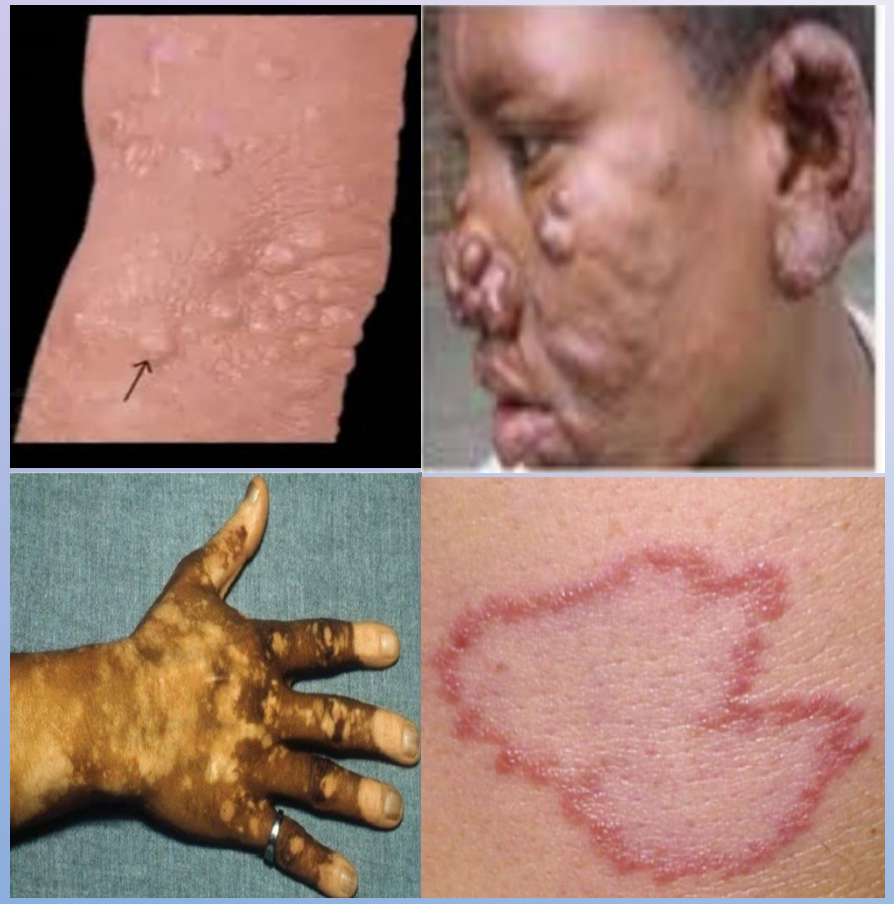
LEPROSY



PRESENTED BY

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ROG NIDAN EVUM VIKRITI VIGYAN

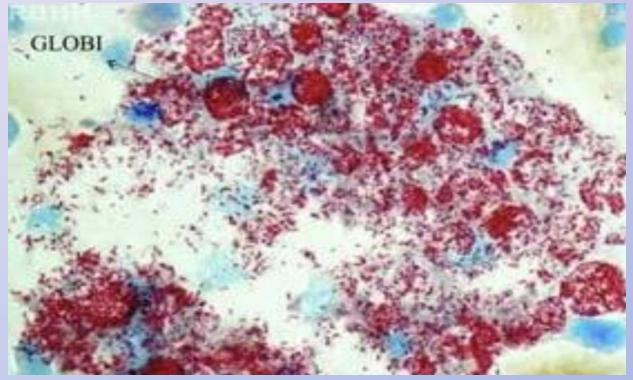
DEPARTMENT

INTRODUCTION

- Leprosy or Hansen disease (after discovery of the causative organism by hansen in 1874)
- It affects mainly the cooler parts of the body such as the skin, mouth, respiratory tract, eyes, peripheral nerves, superficial lymph nodes and testis.
- In leprosy, the earliest and main tissue involvement is of the skin and nerves. However, in bacteraemia from endothelial colonisation or by bacilli filtered from blood by reticuloendothelial system, other organs such as the liver, spleen, bone marrow and regional lymph nodes are also involved.

CAUSATIVE ORGANISM

The disease is caused by **Mycobacterium leprae** which closely resembles mycobacterium tuberculosis but the organism is less acid-fast and has characteristic **neurotropism**. The organisms in tissues appear as compact rounded masses **(globi)** or are arranged in parallel fashion like **Cigarettes-in-pack.**



Lepra bacilli

- Obligate intracellular gram positive and acid fast bacilli
- Short, thick, pink stained rods
- Affinity for schwan cells & cells of R-E system
- Cannot grow in vitro but can grow in mice and nine banded armadillos

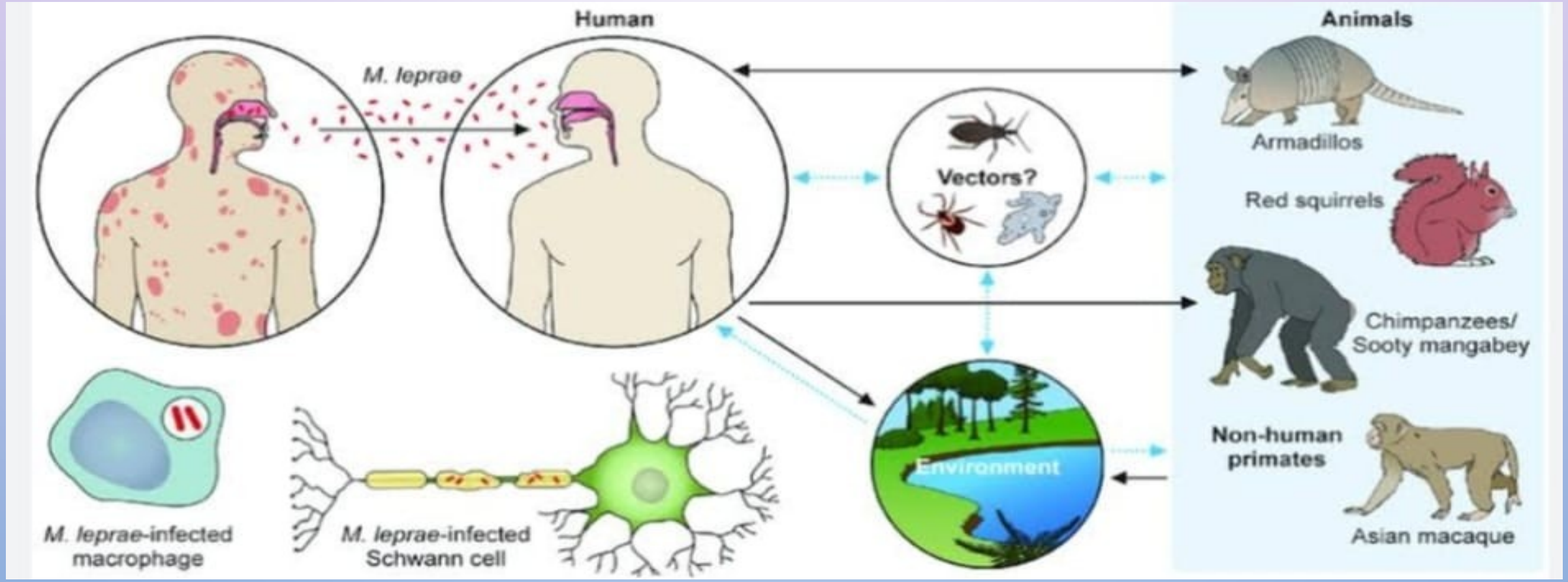
MODE OF TRANSMISSION

- Leprosy is a slow communicable disease and the **incubation period** between first exposure and appearance of signs of disease varies from **2 to 20 years** (average about 3 years). The infection may be transmitted by the following routes :-

Direct contact with **untreated leprosy patients** who shed numerous bacilli from-

- Damaged skin
- Nasal secretions
- Mucous membrane of mouth and
- Hair follicles.

- **Materno-foetal** transmission across the placenta.
- Transmission from **milk of leprosy** affected mother to infant.



IMMUNOLOGY OF LEPROSY

The immune response in leprosy is **T cell-mediated delayed** hypersensitivity (**type IV reaction**) . M. Leprae do not produce any toxins. Instead, the damage to tissues is immune-mediated. This is due to the following peculiar aspects in immunology of leprosy:

Antigens of leprosy bacilli :-

Lepra bacilli have several antigens. The bacterial cell wall contains large amount of M. Leprae- specific **phenolic glycolipid (PGL-1)** and another surface antigen, **lipoarabinomannan (LAM)**. These antigens of the bacilli determine -

The immune reaction of host lymphocytes and macrophages. Another unique feature of leprosy bacilli is invasion in peripheral nerves which is due to binding of trisaccharide of M. Leprae to basal lamina of schwann cells (neurotropism).

Genotype of the host

Genetic composition of the host as known by MHC class (or HLA type) determines which antigen of leprosy bacilli shall interact with host immune cells. Accordingly the host response to the leprosy bacilli in different individuals is variable.

T cell response

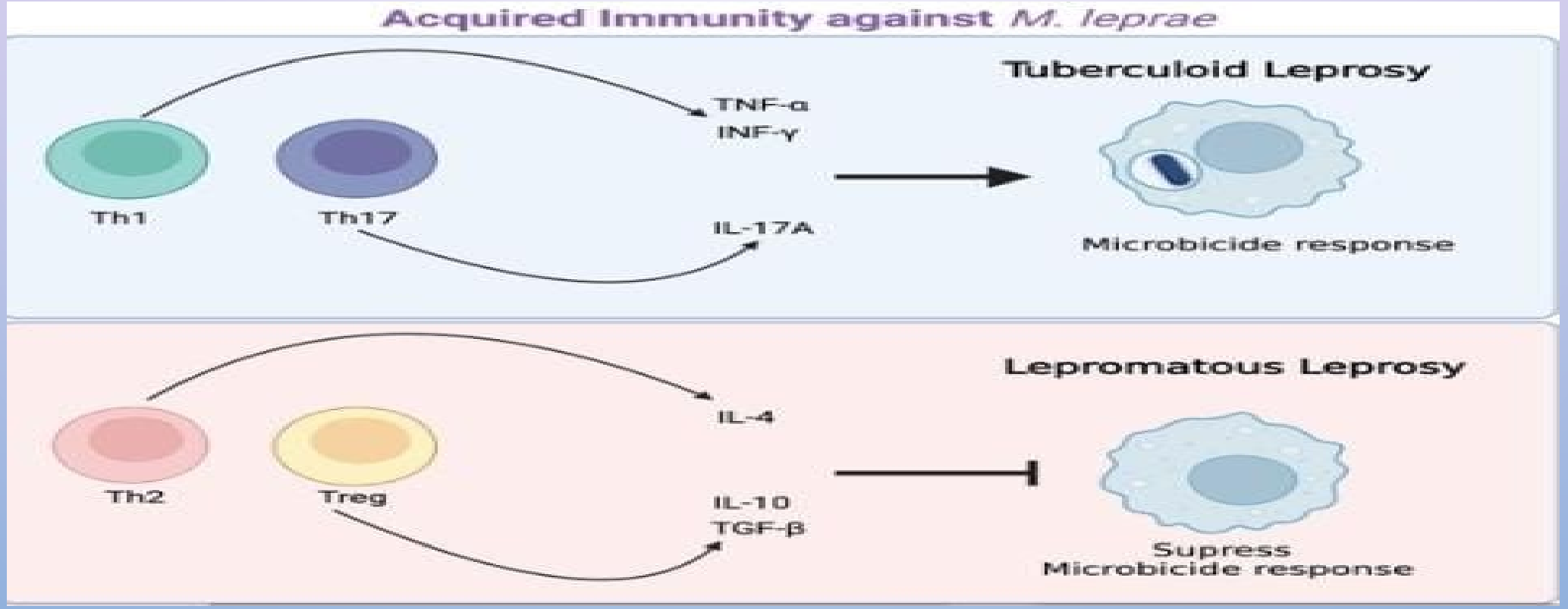
There is variation in T cell response in two main forms of leprosy:

1. Unlike tubercle bacilli, there is not only activation of C D4+T cells but also of C D8+T cells.

2. In tuberculoid leprosy, the response is largely by C D4+T cells, while in lepromatous leprosy although there is excess of C D8+T cells (suppressor T) but the macrophages and suppressor T cells fail to destroy the bacilli due to C D8+T cell defect.

Humoral response

Though the patients of lepromatous leprosy have humoral immune response such as high levels of immunoglobulins (IgG, IgA, IgM) and antibodies to mycobacterial antigens but these antibodies do not have any protective role against lepra bacilli.



PATHOGENESIS OF LEPROSY

Bacilli enter the body usually through respiratory system After entering the body, bacilli migrate towards the neural tissue and enter Schwann cells.

Can also be found in macrophages, muscle cells and endothelial cells of blood vessels.

Slow multiplication inside cells & tissues with lower temperature (about 12-14 days for one bacterium to divide into two)Further progress depends on the immunological status of the infected person

Pathogenesis:

M. Lepae

↓

Enter through respiratory tract

↓

Schwann cells in cooler places
(Cutaneous nerves & peripheral nerve trunks of limbs and face)
Bacilli multiply in the Schwann cells

↓

Good CMI Response

Weak CMI Response

↓

1. No skin/nerve lesion appear, or
2. Skin/nerve lesions appear followed by spontaneous healing , or
3. Pauci-bacillary (PB) Leprosy

↓

1. Multi bacillary / (MB) Leprosy
2. In addition to skin and nerve, eyes, testes, kidney, voluntary/smooth muscles, reticulo endothelial system, and vascular endothelium get involved

↓

Disabilities and deformities

WHO CLASSIFICATION FOR LEPROSY CONTROL

- Used for treatment purposes.
- Segregation into two groups for treatment purposes –

❑ The less bacillated patients could be treated with with lesser number of drugs for shorter period,

❑ More bacillated patients treated with more number of drugs for longer period.

CLINICAL FEATURE ON SKIN LESION	PAUCI BACILLARY LEPROSY	MULTI BACILLARY LEPROSY
Inclunding macular flat lesion papules and nodules	1 to 5 lesions Asymmetrical Definite loss of sensation	More than 5 lesion Symmertrical Loss of sensation may or may not be present

Presently in India, number of nerves involved is also taken into consideration while categorizing the patients into paucibacillary and multibacillary types as per the NLEP (National Leprosy Eradication Programme) of Government of India.

MADRID CLASSIFICATION

- International leprosy congress held at Madrid in 1953.
- Two types-

  Lepromatous (L)

  Tuberculoid (T)

- Two groups-

  Indeterminate

  Borderline or Dimorphous

Lepromatous type (L) - Macular

Nodular

Diffuse

Neuritic

Tuberculoid type (t) - Macular

Minor tuberculoid

Major tuberculoid

Neuritic , pure

Indeterminate Group (I) - macular

neuritic, pure

Borderline Group (B) - infiltrated

NEW IAL CLASSIFICATION

5 GROUP CLASSIFICATION

- INDETERMINATE TYPE
- TUBERCULOID TYPE
- BORDERLINE TYPE
- LEPROMATOUS TYPE
- PURE NEURITIC TYPE

RIDLEY AND JOPLING CLASSIFICATION

Traditionally two main forms of leprosy are distinguished

1. Lepromatous type representing **low resistance,**

2. Tuberculoid type representing **high resistance**.

Since both these types of leprosy represent two opposite poles of host immune response, these are also called polar forms of leprosy.

Cases not falling into either of the two poles are classified as borderline and indeterminate types.

Based on clinical, histologic and immunologic features, modified ridley and jopling classification has been described which divides leprosy into 5 groups as under:

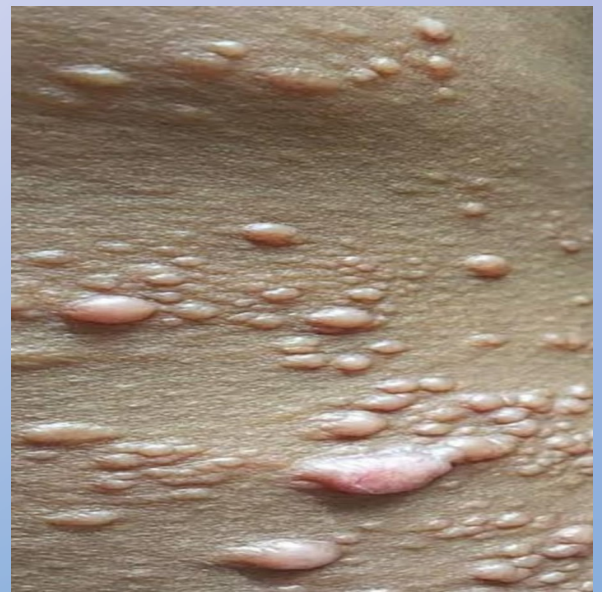
- TT - TUBERCULOID POLAR (HIGH RESISTANCE)
- BT - BORDERLINE TUBERCULOID
- BB - MID BORDERLINE (DIMORPHIC)
- BL - BORDERLINE LEPROMATOUS
- LL - LEPROMATOUS POLAR (LOW RESISTANCE)

VARIANTS in addition, a few variant forms of leprosy which are not included in ridley-jopling classification have been described:

INDETERMINATE LEPROSY - This is an initial non-specific stage of any type of leprosy.

HISTOID LEPROSY- This is a variant of LL in which the skin lesions resemble nodules of dermatofibroma and the lesions are **Dome** shaped and highly positive for lepra bacilli.

Clinical, histopathological, bacteriological and immunological features show slow continous change from one pole to another.



REACTIONAL LEPROSY

REACTIONAL LEPROSY based on shift in immune status, or in patients of leprosy on treatment, two types of reactional leprosy are distinguished: Type I (Reversal Reactions) and Type II (Erythema Nodosum Leprosum).

TYPE I

Reversal reactions the polar forms of leprosy do not undergo any change in clinical and histopathological picture.

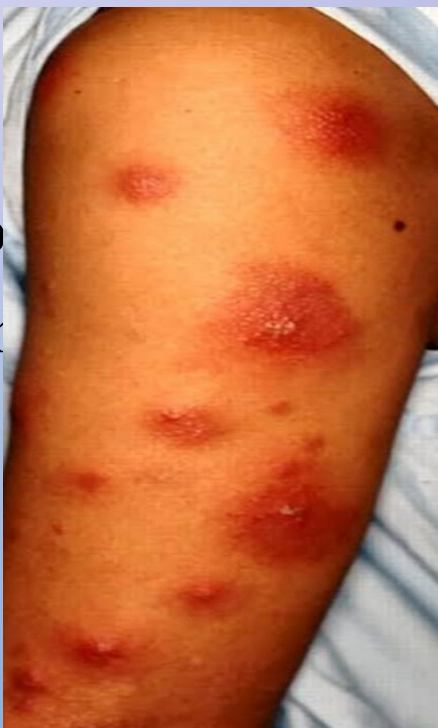
The borderline groups are unstable and may move across the spectrum in either direction with upgrading or downgrading of patient's immune state.

Accordingly, there may be two types of borderline reaction:

- **UPGRADING REACTION -** Is characterised by increased cell- mediated immunity and occurs in patients of borderline lepromatous (BL) type on treatment who upgrade or shift towards tuberculoid type
- **DOWNGRADING REACTION -** Is characterised by lowering of cellular immunity and is seen in borderline tuberculoid (BT) type who downgrade or shift towards lepromatous type.

TYPE II

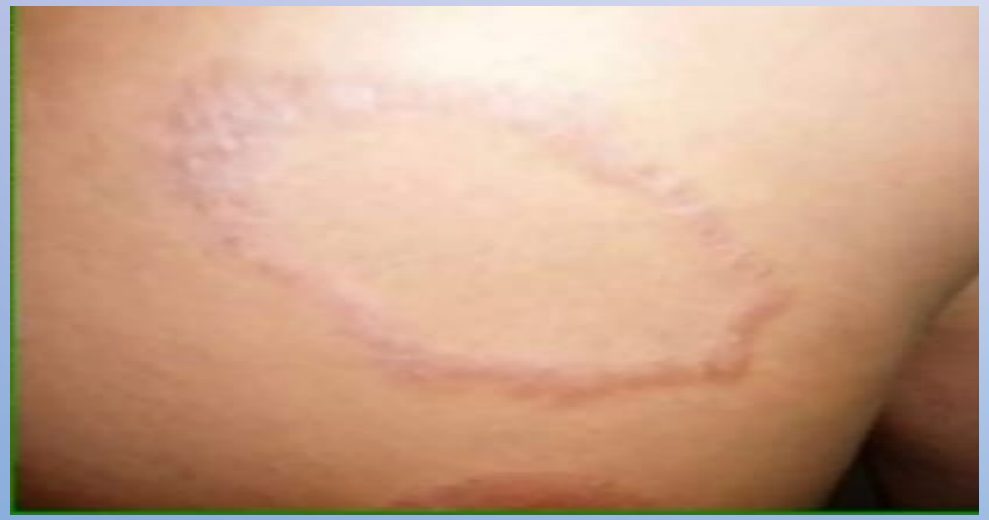
ERYTHEMA NODOSUM LEPROSUM (ENL)- ENL occurs in lepro patients after treatment. It is characterised by tender cutaneous r fever, iridocyclitis, synovitis and lymph node involvement.

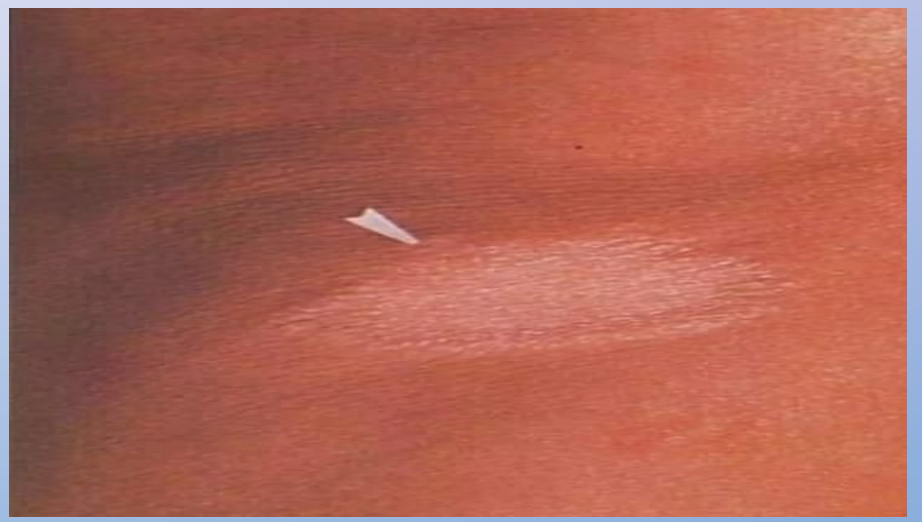


TUBERCULOID LEPROSY (TT)

- Benign and stable
- Number of lesions - 1 to 3.
- **MORPHOLOGY**- Well defined erythematous plaques with raised and clear cut edges sloping inwards. Lesions may be flat in the center with a raised well defined margin(annular).
- **SURFACE -** Dry, hairless, anesthetic and usually scaly.
- Nerve involvement occurs as a result of extension from or through cutaneous nerve branches.

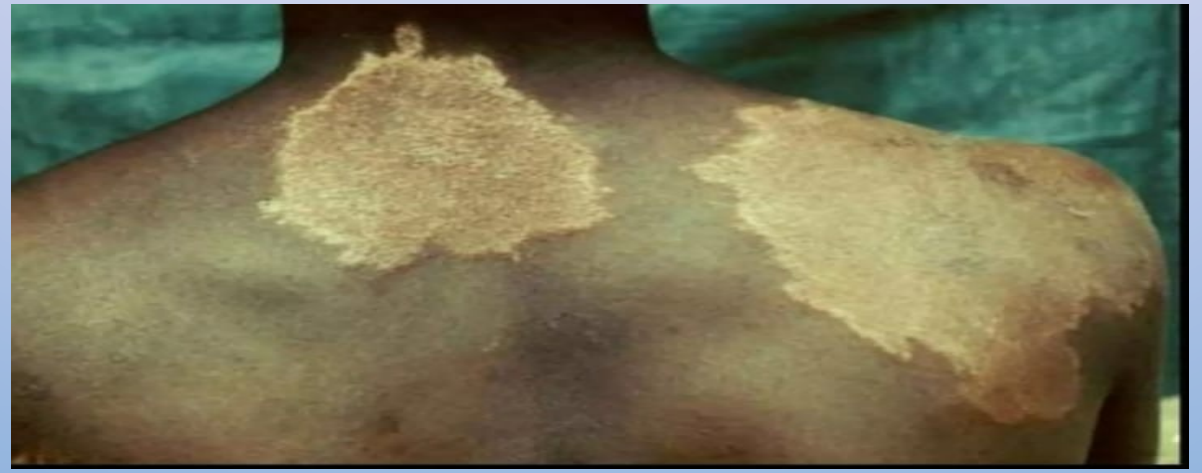
- Peripheral nerve - sensory loss
- Autonomic nerve - dry surface and loss of sweating, rough skin.
- A solitary peripheral nerve trunk may be thickened in the vicinity of a tt lesion (feeding nerve)
- No AFB found on slit skin smear.
- Lepromin test strongly +ve.





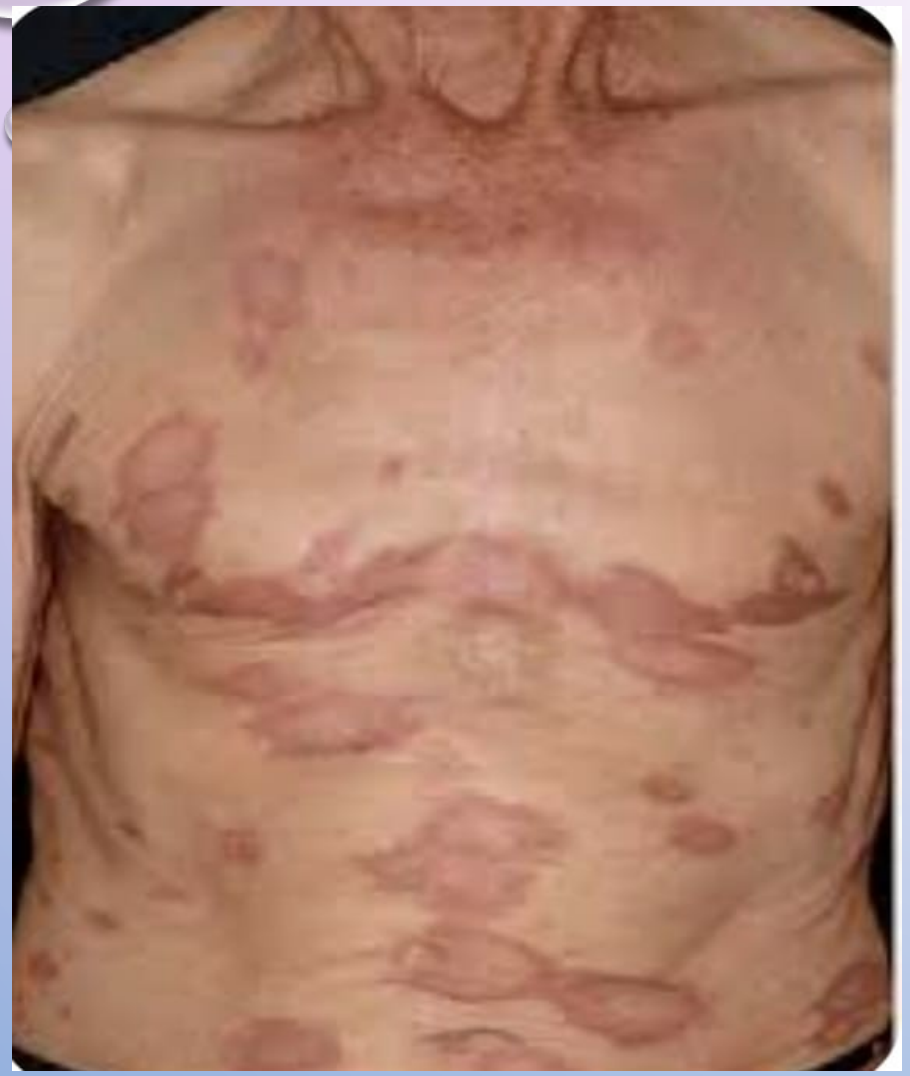
BORDERLINE TUBERCULOID (BT)

- 3 to 10 skin lesions
- 0 lesions similar to TT, but there is evidence of the disease not being contained. Small extension of the lesion at one edge (pseudopodium) or there may be satellite lesions. Lesions have less defined margins and the border may fade into the normal skin.
- Loss of sensations, dryness, scaling, erythema or hypopigmentation less conspicuous than that in TT.



BORDERLINE BORDERLINE(BB)

- Most unstable BB state is short lived and rapidly shifts to other poles, more often to BL.
- Mostly downregulates towards lepromatous pole if untreated.
- Presence of dimorphous type of lesions.
- Multiple skin lesions with a tendency to symmetry. Lesions are of all shapes and sizes including papules, plaques, circinate lesions or rarely even nodules.



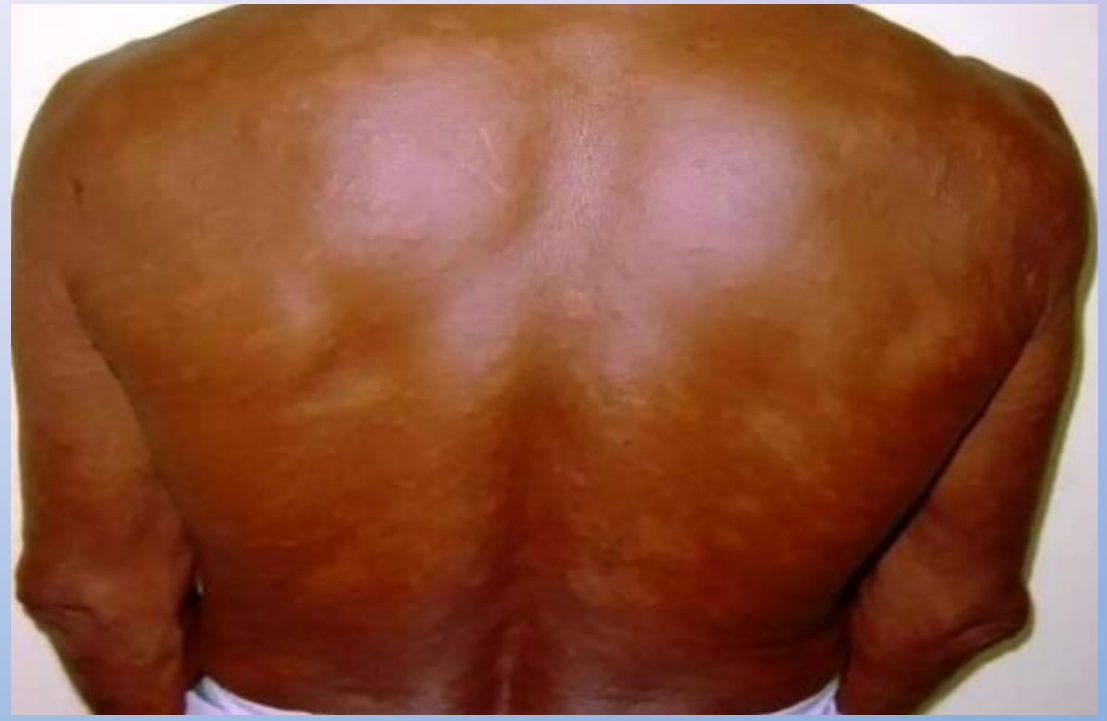
• Characerstic skin lesions are the annular lesions where the inner edge is well demarcated and the outer edge is ill defined and slopes towards normal skin. 'Punched out' appearance (**INVERTED SAUCER SHAPE).**

- Clinically, normal looking skin within such plaques gives a **"Swizz cheese"** appearance.
- Face may show inflitration with occasional nodules over ears and chin.

BORDERLINE LEPROMATOUS (BL)

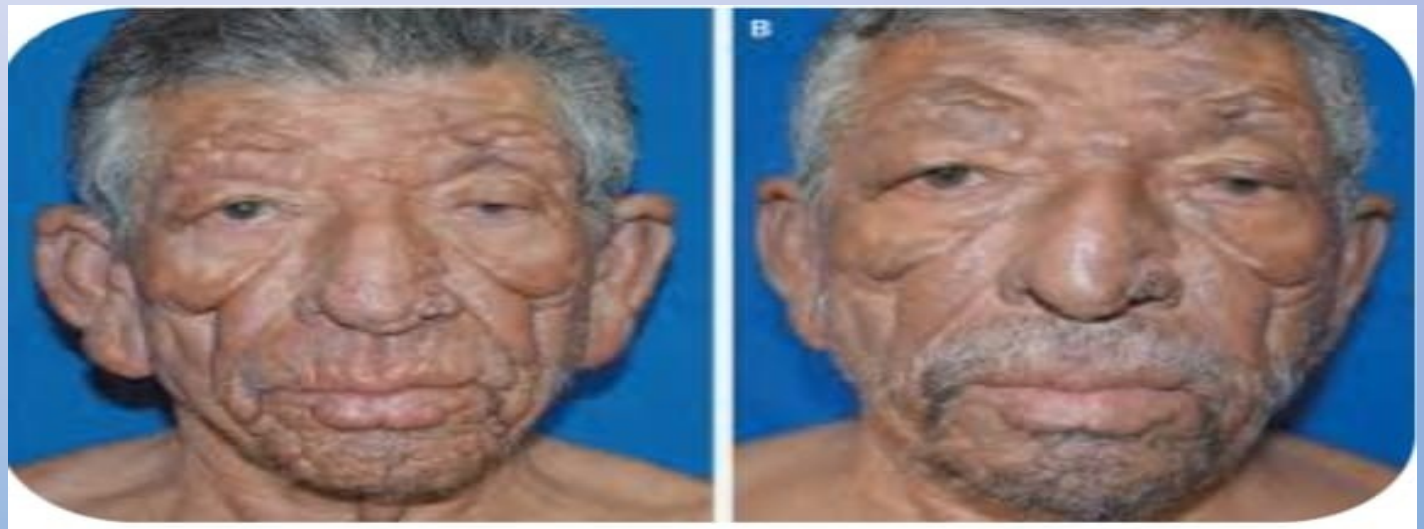
- Numerous skin lesions (>30)
- Ill defined showing tendency to bilateral symmetry.
- Infiltrated macules with copper hue, round or oval about 2-3cm in diameter. With disease progression, papules, nodules and plaques may develop, with sloping margins which merge into the normal skin.
- Infiltration takes place within the itinial macules, creating a plaque like appearance on face and ears. Surface of lesions shiny.
- Nerve trunks get damaged (not so symmetrically)

- Eyebrows involvement absent or partial.
- Systemic symptoms of involvement of oral cavity or eyes, testes appear later.
- More prone to develop type 2 reactions (erythema nodosum leprosum).
- Many AFBs seen on sss.
- Lepromin test negative.



LEPROMATOUS LEPROSY (LL)

- Multiplication and universal spread of M.Leprae
- Early lesions - innumerable small infiltrated, shiny, erythematous macules, with indistinct edges, widely disseminated and distributed symmetrically.
- Insidious onset and steady progression.
- LL with with infiltrated lesions presents as 3 distinct forms- diffuse, infiltrated and nodular forms.
- AFB positive in sss.
- Lepromin reaction negative.



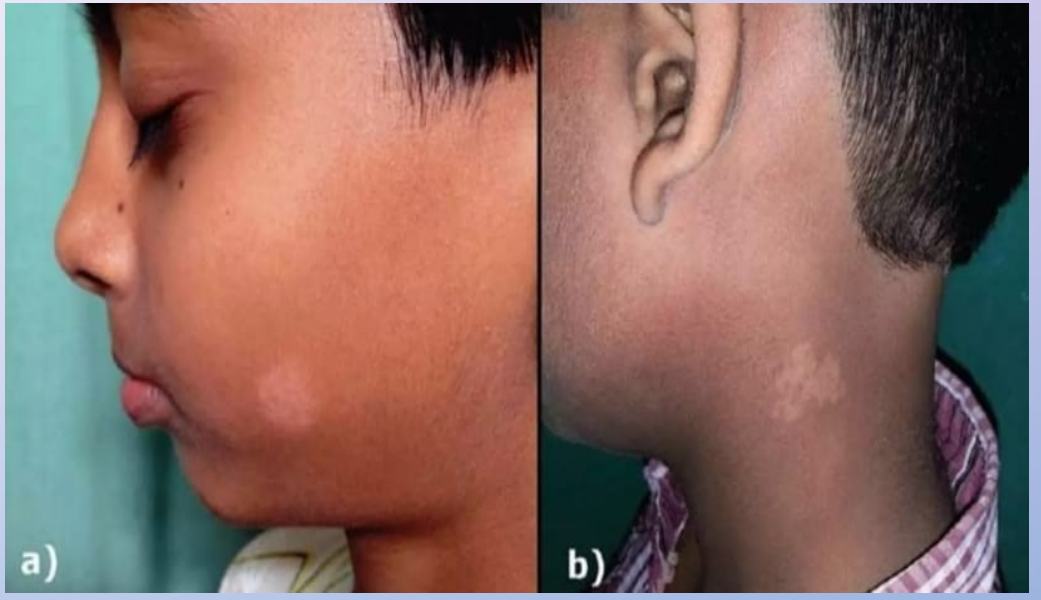
INDETERMINATE LEPROSY

• Medium to large hypopigmented patches which are faintly visible, often on the external aspect of the thigh, face, extensor aspect of limbs.

• Vague edges

• Some loss of tactile and thermal sensations

• Commonly misdiagnosed as P. Alba



• Excellent prognosis

• Lepromin reaction is variable

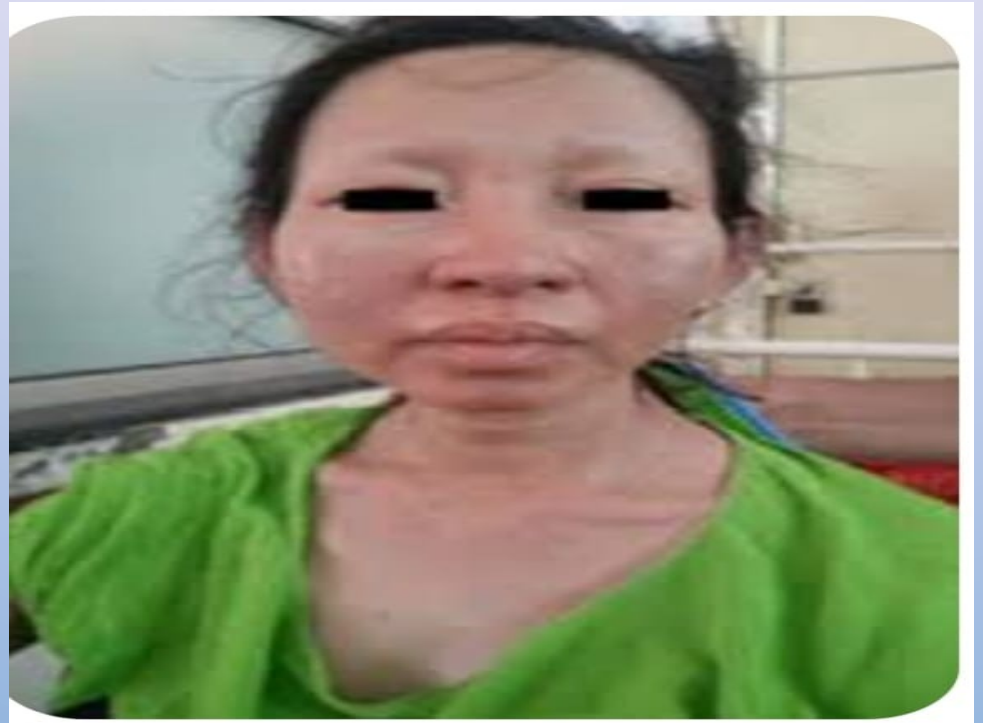
• AFB mostly not detectable.

• Diagnosis can only be confirmed with a biopsy- typical perineurovascular infiltrate.

SPECIAL FORMS OF LEPROSY

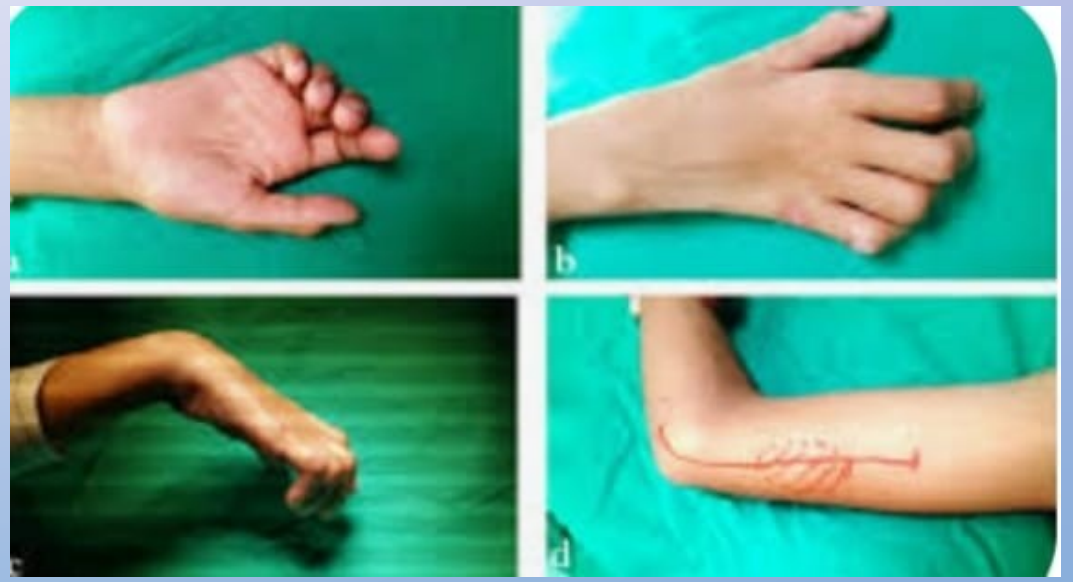
LUCIO LEPROSY/ LEPRA BONITA'/ BEAUTIFUL LEPROSY

- Rare form of lepromatous leprosy, described in mexico. Diffuse widespread infiltration of skin, loss of body hair, loss of eyebrows & eyelashes, and widespread sensory loss.



PURE NEURITIC LEPROSY

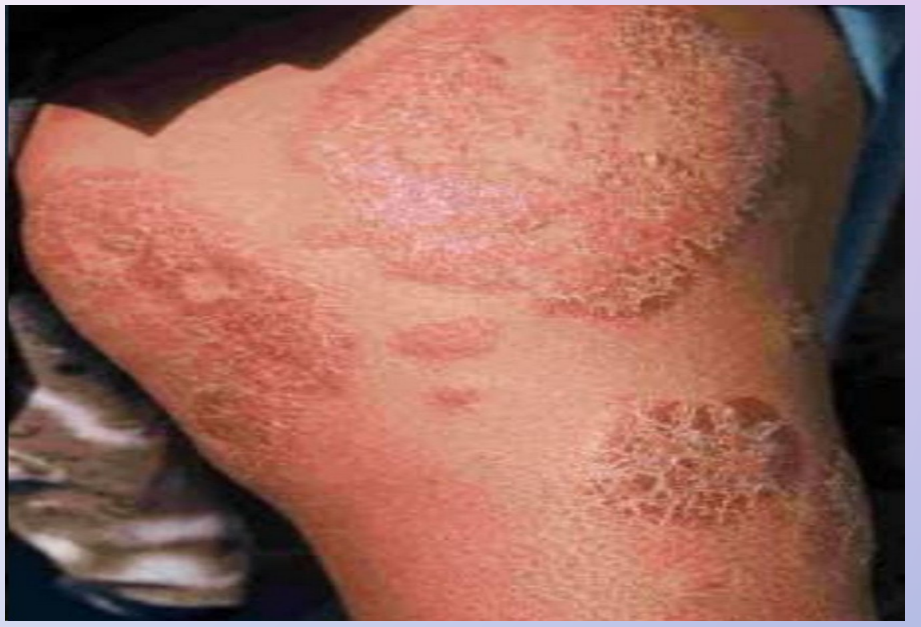
- Area of sensory loss in the absence of any skin patch along the distribution of an involved nerve trunk with or without motor deficit.
- Neuritic manifestations- tingling, heaviness, numbness, peresis, hypotonia, atrophy,claw hand and toes, wrist drop and foot drop, neuropathic ulcers, bone resorption.
- Most frequently in india and nepal
- Accounts for 5-10 percent

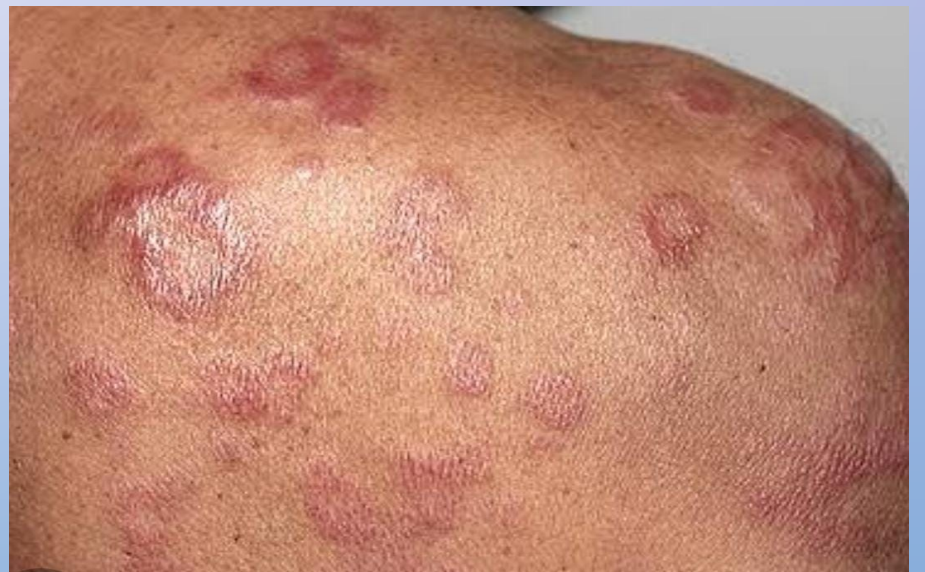


CLINICAL FEATURES

SKIN:

- Variable lesions: macules, papules, nodules.
- Single / multiple.
- Hypopigmented, sometimes reddish.
- Sensory loss typically (anaesthesia/hypothesia).



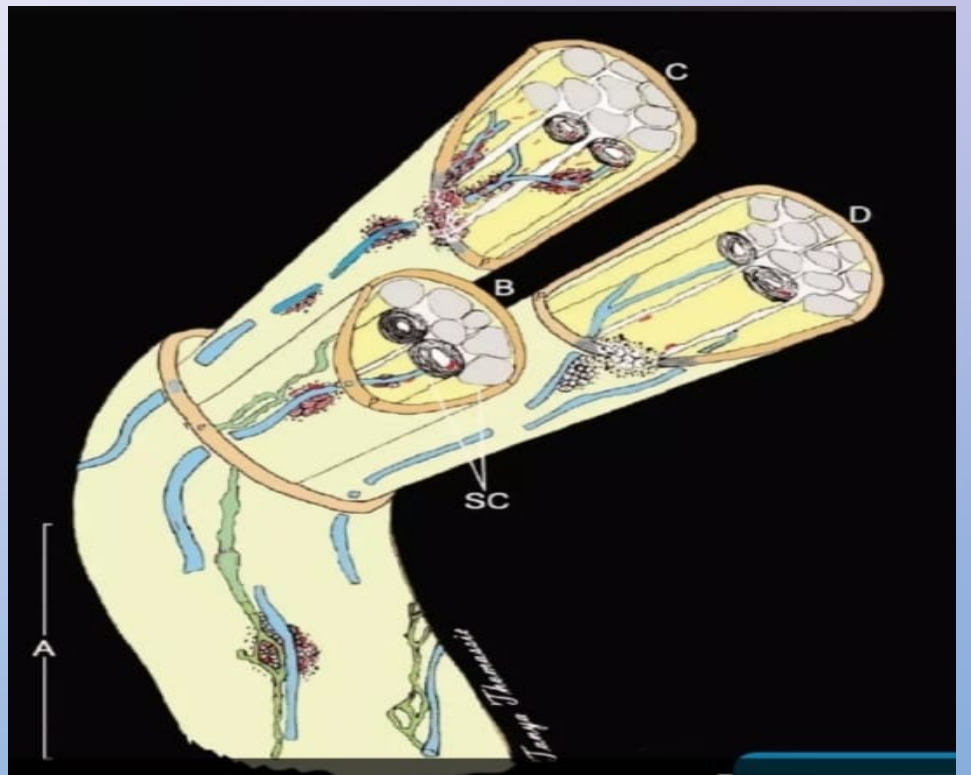


NERVES

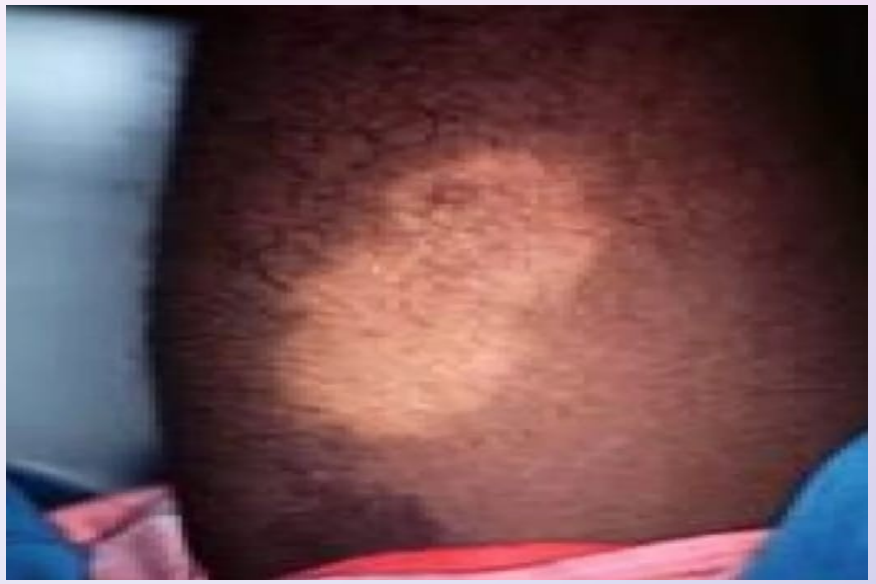
- Thickened.
- Loss of sensation.
- Muscle weakness.

Mechanism Of Nerve Damage

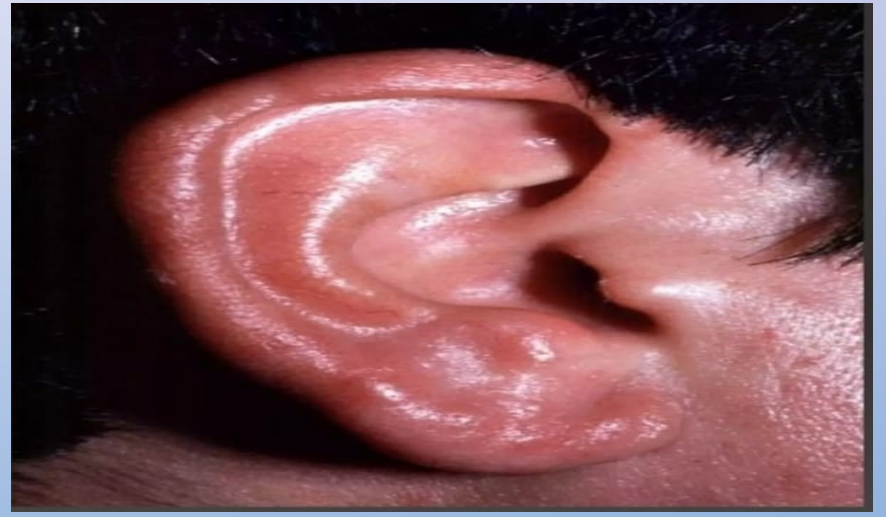
1. Entry through blood vessels
2. Inflammatory response
3. Demyelination



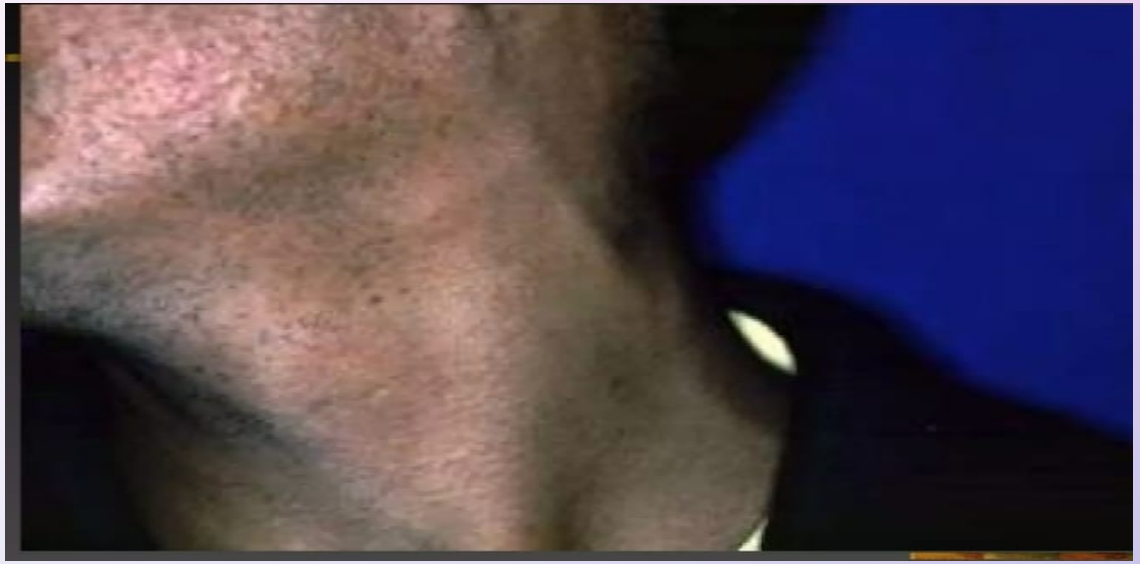
- ***HYPOPIGMENTED PATCH***



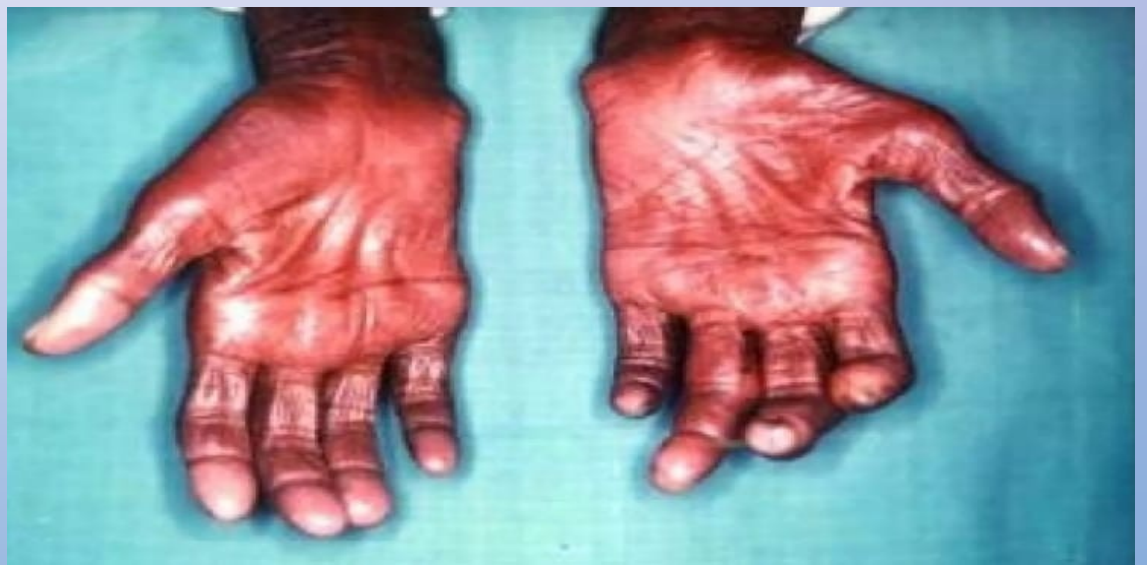
- ***EAR NODULES***



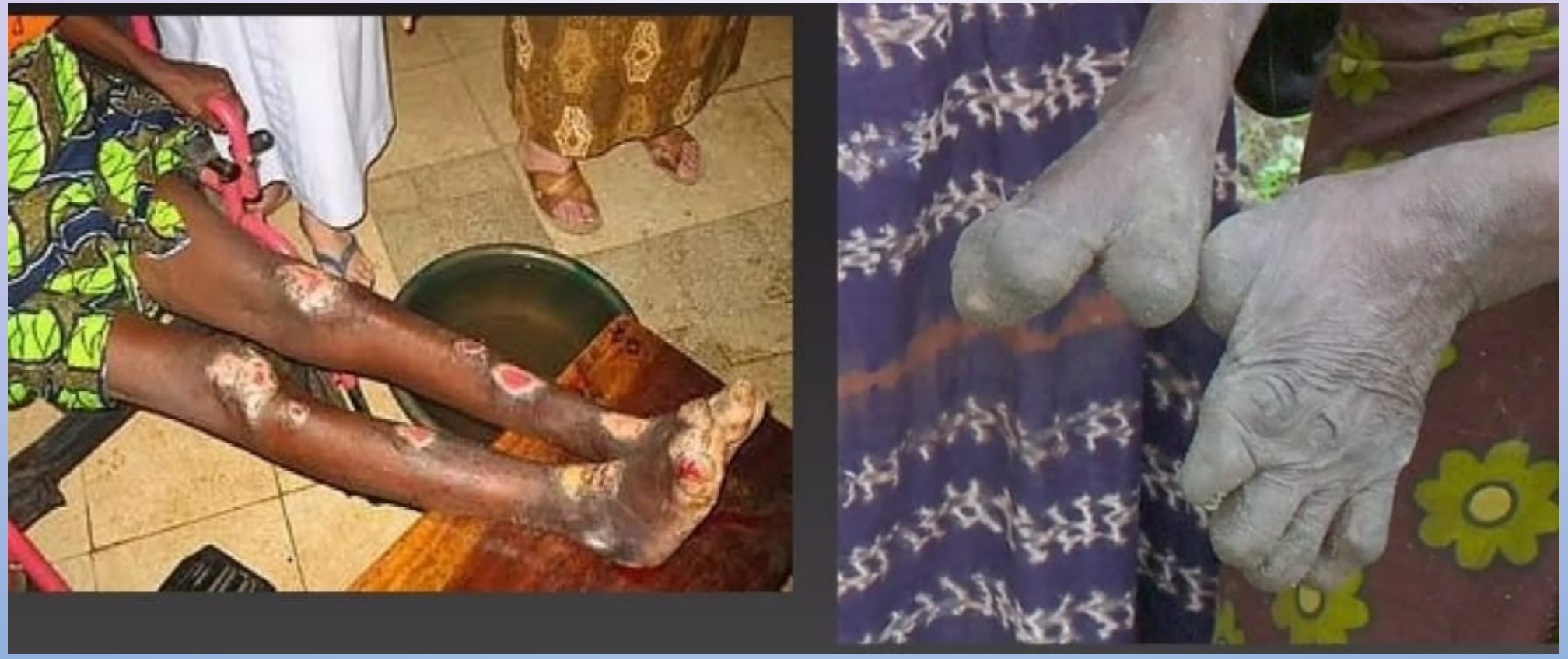
NERVE ENLARGEMENT



NEUROLOGICAL DEFECT



SENSORY LOSS CAN LEAD TO SECONDARY INFECTIONS AND SEVERE DEFORMITIES



CLINICAL EXAMINATION

1. General physical examination
2. Cutaneous and mucosal involvement
3. Ocular involvement
4. Palpation of peripheral nerves and testing for sensory impairment
5. Examination of musculoskeletal system
6. Examination of external genitalia
7. Other systemic examination

SIGN THAT LOOK LIKE LEPROSY

SKIN CONDITION

1. Tinia circinata,
2. Psoriasis
3. Vitiligo,
4. Naevus (birth mark)
5. Dermal leshmaniia

6. Neurofibromatosis

7. Nutritional dyschromia

8. Lichen planus

9. Pityriasis rosea

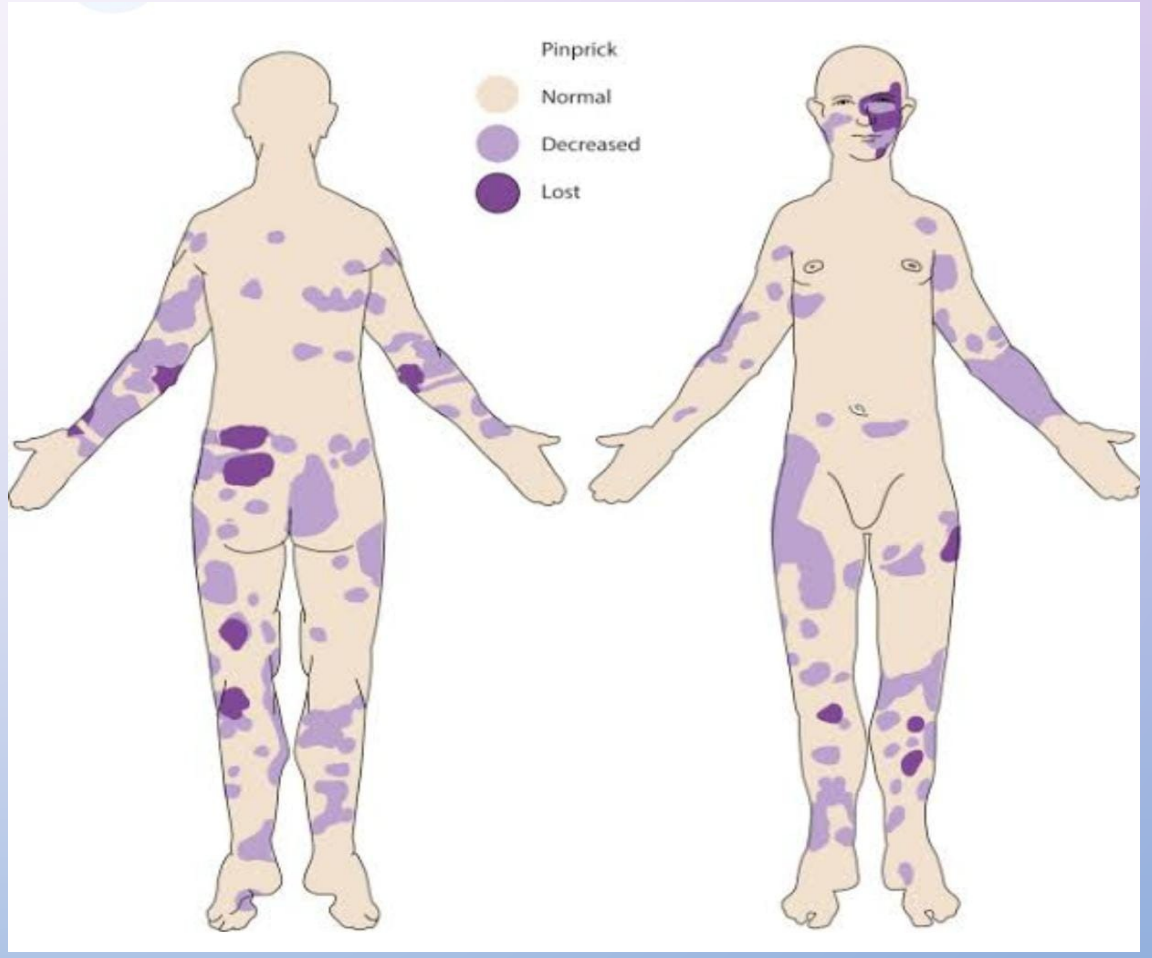
10. Lupus vulgaris

11. Scar & keloid

12. Xanthomatosis

NEUROLOGICAL CONDITION

1. Diabetic neuropathy
2. Alcoholic neuritis
3. Syringomyelia
4. Tabes dorsalis



SURFACE ANATOMY OF NERVES

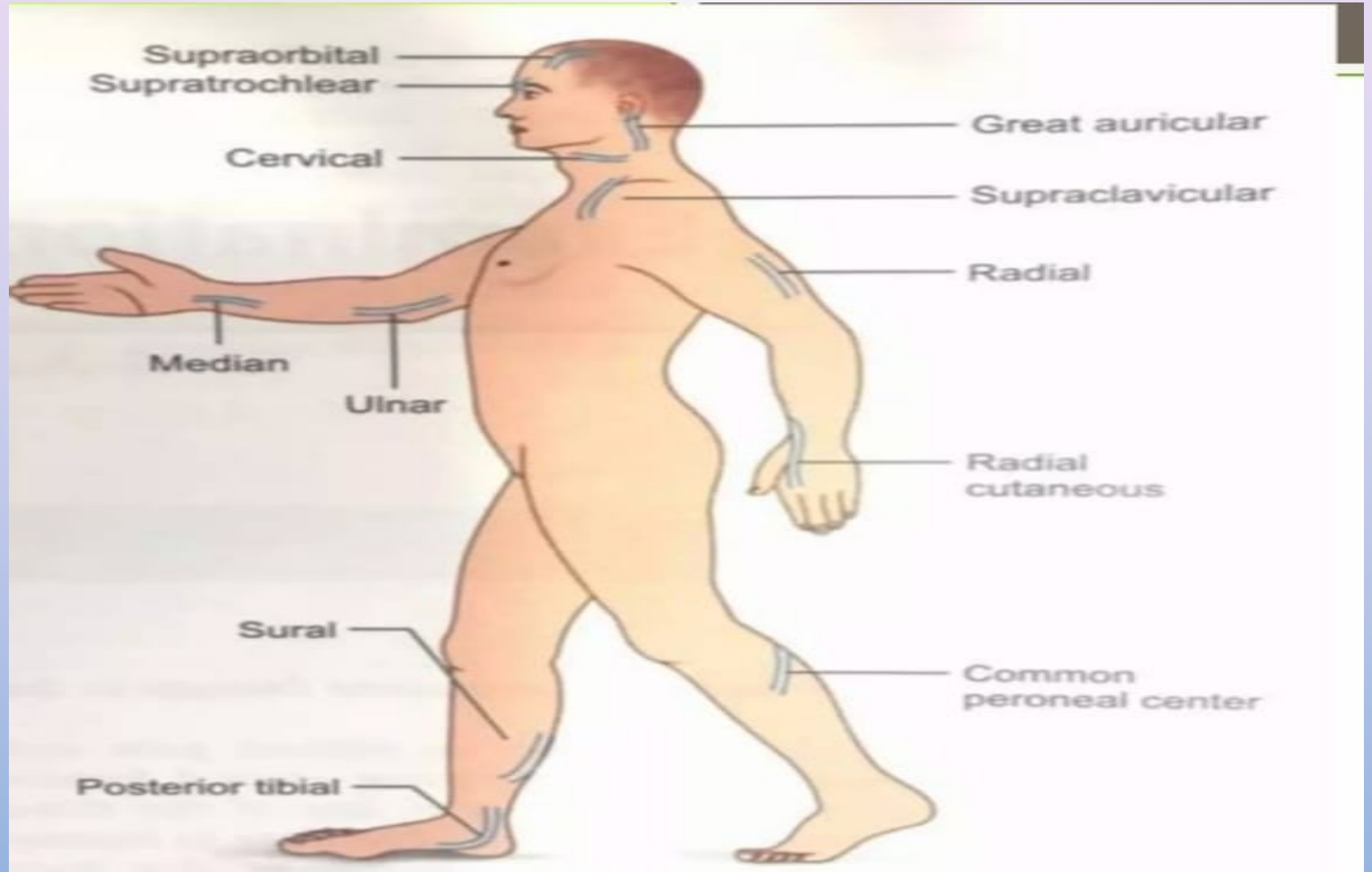
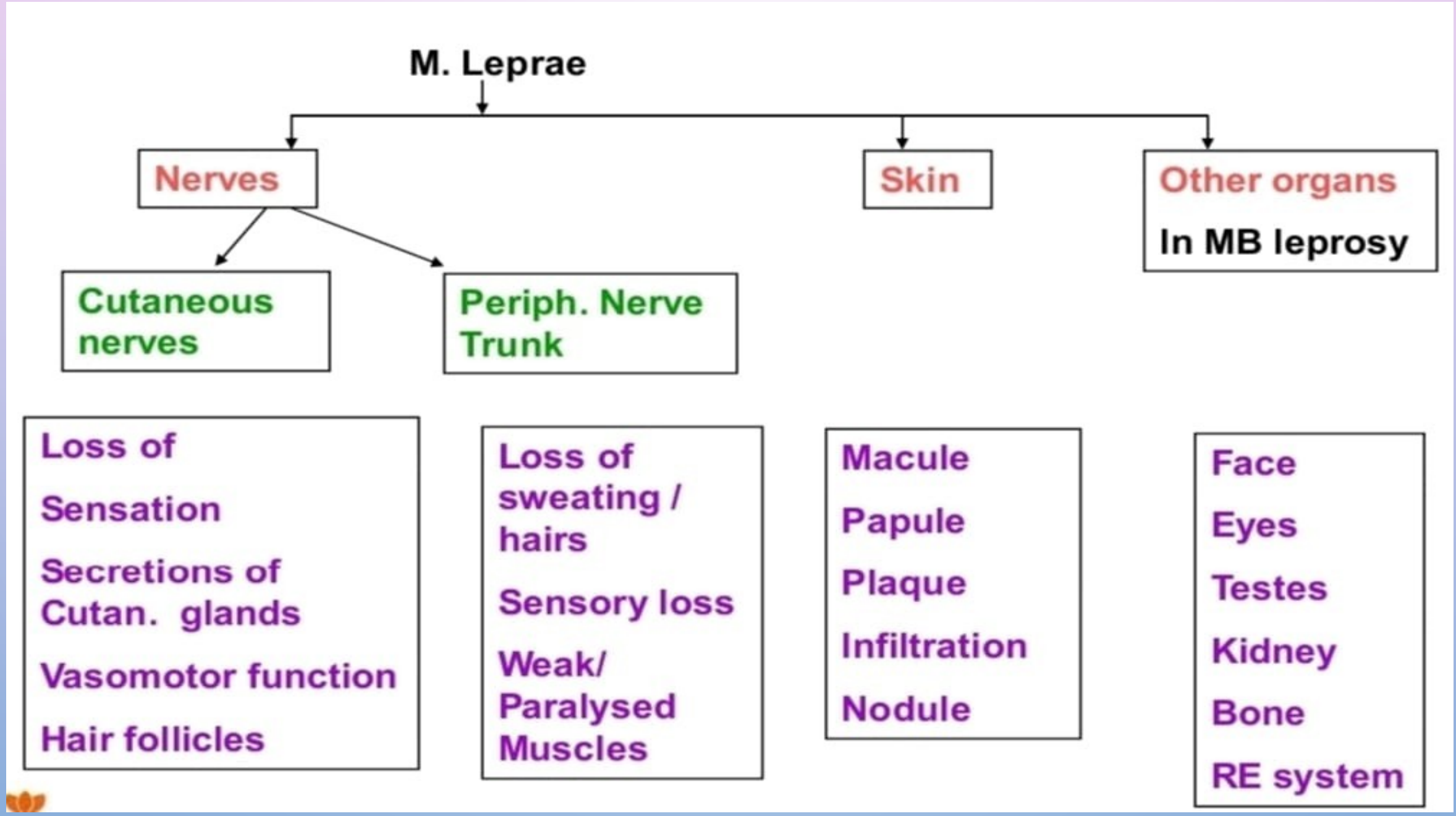
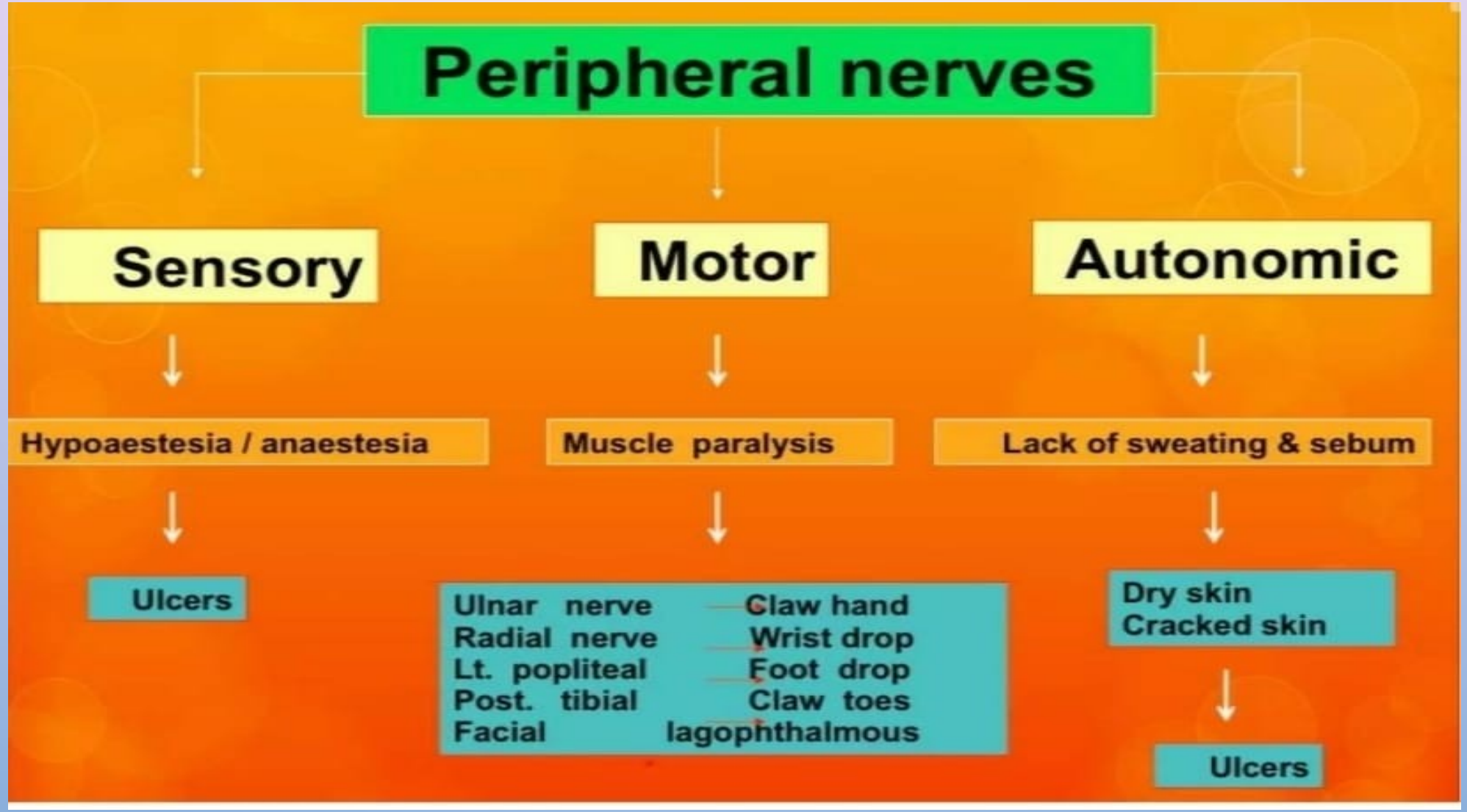


Fig. 17.1: Surface marking of nerves commonly affected in leprosy


M. Leprae
Nerves
Skin
Other organs
In MB leprosy
Cutaneous nerves
Periph. Nerve Trunk
Loss of
Sensation
Secretions of Cutan. glands
Vasomotor function
Hair follicles
Loss of sweating / hairs
Sensory loss
Weak/ Paralysed Muscles
Macule
Papule
Plaque
Infiltration
Nodule
Face
Eyes
Testes
Kidney
Bone
RE system

PERIPHERAL NERVES

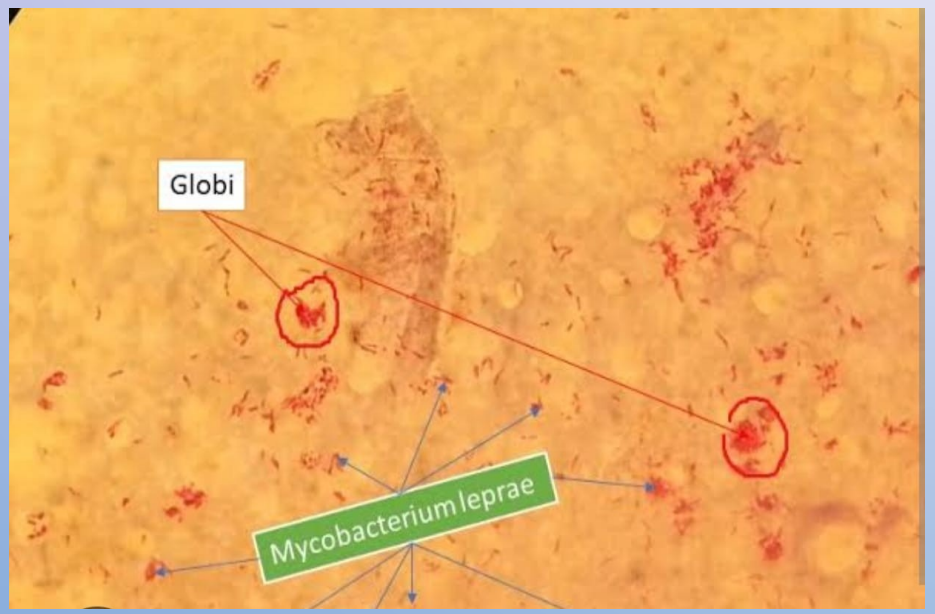


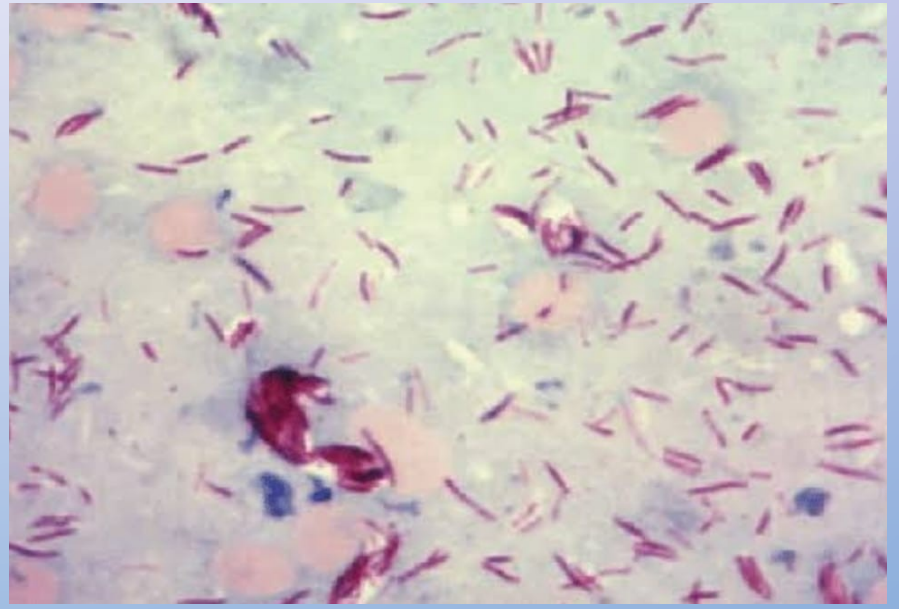
DIAGNOSIS OF LEPROSY

- Diagnosis of leprosy is most commonly based on the clinical signs and symptoms.
- Sample collection from lesion.
- Specimen are collected from nasal mucosa, skin lesion and clear lobules.
- Blunt, narrow scalpel is introduced into the nose and a piece of mucous membrane is taken. - **Nasal mucosa**
- Skin is pinched and cut about 5mm and a deep infiltrated layer is taken with a scalpel. - **Skin lesion**

1. **Acid-fast (ziehl-neelsen or ZN) staining** the staining procedure is similar as for demonstration of M. Tuberculosis but can be decolourised by lower concentration (5%) of sulphuric acid (less acid-fast).

2**. Fite-faraco staining** this procedure is a modification of ZN procedure and is considered better for more adequate staining of tissue sections .





3. **Gomori methenamine silver (GMS) staining** can also be employed.

4. Molecular methods, e.g. **PCR**.

5. IgM antibodies to **PGL-1 antigen** is seen in 95% cases of lepromatous leprosy but only in 60% cases of tuberculoid leprosy.

- The **slit smear technique** gives a reasonable quantitative measure of **M. Leprae** when **stained** with **ZN method** and examined using **100x oil** objective for determining the **density of bacteria** in the lesion **(bacterial index, BI).** BI is scored from **1 + to 6 +** (range from 1 to 10 bacilli per 100 fields to > 1000 per field) as **Multibacillary leprosy** while BI of **0+ is termed Paucibacillary leprosy**. This forms the basis of WHO classification of leprosy practiced by field workers.

- **Lymphocyte Migration Inhibition Test (LMIT)**:

As determined by a lymphocyte transformation and LMIT, cell- mediated immunity to M leprae is absent in patients with lepromatous leprosy but present in those with tuberculoid leprosy.

- **Contact or family screening for history of leprosy**.

LEPROMIN TEST

Intradermal injection of lepromin, an antigenic extract of M. Leprae, reveals delayed hypersensitivity reaction in patients of tuberculoid leprosy:

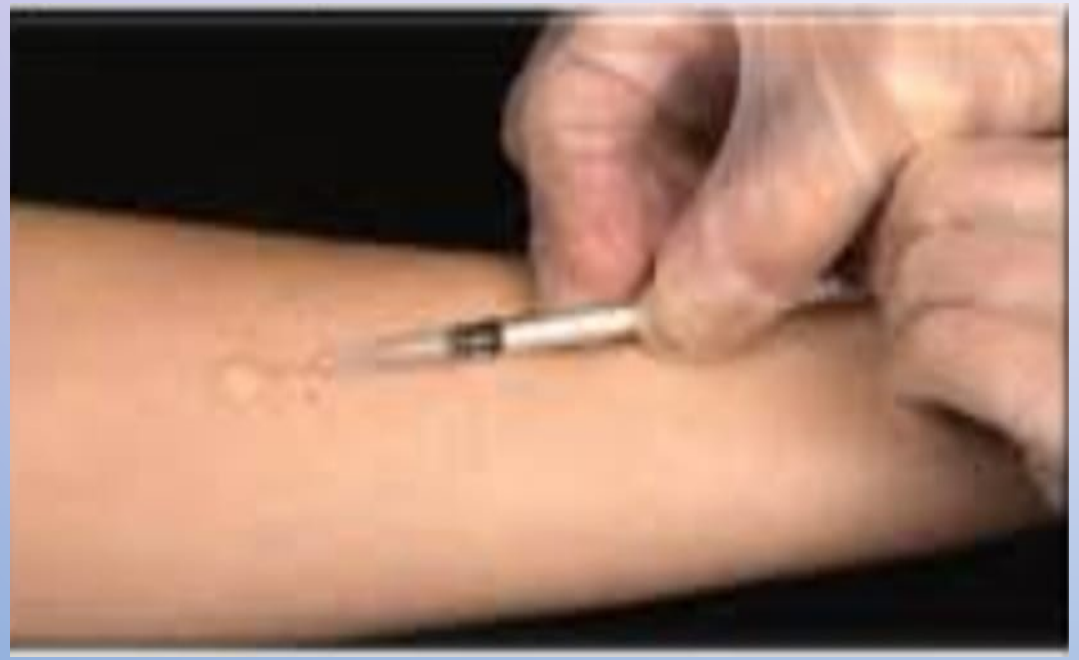
1) An early positive reaction appearing as an indurated area in 24-48 hours is called Fernandez reaction.

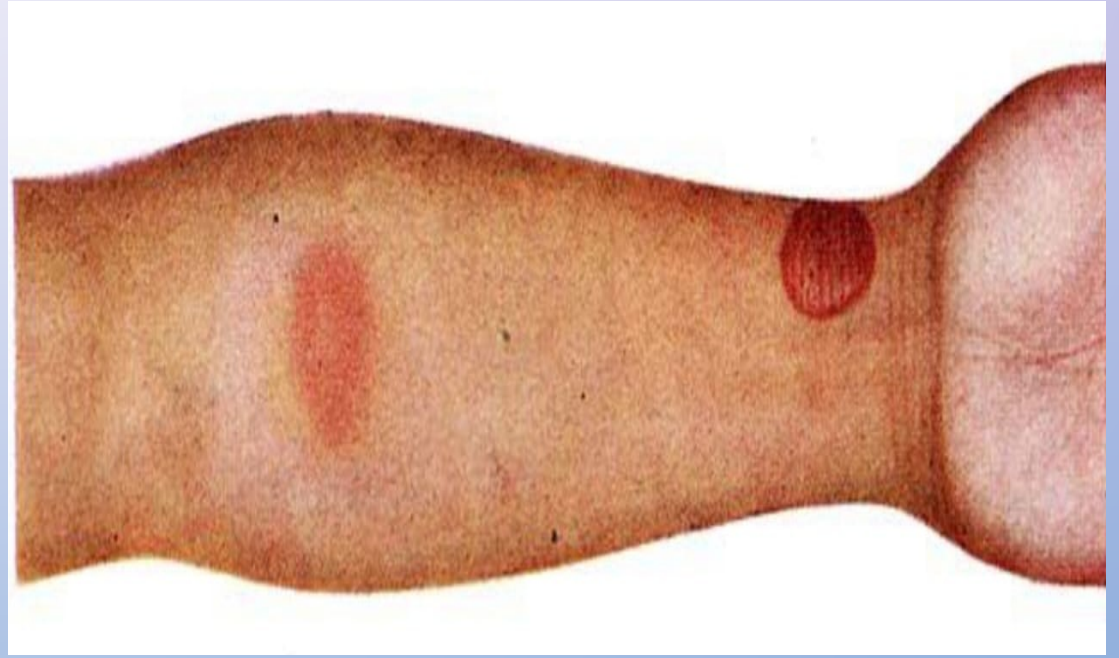
2) A delayed granulomatous lesion appearing after 3-4 weeks is called Mitsuda reaction.

This test indicates that cell-mediated immunity patients of -

- Tuberculoid leprosy show good immune response.
- On the other hand, patients of lepromatous leprosy are negative by the lepromin test. It indicates that cell-mediated immunity is greatly suppressed in lepromatous leprosy.

- Delayed type of hypersensitivity is conferred by T helper cells. The granulomas of tuberculoid leprosy have sufficient T helper cells and fewer T suppressor cells at the periphery while the cellular infiltrates of lepromatous leprosy lack T helper cells.





CASE PRESENTATION

- NAME OF PATIENT:
- FATHER'S NAME:
- AGE: 21 YRS
- SEX: MALE
- CAST:
- RELIGION: HINDU
- OCCUPATION: LABOUR (~5000P.M.)
- MARITAL STATUS: MARRIED
- FAMILY MEMBERS: TOTAL 5 (3 CHILDREN =2F+1 M)
- ADDRESS: VILLAGE BHAGWANPUR, V.P.O RAJPUR, DIST. BAXAR, BIHAR (MOB. 07891222169)
- CHIEF COMPLAINTS:

* **REDDISH PATCH WITH NUMBNESS AT RT. LEG - 4 MONTHS**

HISTORY OF PRESENT ILLNESS:

Patient was apparently asymptomatic about 4 months back then reddish patch develop at Rt. outer leg. Gradually it increased in size and numbness.

HISTORY OF PAST ILLNESS:

No history of any specific past illness and previous hospitalization.

*FAMILY HISTORY: Not significant.

*5 members in the family, one male i.e. patient himself 21 yrs old and o his WIFE 20 yrs old. 3 CHILDREN, one male & 2 female.

*PERSONAL HISTORY:

*Patient is purely vegetarian, Non Alcoholic

*Smoker 10-15 biddies per day, Tobacco chewer 5~7 packet per day,

* Bowel and bladder habit normal.

- *DRUG HISTORY: NO HISTORY OF ANY DRUG ALLERGY.
- *IMMUNISATION HISTORY: UNKNOWN
- *SOCIO ECONOMIC STATUS:
- *PATIENT IS MIGRATORY FROM BIHAR. RESIDING AT KACHHI BASTI NEAR TRANSPORT NAGAR; JAIPUR SINCE 2 YEARS.
- * AND LIVES IN RENTED PUCCA HOUSE 2 ROOMS WITHOUT LATRINE AND BATHROOM FACILITIES.
- *LABOUR BY OCCUPATION AND EARNS A MONTHLY INCOME OF RS.5000.

- *GENERAL PHYSICAL EXAMINATION:
- GENERAL CONDITION FAIR.

➤ PATIENT IS WELL CONSCIOUS AND WELL ORIENTED TO TIME PLACE

- **VITALS:**
- ➤BLOOD PRESSURE: 120/70 MMHG, PULSE RATE: 84/MIN/REGULAR
- ➤RR-20/MIN/REGULAR, TEMP- AFEBRILE
- ➤NO PALLOR, ICTERUS, CYANOSIS, LYMPHADENOPATHY, OEDEMA.
- **LOCAL EXAMINATION**:
- **➤SINGLE ERYTHAMATOUS SKIN PATCH IS PRESENT OVER THE RT. LEG LOWER ON LATERAL SIDE.**
- **➤WELL DEFINE MARGIN; SIZE~5CM *2.5 CM**
- **➤DECREASE SENSATION OF TOUCH, TEMPERATURE, PAIN**
- **NO OTHER PATCH AND THICKENED PERIPHERAL NERVE SEEN.**

- **SYSTEMIC EXAMINATION**:
- RESPIRATORY SYSTEM: BILATERAL SYMMETRY OF THE CHEST IS NORM BILATERAL CHEST SOUNDS CLEAR.
- CVS: S1 S2 NORMAL, NO MURMUR SOUND HEARD.
- CNS: NORMAL.
- INVESTIGATION DONE:
- HEMATOLOGICAL INVESTIGATION:
- ➤C.B.C - NAD
- ➤SKIN BIOPSY :

  ➤**TUBERCULOID LEPROSY**


Thank
You