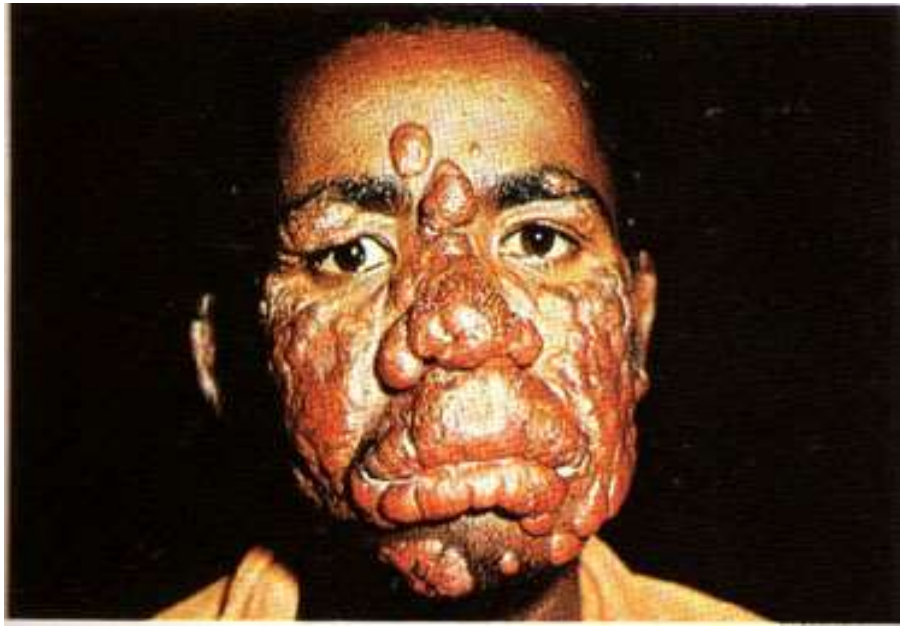
Anti Leprotic Drugs

Leprosy



- Mycobacterium leprae
- strongly acid-fast rod-shaped
- Also known as Hansen's disease, after the scientist ho discovered *M. leprae* in 1873
- Long Incubation period (3 – 5 years)

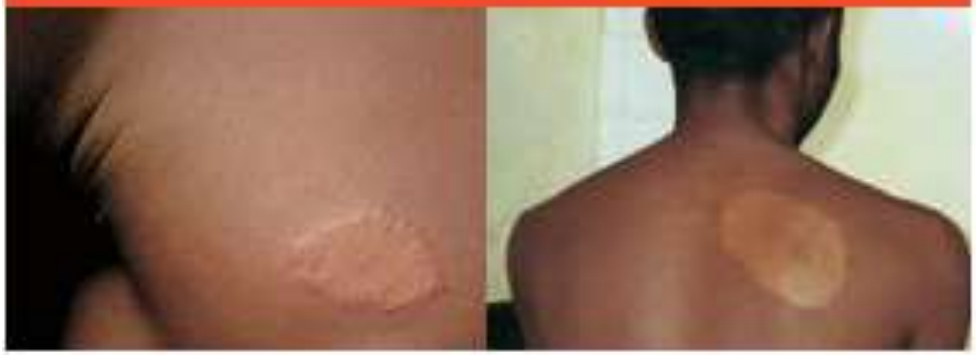
- primarily affect superficial tissues, especially the skin and peripheral nerves.

- A leprosy patient is someone who: has a skin patch or patches with a definite loss of sensation;
- Leprosy patches:
- Can be pale or reddish or copper-coloured;
- Can be flat or raised;
- Do not itch;
- Usually do not hurt;
- Lack sensation to heat, touch or pain;
- Can appear anywhere.

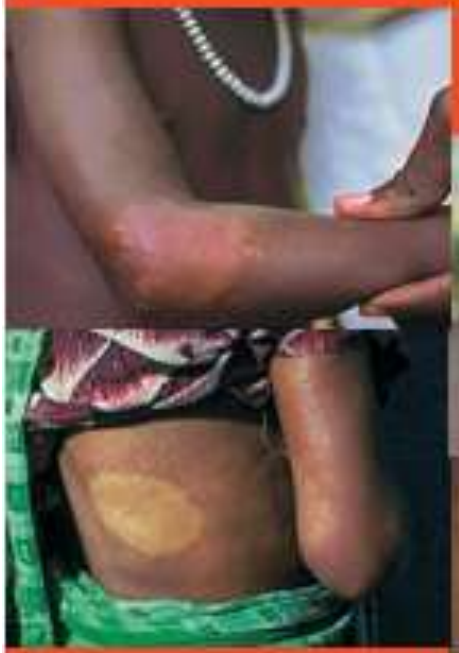
Leprosy patches...

...can be pale or reddish
or copper-coloured.

...can be flat or raised.



Leprosy patches...



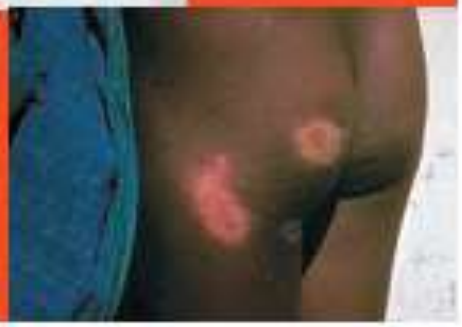
...usually do not hurt.

...lack sensation
to heat, touch or pain.

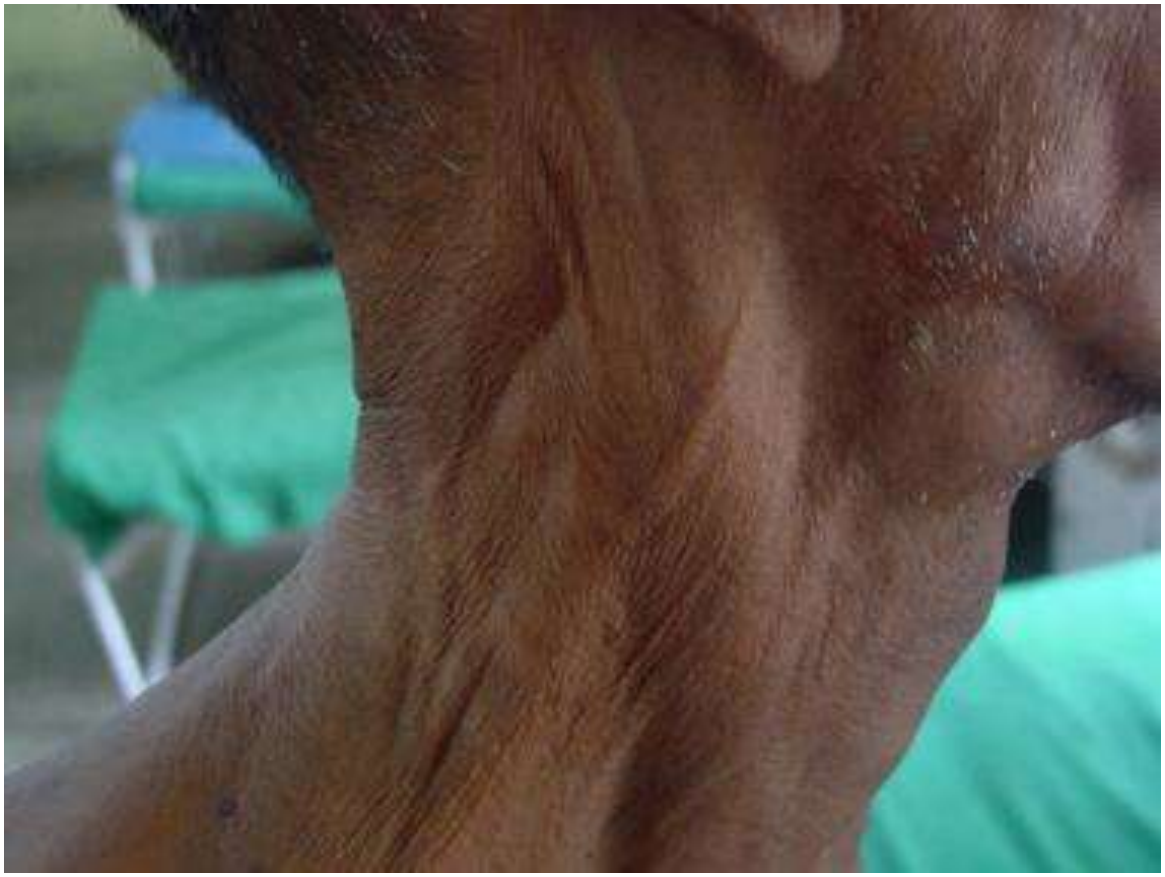
...can appear anywhere.

...do not
itch.

Leprosy can be
diagnosed
on clinical signs
alone.



Peripheral nerve thickening in leprosy



Hand deformities in leprosy

Classification

1. Sulfone	Dapsone (DDS)
2. Phenazine derivative	Clofazimine
3. Antitubercular drugs	Rifampin, Ethionamide
4. Other antibiotics	Ofloxacin, Moxifloxacin, Minocycline, Clarithromycin

Dapsone (DDS)

- diamino diphenyl sulfone (DDS)
- simplest, oldest, cheapest, most active and most commonly used member of its class.

- Mechanism of action
- inhibition of PABA incorporation into folic acid by folate synthase.

- Dapsone-resistance among M. leprae, first noted in 1964, has spread and has necessitated the use of multidrug therapy (MDT).

Dapsone Resistance

Primary	**Infection was contacted from a patient harbouring resistant bacilli.**
Secondary	Resistance which develops during monotherapy in an individual patient with dapsone
Persisters	Drug sensitive bacilli which become dormant, hide in some tissues and are not affected by any drug. They may stage a comeback after the drug is withdrawn.

Dapsone

- Pharmacokinetics
- Dapsone is completely absorbed after oral administration and is widely distributed in the body, though penetration in CSF is poor.
- The plasma t½ of dapsone is variable, though often > 24 hrs.

Dapsone

- Adverse effects
- Mild haemolytic anaemia
- Gastric intolerance
- Cutaneous reactions: allergic rashes, fixed drug eruption, hypermelanosis, phototoxicity and rarely exfoliative dermatitis.
- Hepatitis and agranulocytosis are rare complications.

Dapsone

- Sulfone syndrome: develops 4–6 weeks after starting dapsone treatment: consists of fever, malaise, lymph node enlargement, desquamation of skin, jaundice and anaemia.

- Its treatment consists of stopping dapsone and instituting corticosteroid therapy along with supportive measures.

Dapsone

- Contraindications
- Dapsone should not be used in patients with severe anaemia (Hb < 7 g/dl),
- G-6-PD deficiency
- hypersensitivity reactions.

Clofazimine (Clo)

- It is a dye with leprostatic and antiinflammatory properties.

Clofazimine (Clo)

The putative mechanisms of anti-leprotic action of clofazimine are:

- Interference with template function of DNA in M.leprae
- Alteration of membrane stucture and its transport function.
- Disruption of mitochondrial electron transport chain.

Clofazimine (Clo)

- Orally active (40–70% absorbed).
- It accumulates in macrophages and gets deposited in many tissues including subcutaneous fat, as needle-shaped crystals.
- entry in CSF is poor.
- The t½ is 70 days so that intermittent therapy is possible.

Clofazimine (Clo)

- Because of its antiinflammatory property, it is valuable in lepra reaction.

Clofazimine (Clo)

- Adverse effects
- Skin
    - Reddish-black discolouration of skin.
    - Discolouration of hair and body secretions
    - Dryness of skin and itching
    - Acneform eruptions
    - Phototoxicity

Clofazimine (Clo)

- GI symptoms
- **early syndrome:** Nausea, anorexia, abdominal pain, weight loss and enteritis with intermittent loose stools
- **late syndrome:** deposition of clofazimine crystals in the intestinal submucosa.

Rifampin (R)

- Most potent cidal drug for M.leprae
- Rifampin remains effective in leprosy even if given once a month.
- It should not be given to patients with hepatic or renal dysfunction, as well as during ‘erythema nodosum leprosum’ (ENL) and ‘reversal reaction’ in leprosy patients, because it can release large quantities of mycobacterial antigens by inducing rapid bacillary killing.

Ofloxacin

- cidal to M.leprae
- can be used in alternative regimens in case rifampin cannot be used,
- to shorten the duration of treatment
- reduce chances of drug resistance.

Minocycline

- Because of high lipophilicity, this tetracycline penetrates into M.leprae.
- Vertigo is the only serious complication of its long-term use.
- It is being tried in alternative MDT regimens.

Clarithromycin

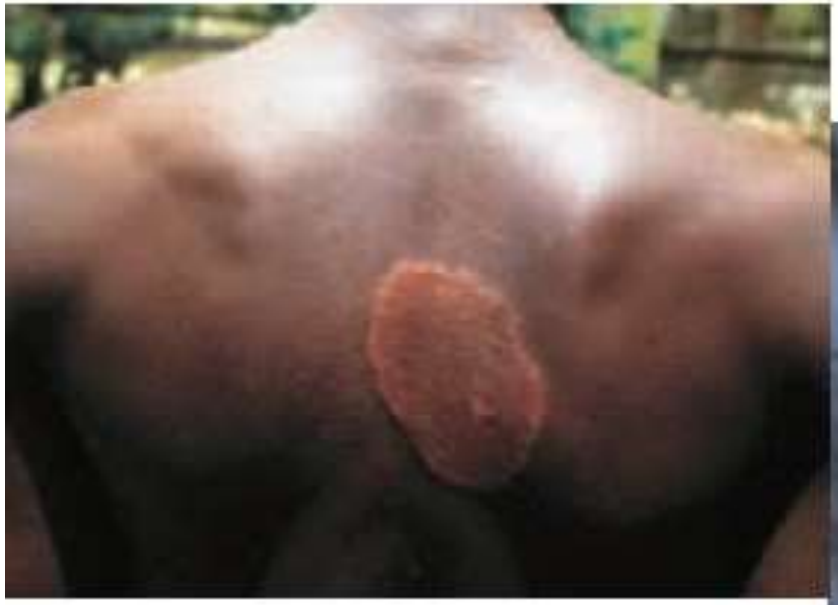
- Less bactericidal than rifampin.
- being included in alternative MDT regimens.

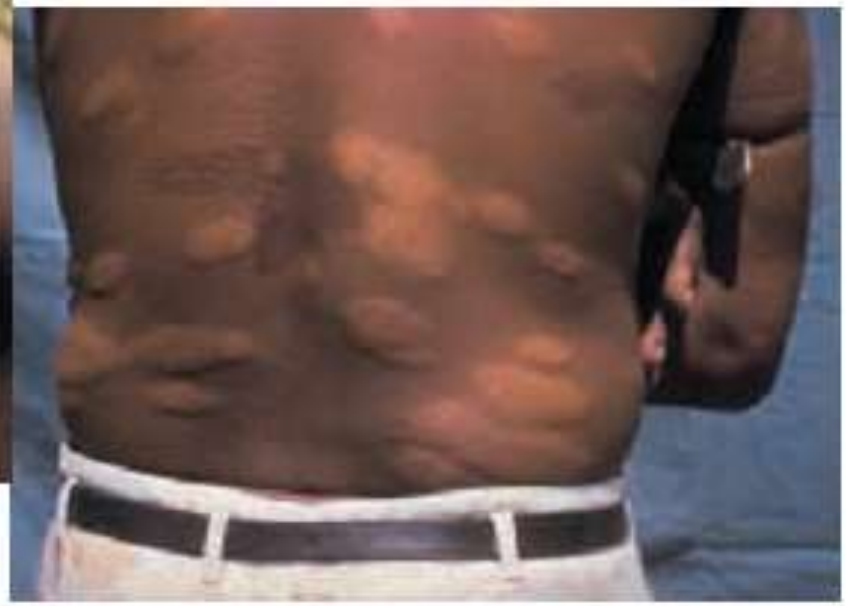
- Though the burden of leprosy has fallen drastically after introduction of MDT, both globally and in India, WHO data (2010) show that 65% of all new leprosy cases worldover are from India.

NLEP (2009) Classification of Leprosy

Paucibacillary (PB)	Multibacillary (MB)
1-5 skin lesions	6 or more skin lesions
No nerve/only one nerve involvement, + 1–5 skin lesions	> 1 nerve involved irrespective of number of skin lesions
Skin smear negative at all sites	Skin smear positive at any one site

1–5 patches?
It is paucibacillary (PB) leprosy. Treatment:
6 PB blister packs.





More than 5 patches?
It is multibacillary (MB) leprosy.
Treatment: 12 MB blister packs.

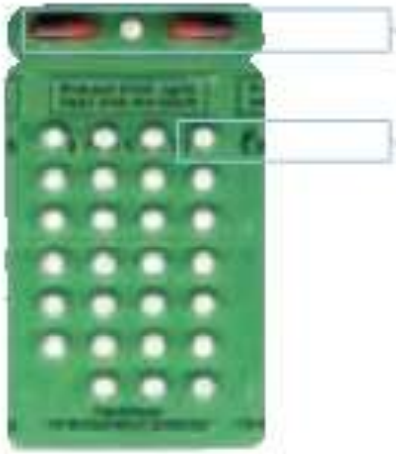
Multidrug therapy (MDT) of leprosy

- To deal with dapsone resistant strains of M. leprae
- to shorten the duration of treatment
- Multidrug therapy with rifampin, dapsone and clofazimine was introduced by the WHO in 1981.

- Advantages
- Effective in cases with primary dapsone resis tance.
- Prevents emergence of dapsone resistance.
- Affords quick symptom relief and renders MBL cases noncontagious within few days.
- Reduces total duration of therapy

Multidrug therapy (MDT) of leprosy

	Multibacillary	Paucibacillary
Rifampin	600 mg once a month supervised	600 mg once a month supervised
Dapsone	100 mg daily self administered	100 mg daily self administered
Clofazimine	300 mg once a month supervised and 50 mg daily self administered	—
Duration	12 months	6 months



PB adult blister pack

PB adult treatment:

Once a month: Day 1
– 2 capsules of rifampicin (300 mg X 2)
– 1 tablet of dapsone (100 mg)

Once a day: Days 2–28
– 1 tablet of dapsone (100 mg)

Full course: 6 blister packs

MB adult blister pack

MB adult treatment:

Once a month: Day 1
– 2 capsules of rifampicin (300 mg X 2)
– 3 capsules of clofazimine (100mg X 3)
– 1 tablet of dapsone (100 mg)

Once a day: Days 2–28
– 1 capsule of clofazimine (50 mg)
– 1 tablet of dapsone (100 mg)

Full course: 12 blister packs

Alternative regimens

- used only in case of rifampin-resistance or when it is impossible/inadvisable to employ the standard MDT regimen.

Alternative regimens

- **Intermittent ROM:** Rifampin 600 mg + ofloxacin 400 mg + minocycline 100 mg are given once a month for 3–6 month for PBL and for 12 or 24 month for MBL cases, without any drug in between.

- **Intermitent RMMx:** Moxifloxacin 400 mg + minocycline 200 mg + rifampin 600 mg is administered once a month:6 doses given for PBL and 12 doses given for MBL cases

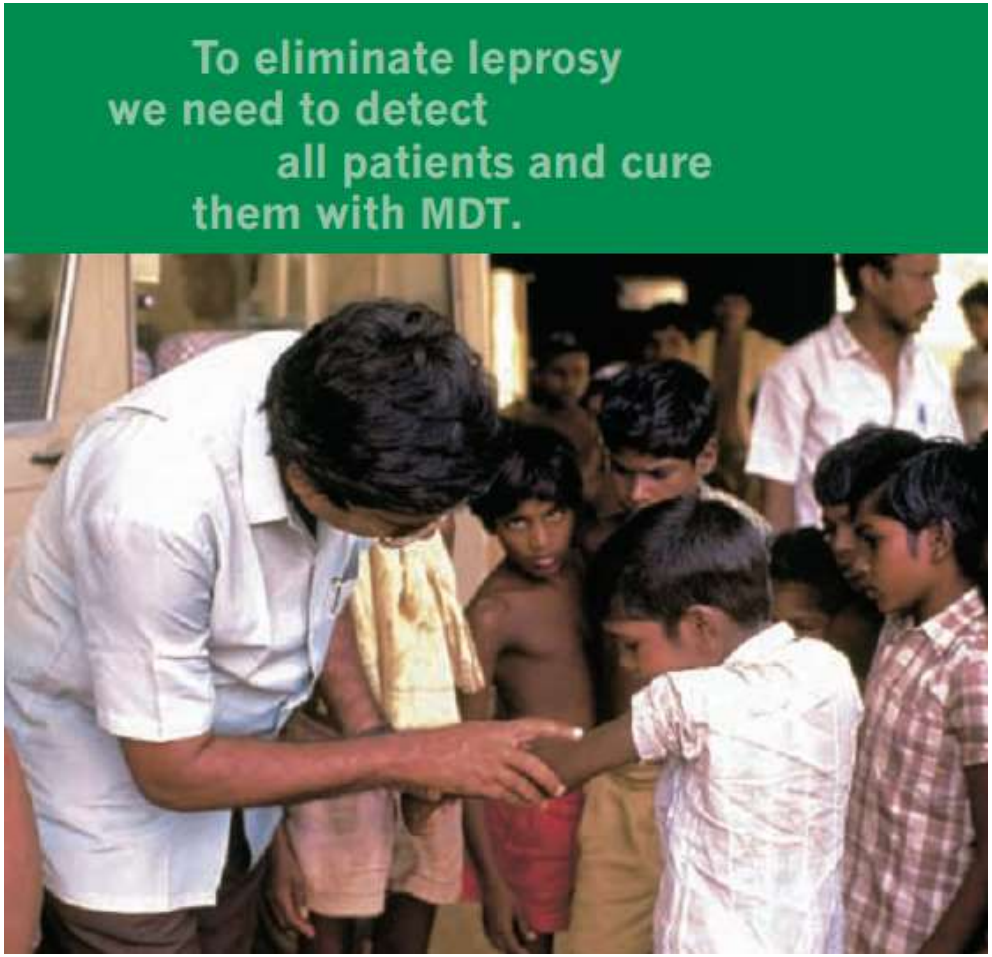
Reactions in leprosy

- Lepra reaction
- occurs in LL
- coincides with institution of chemotherapy
- due to release of antigens from the killed bacilli.
- Lepra reaction is of abrupt onset; existing lesions enlarge, become red, swollen and painful; several new lesions may appear.
- Malaise, fever and other constitutional symptoms generally accompany and may be marked.

Lepra reaction

- Temporary discontinuation of dapsone is recommended only in severe cases.
- Clofazimine (200 mg daily) is effective in controlling the reaction (except the severe one).
- Prednisolone 40–60 mg/day for severe reaction

Thank You


To eliminate leprosy
we need to detect
all patients and cure
them with MDT.