopsy.

3.Ear lobules (Slit skin smear).

5. Lepromin test : To know prognosis.
Not for diagnosis.

6. Serological test :

(a). MLPA (b). ELISA (Antibody against PGL-I).

7.Molecular diagnosis: Identifying DNA codes for 65 & 18-kDa M.leprae proteins.

Treatment :

Until 1982 : Dapsone only.

Now MDT being given because of resistant strains.

WHO recommended Multi drug therapy

Paucibacillary case.

Rifampicin 600 mg/ month

Dapsone 100mg / day

} 6months

Multi bacillary case:

Rifampicin 600mg / month

Dapsone 100 mg / day

Clofazimine 300 mg / month
+
50 mg / day

} 2 or more years

Vaccines: BCG, MAI complex vaccine.
Mycobacterium w vaccine.

Chemoprophylaxis: MDT