Pharmacotherapy of Leprosy

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Contents

- History
- Leprosy classification
- Drugs – classification and pharmacology
- Drug resistance
- MDT
- Lepra reactions and management
- Conclusion

History of Treatment

- Chaulmoogra oil was used an antileprotic agent in Indian medicine for centuries
- 1949 - Cochrane et al employed parental Dapsone at Chenglepet , Madras.
- 1949 - Lowe and Smith used Dapsone orally
- 1981- WHO introduced MDT of Leprosy

Leprosy classification

Types

- Lepromatous leprosy (LL)
- Tuberculoid leprosy (TL)
- Borderline lepromatous leprosy (BL)
- Borderline tuberculoid leprosy (BT)
- Indeterminate

Classification ….contd

WHO classified for therapeutic purpose

Paucibacillary leprosy (non infectious)-
TL, BT- with 2-5 skin lesions

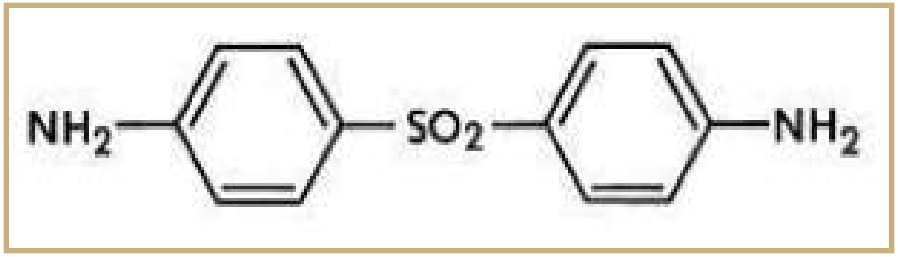
Multibacillary leprosy (Infectious) –
LL, BL.- more than 6 skin lesions

.

Drugs classification

- Sulfones : Dapsone(DDS)
- Phenazine drivatives : Clofazimine
- Antitubercular drugs : Rifampin, Ethionamide
- Other Antimicrobials : Ofloxacin, Moxifloxacin, Minocycline, Clarithromycin

Dapsone



- Acts through inhibition of bacterial folate synthesis.
- Exhibits **bacteriostatic** effect.
- Given orally,well absorbed and widely distributed .
- Produces ten times more concentration in diseased skin than in normal skin.
- Plasma half-life is 24-48 h.
- Dose is 100mg once daily.

Dapsone

ADVERSE DRUG REACTIONS

- Haemolysis of red cells
- Methaemoglobinaemia,
- Anorexia, nausea and vomiting,
- Fever, allergic dermatitis and neuropathy.
- *Lepra reactions* (an exacerbation of lepromatous lesions) can occur
- Contraindicated:
  - severe anaemia (Hb < 7g/dl)
  - G6PD deficiency

Clofazimine

- Clofazimine is a phenazine dye
- It interferes with template function of DNA.
- has anti-inflammatory activity and
- useful in patients in whom dapsone causes drug reactions
- t ½ is 70 days

Clofazimine

ADVERSE DRUG REACTIONS

- Relate to the fact that clofazimine is a dye.
- The most prominent untoward effect is red-brown to black skin discoloration.
- Dose-related nausea, giddiness, headache and gastrointestinal disturbances can also occur

Rifampicin

- Anti tubercular drug also effective in leprosy
- A bactericidal drug
- Relieves nasal symptoms in 2-3 weeks and skin lesions start regression in 2-3 months
- Used in MDT at a dose of 600mg once a month

Rifampicin

ADVERSE DRUG REACTIONS

- Urine & secretions may become red
- Respiratory syndrome:
  - Breathlessness, shock, collapse
- Cutaneous syndrome:
  - Flush, pruritis, rash, watering in eyes
- Flu syndrome:
- Abdominal syndrome
- CONTRAINDICATED: Hepatic & renal dysfunctions, ENL & Reversal reaction

Ethionamide

- It is Ethyl Isothionicotinamide
- Chemically related to Isoniazid
- Acts synergistically with dapsone
- Dose : 250mg / day

Fluoroquinolones

- Ofloxacin, moxifloxacin, sparfloxacin are effective.
- These are BACTERICIDAL.
- 400mg/day of Ofloxacin can kill 99.9% bacilli.(22 daily doses)
- Used as an alternate drug
- Moxifloxacin is the most potent drug.

Minocycline

- Lipid soluble tetracycline
- Penetrates M. leprae
- Inhibit bacterial protein synthesis
- A dose of 100mg/day produces plasma levels that exceed MIC of M. leprae 10 – 20 times.
- ADVERSE EFFECTS : vertigo

Clarithromycin

- O-methyl derivative of Erythromycin.
- 500mg daily dose kills 99.9% bacilli of Lepromatous Leprosy patients in 8 weeks.

- **Metabolism** - in the liver converted to 14 a- hydroxy clarithromycin which also has antimicrobial activity
- **Excretion** - through Urine
- Dose adjustment needed in Kidney disease

Bacterial Resistance

Mycobacterium leprae - resistant gene		
Drug	gene	Function of gene
RFP	rpoB	DNA dependent-RNA polymerase β subunit
DDS	folP	Dihydropteroate synthesis
OFLX	gyrA	DNA gyrase

MDT of Leprosy

- Irregular and inadequate duration of treatment with single drug have allowed emergence of resistance
- WHO introduced MDT in 1981
- Implemented under NLEP in India

MDT of Leprosy

Goals:

- To prevent the emergence of Dapsone resistance
- To render MBL cases noncontagious
- To reduce the duration of Therapy
- To eliminate dormant forms

WHO recommended regimes

Paucibacillary leprosy (D+R)	Dapsone 100mg daily (**self administered**) Rifampicin 600mg once a month (**supervision)**	**6 months**
Multibacillary leprosy (DC+RC)	Dapsone 100mg + Clofazimine 50mg daily (**self administered)** Rifampicin 600mg + Clofazimine 300mg once a month (**supervision**)	**12 months**

Alternative Regimens

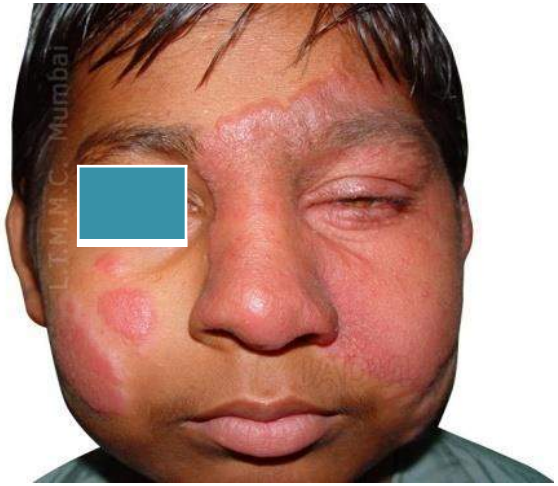
- **Indicated in**
  - Dapsone resistance
  - MDT regimen is NOT advisable
- **Include**
  - Intermittent ROM
  - Four drug regimen
  - Intermittent RMMx.

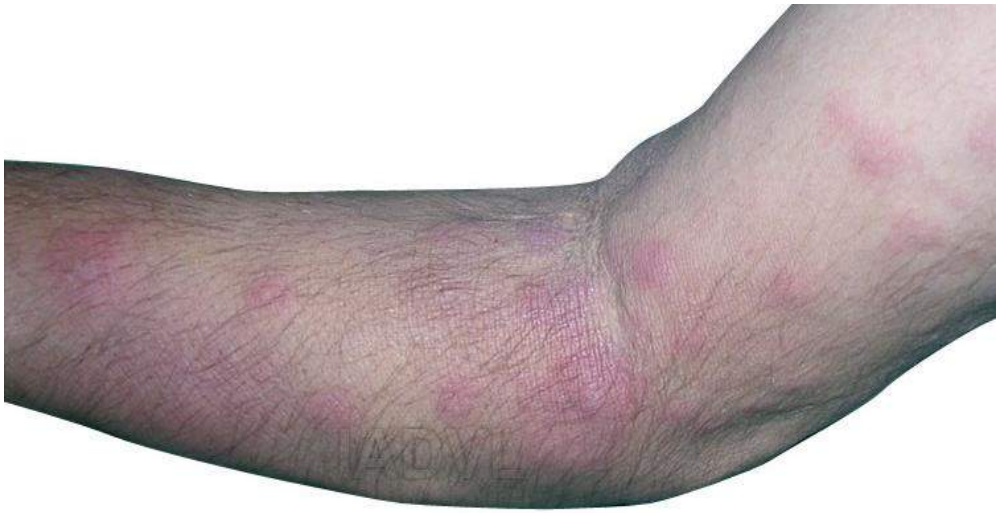
Alternative Regimens

Regimen	PBL	MBL
Intermittent ROM	R(600mg)+ Ofl(400mg)+Min(100 mg) once in month- upto 6 months	R(600mg)+Ofl(400mg)+Min(100mg) once in month- upto 24 months
Intermittent RMMx	Mox(400mg)+Min(20 0mg)+R(600mg) once in month-upto 6 months	Mox(400mg)+Min(20 0mg)+R(600mg) once in month-upto 12 months
Four drug Regimen		R(600mg)+Spar(200m g)+Clar(500mg)+Min(100mg)- 3 months

Lepra reactions

- Due to release of Ag from killed bacilli

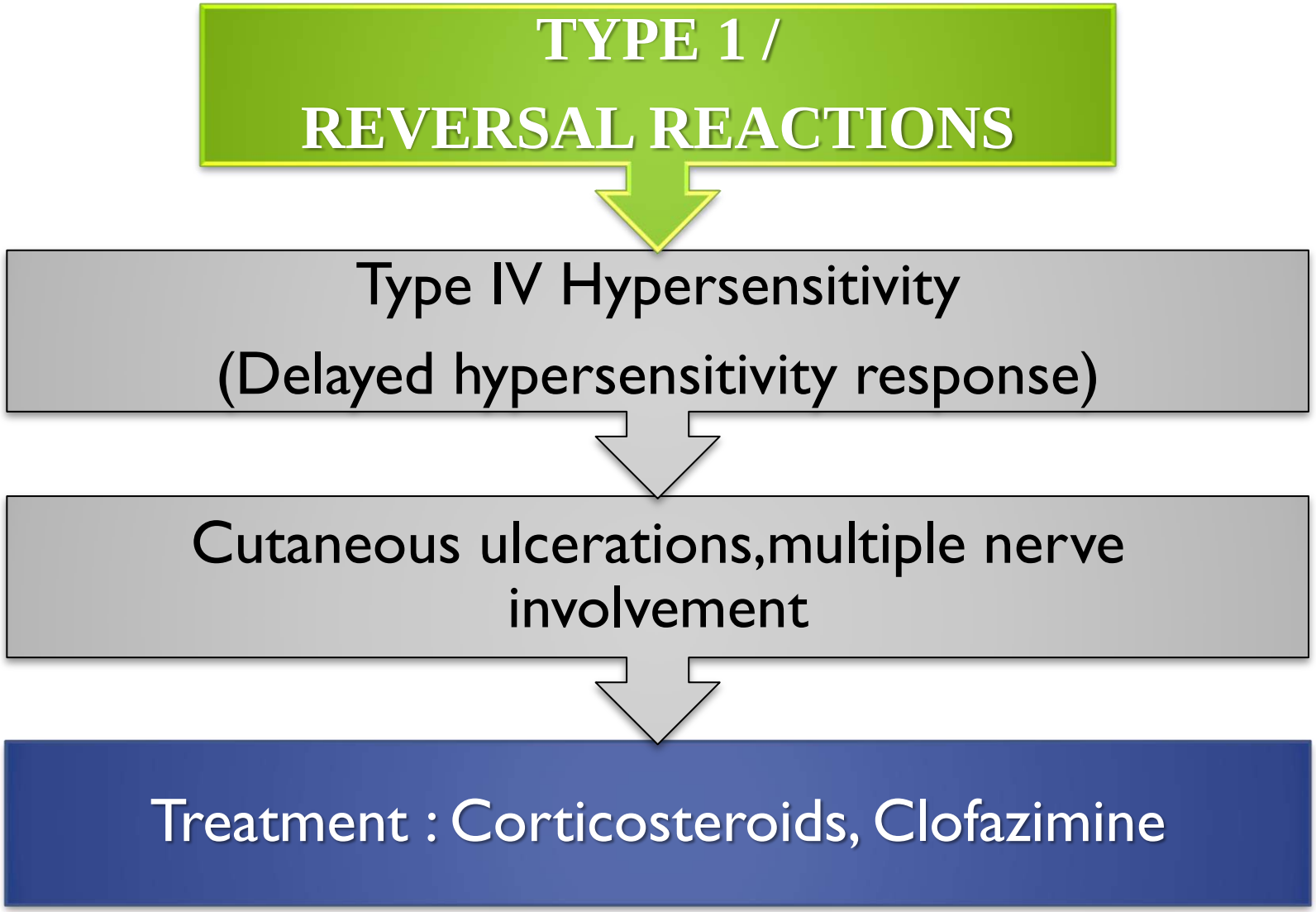




- Type I

Type II

Type -1 Lepra Reaction



Type -1I Lepra Reaction

TYPE2 / ERYTHEMA NODOSUM LEPROSUM

Type III Hypersensitivity

(Humoral antibody response)

Existing lesions enlarge , become red, inflamed and painful

Treatment : Clofazamine

(200mg OD),corticosteroids(40-60 mg/day),

Thalidomide(alternative to steroids)

Conclusion

- Drug therapy of Leprosy started with chalmoogra oil .
- Currently MDT therapy is advised.
- Alternative regimens are ROM, RMMx and Four drug regimen.
- Drug of choice in lepra reaction is corticosteroids.

THANK YOU