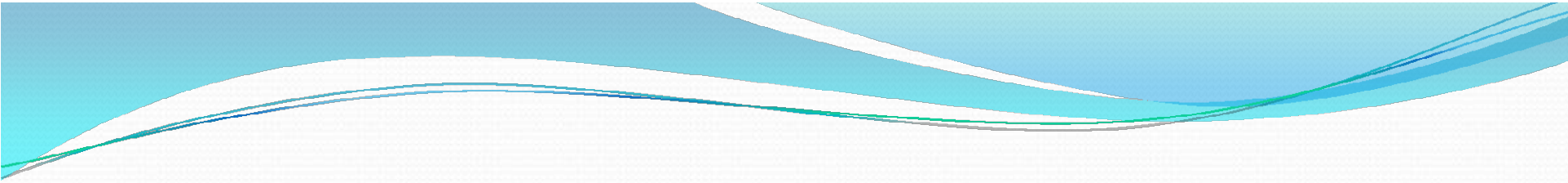


Management of Lepra Reactions

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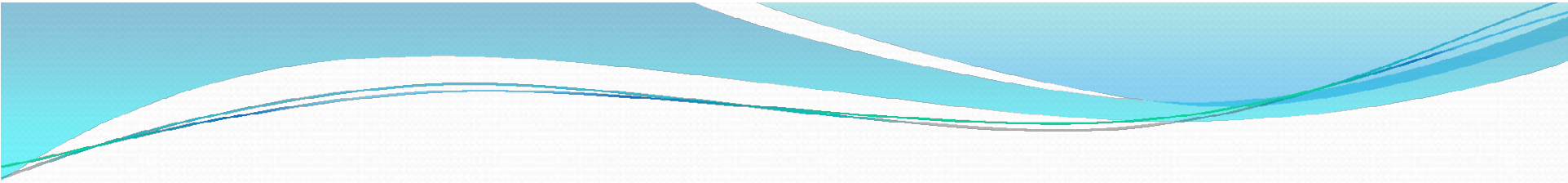


DEFINITION

- acute inflammatory response occurring in the course of the disease.
- It can occur at any time **before, during or after** the treatment
- Patients developing reactions are at a **higher risk of developing disabilities** compared to the people who do not develop reaction.

Persons with following features are more likely to develop reactions:

- Multiple lesions
- Lesions close to the peripheral nerve (predisposes to neuritis)
- Lesions on the face
- High B.I bacillary index in SSS



Precipitating factors:

- Infections and infestations
- Hormonal changes: Puberty, Pregnancy and Childbirth
- Psychological stress

Types of Reactions

(1) Type 1 Reaction: Reversal Reaction

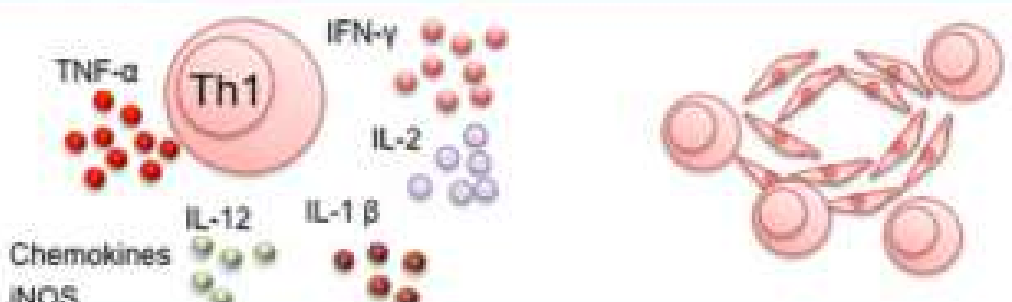
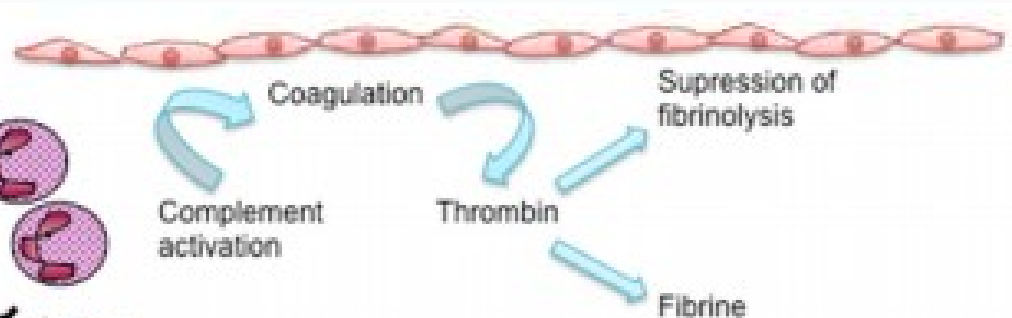
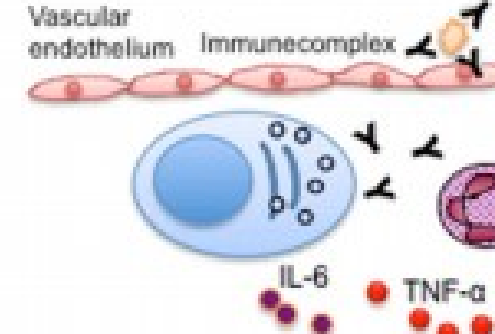
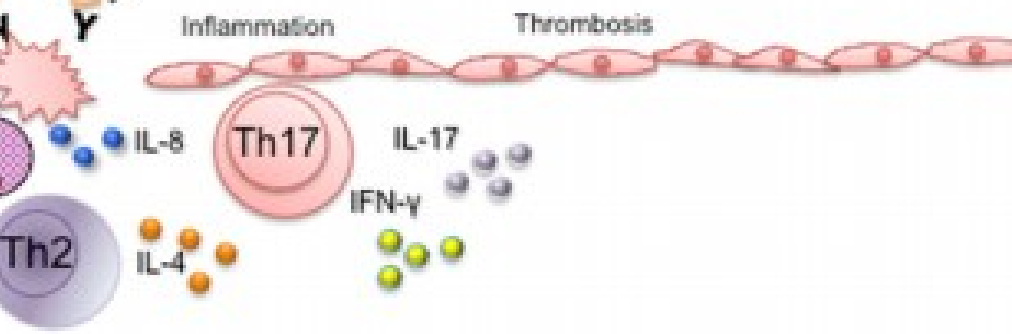
can occur in any patient with unstable CMI .

Type 4 hypersensitivity reaction.

(2) Type 2 Reaction: Erythema Nodosum Leprosum (ENL)

- usually seen in MB Leprosy having a heavy load of bacilli.
- Type 3 hypersensitivity reaction

Leprosy reactions - Clinical and immunological characteristics

a RR	Type IV hypersensitivity – Cell-mediated lesions
• TT, BT, BB and BL before, during or after treatment switch Th2/Th1 • Th1 cells specific for <i>M. leprae</i> • Cell-mediated immunity • Chemokines CXCL10/IP10, CCL2/MCP-1, RANTES • iNOS	 The diagram illustrates the Type IV hypersensitivity reaction. A central Th1 cell is shown releasing several cytokines: TNF-α (red dots), IFN-γ (pink dots), IL-2 (purple dots), IL-12 (green dots), and IL-1β (red dots). These cytokines, along with chemokines (green dots) and iNOS (red dots), are shown acting on a cluster of cells on the right, leading to tissue damage.
b ENL	Type III hypersensitivity - Immune complex-mediated lesions
• LL and BL before, during or after treatment switch Th2/Th1 • Immune complex deposits • Neutrophil infiltrates • Up-regulation of Th2 and Th17 cytokines • Down-regulation of T regulatory response	 The diagram illustrates the Type III hypersensitivity reaction. It shows a sequence of events: Coagulation leads to Thrombin, which leads to Fibrine. Complement activation leads to Inflammation. Thrombin also leads to Suppression of fibrinolysis. The diagram shows immune complexes (orange dots) depositing on the vascular endothelium, leading to inflammation and thrombosis. Cytokines released include IL-6 (purple dots), TNF-α (red dots), IL-8 (blue dots), IL-4 (orange dots), IL-17 (purple dots), and IFN-γ (pink dots). Th2 and Th17 cells are also shown.
Vascular endothelium  The diagram shows immune complexes (orange dots) depositing on the vascular endothelium (red line). This leads to the recruitment of neutrophils (purple cells) and the release of cytokines (IL-6, TNF-α, IL-8, IL-4, IL-17, IFN-γ) and chemokines (green dots). Th2 and Th17 cells are also shown.	Inflammation Thrombosis  The diagram shows the process of inflammation and thrombosis. Immune complexes (orange dots) deposit on the vascular endothelium (red line), leading to the recruitment of neutrophils (purple cells) and the release of cytokines (IL-6, TNF-α, IL-8, IL-4, IL-17, IFN-γ) and chemokines (green dots). Th2 and Th17 cells are also shown.

Clinical features

TYPE 1 REACTION

1. Inflammation of skin lesions in the **existing skin lesions** AND/OR Appearance of new skin lesions

2. Inflammation of nerves frequently affected in **type 1 reaction**.

- **Acute Neuritis:** Existing involved or new nerves become enlarged, painful/tender
- **Silent Neuropathy/Quiet Nerve Paralysis:** nerve function may get affected without any pain or tenderness of the nerve or inflammation of skin lesions
- **Nerve abscess** along the course of the nerve.

Mild Type 1 reaction

Occurs in some of the **pre-existing skin lesions only**
(Other than those on face)

Erythema and swelling of skin lesions without
ulceration

Nerves are not affected

No constitutional symptoms

No edema of hands and feet



Severe Type 1 reaction

- Red, painful, inflamed **skin lesions with ulceration**
- **Neuritis** with or without NFI
- erythematous, swollen skin **patch on the face** around the eye
- Skin lesion overlying major nerve trunk
- **Marked oedema** of the hands, feet or face
- Clinically mild reaction not responding to NSAIDs for a period of 2 - 4 weeks.





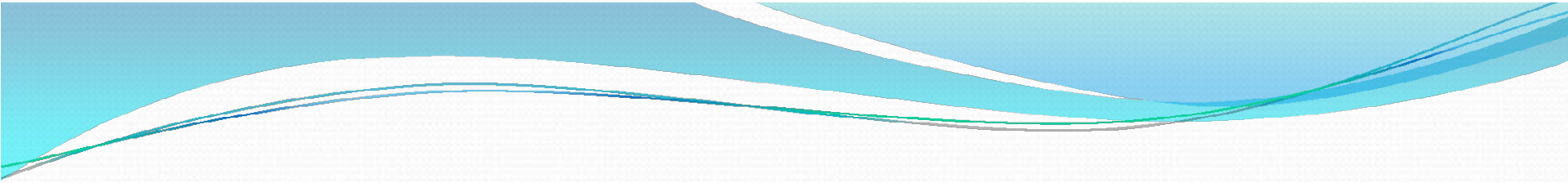
TYPE 2 LEPRA REACTION

- **General condition**

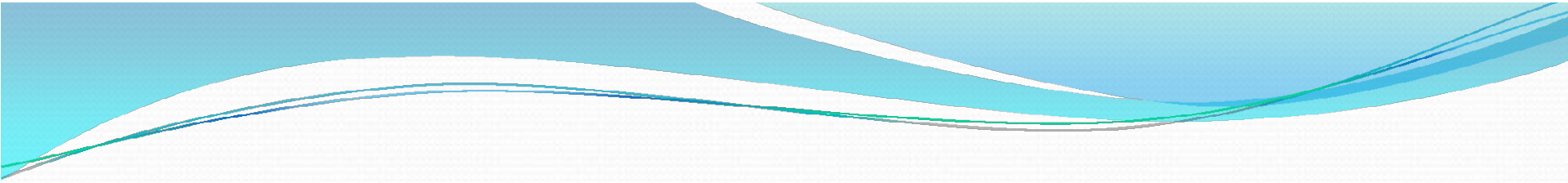
fever, headache and body ache appear before or along with the characteristic nodules that appear on the skin.

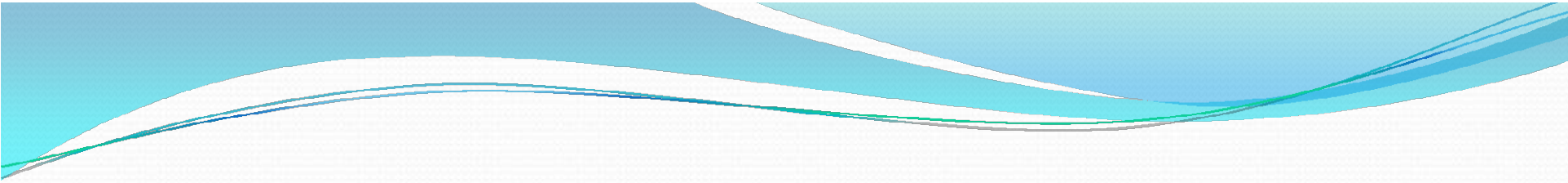
- **Skin lesions**

- red, firm, painful, tender cutaneous and **subcutaneous nodules** (about 1–2 cm across) **appear in crops**.
- Nodules blanch on pressure. Usually multiple, they tend to be distributed bilaterally and symmetrical.
- Ulcerated, pustular and necrotic forms .

- 
- **Inflammation of the nerves:** may get involved in type 2 reaction
 - **Eyes** – iritis or irido-cyclitis and impairment of vision
 - **Swelling of hands and feet** may be seen.

 - **Involvement of other organs:**
 - **Periosteal pain** (especially tibiae), (**myositis**),
 - Pain and swelling of the tendons and joints, painful **dactylitis**,
 - Swollen **tender lymph nodes** especially femoral,
 - **Acute epididymo- orchitis**,
 - **Hepato-splenomegaly**
 - **Endocarditis** with/without arrhythmia.
 - **Glomerulonephritis** - presence of protein and red cells in urine due to deposition of immune complex in renal glomeruli.

- 
- **Chronic ENL**
 - persist for more than three months in spite of adequate treatment
 - **Recurrent ENL**
 - more than four episodes in a year



Mild Type 2 Reaction

- Intermittent crops of **few nodules**
- Nerves are **not affected**
- **Mild fever** (less than 100 F)
- **No other organs involved**

Severe Type 2 Reactions

- Red, painful, multiple nodules in crops
- Pain or tenderness in nerves with or without loss of nerve function
- ENL that becomes ulcerated
- Accompanied by a high fever (>100F)
- Pain and/or redness of the eyes with or without loss of visual acuity (Involvement of eye)
- Generalized symptoms with painful swelling of the small joints with fever
- Enlargement of Lymph glands/testes with pain,
- Involvement of vital organs





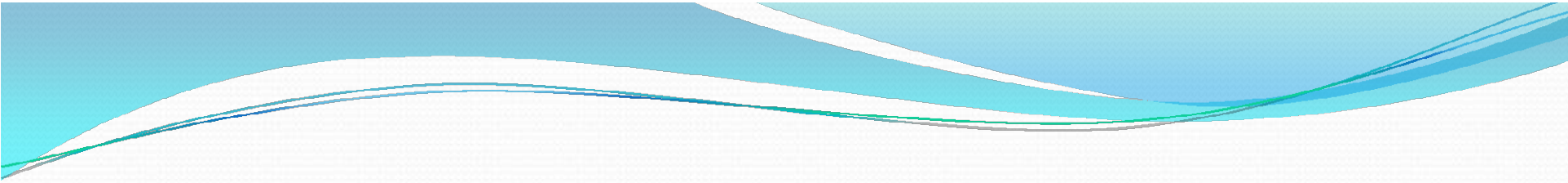




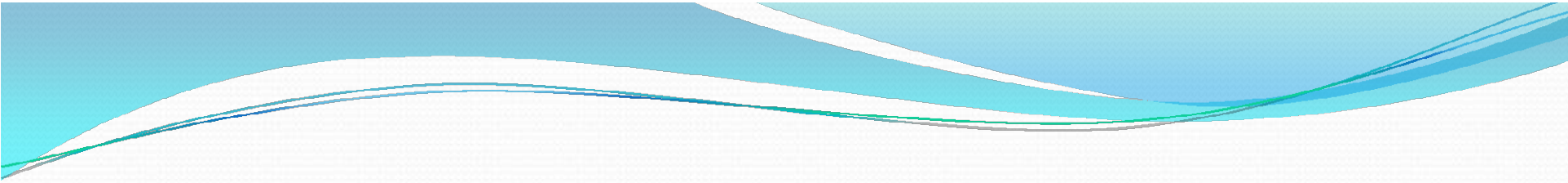


Difference between Type 1 and Type 2 reactions

signs	Type 1	Type 2
Type of reaction	Cell mediated delayed hypersensitivity	Antigen antibody (Immune complex), reaction
Inflammation of the skin	Skin lesions suddenly becomes reddish, swollen, warm, Painful but the rest of the skin is normal, fresh lesions may be noticed	Red, painful, tender, nodules appear (not associated with Leprosy patches).
Nerve involvement	Nerves close to skin maybe enlarged, tender, painful (neuritis) with loss of nerve function and may appear suddenly/rapidly	Nerves may get involved
General condition (Constitutional symptoms)	Good, with little or no fever /other constitutional symptoms	Poor, with prominent fever and general malaise
Other	Not affected	May be affected



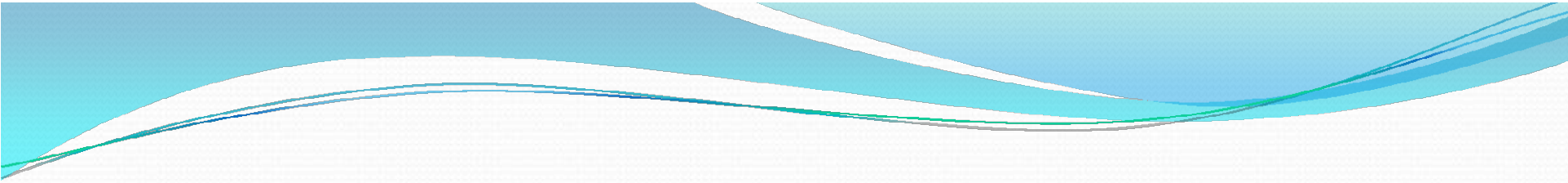
Management of Lepra reactions



Principles of Management

Type 1 Reactions

- Anti-Leprosy drugs to be continued.
- Mild reactions are treated symptomatically without steroids
- Reassurance and counseling to relieve stress
- Treatment of inter-current infections and infestations
- Analgesics, anti-inflammatory drugs (NSAIDS)
- Anxiolytics (at bedtime)



Severe type 1 lepra reaction

- Inpatient admission and bed rest as required.
- Prednisolone: according to dosing schedule.
- Analgesics
- Nerve decompression
- Surgical intervention at referral centre - **abscess** along the course of the nerve

Rest to the affected nerve using **splint**: applied by involving the joint in the vicinity of the affected nerve.

Ulnar nerve

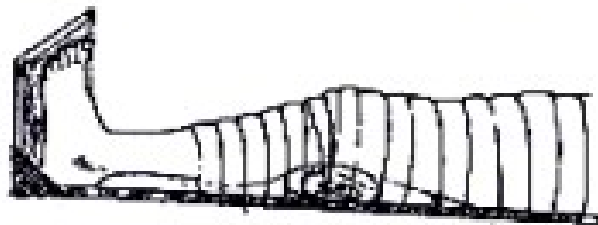
: Elbow flexed to an angle of 90°

Median nerve

: Wrist extended to 40°

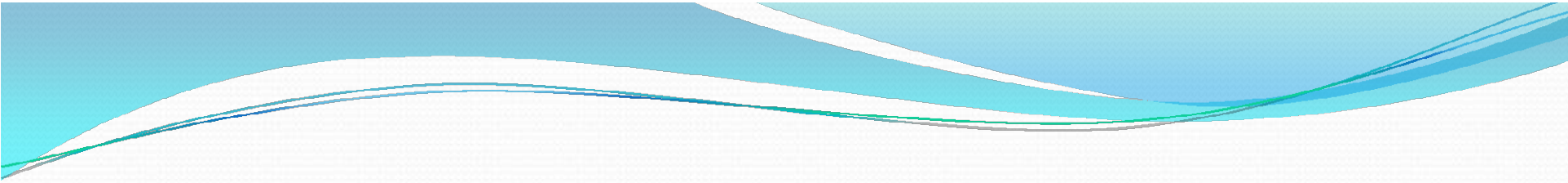


Common peroneal nerve : Knee flexed to 10°



Posterior tibial nerve

: Ankle in neutral position of 90°



Treatment of Type 2 Lepra Reactions

Mild ENL reactions

NSAIDS,

Reassurance and Bed rest

Moderate to severe ENL reactions

- Admission and observe vitals regularly
- Investigations - complete hemogram, LFT RFT
- I.V fluids
- Anxiolytics for stress management
- Antibiotics for pustular lesions and ongoing septicemia

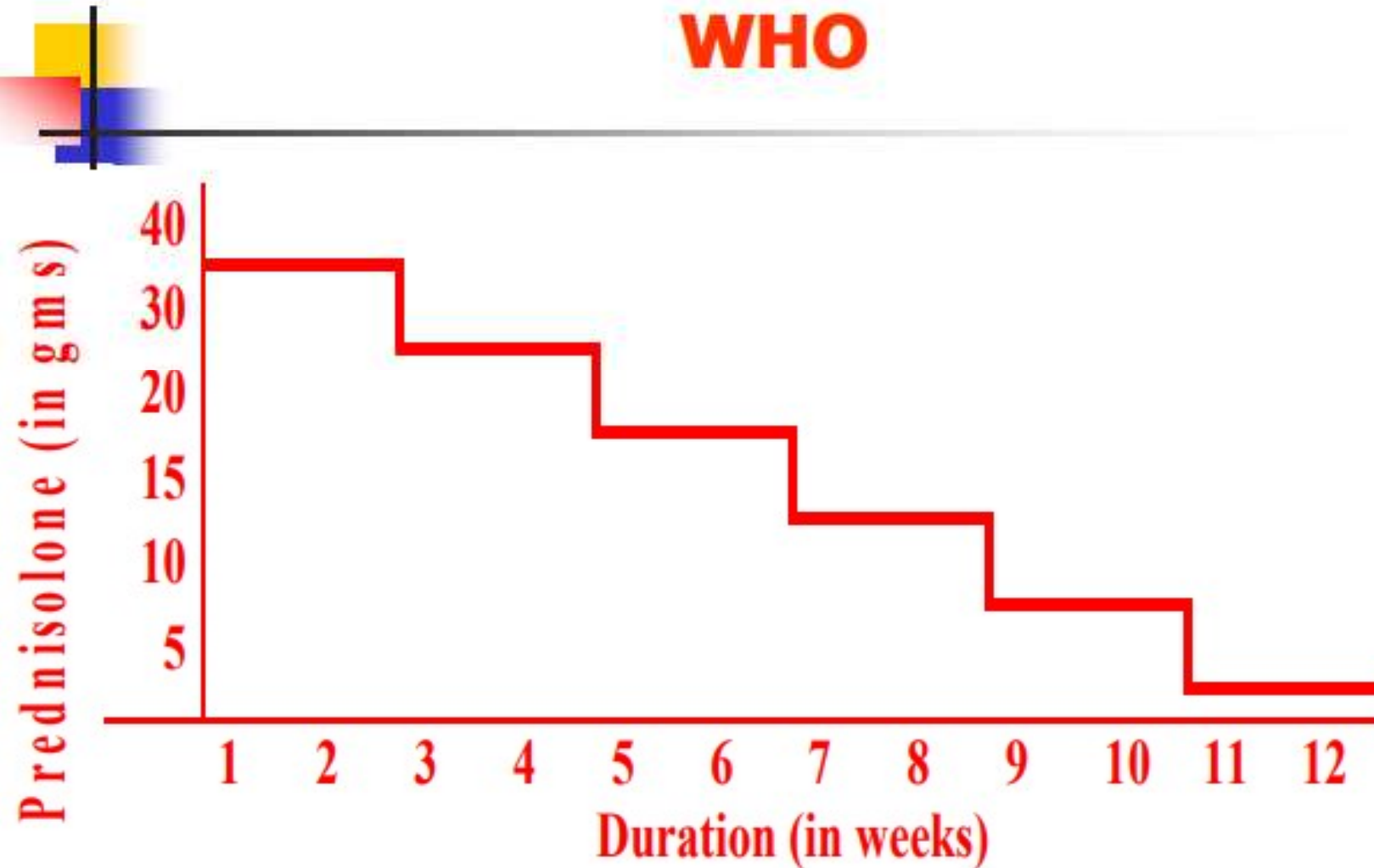
STEROIDS – 1st choice of drugs



- start with higher dose and taper
- 40-60 mg/day or 1 mg/kg/day OD
- assess fortnightly
- In neuritis treatment may be prolonged.

Persons who suffer chronic or recurrent ENL second line drugs may be considered

Standard steroid schedule - WHO



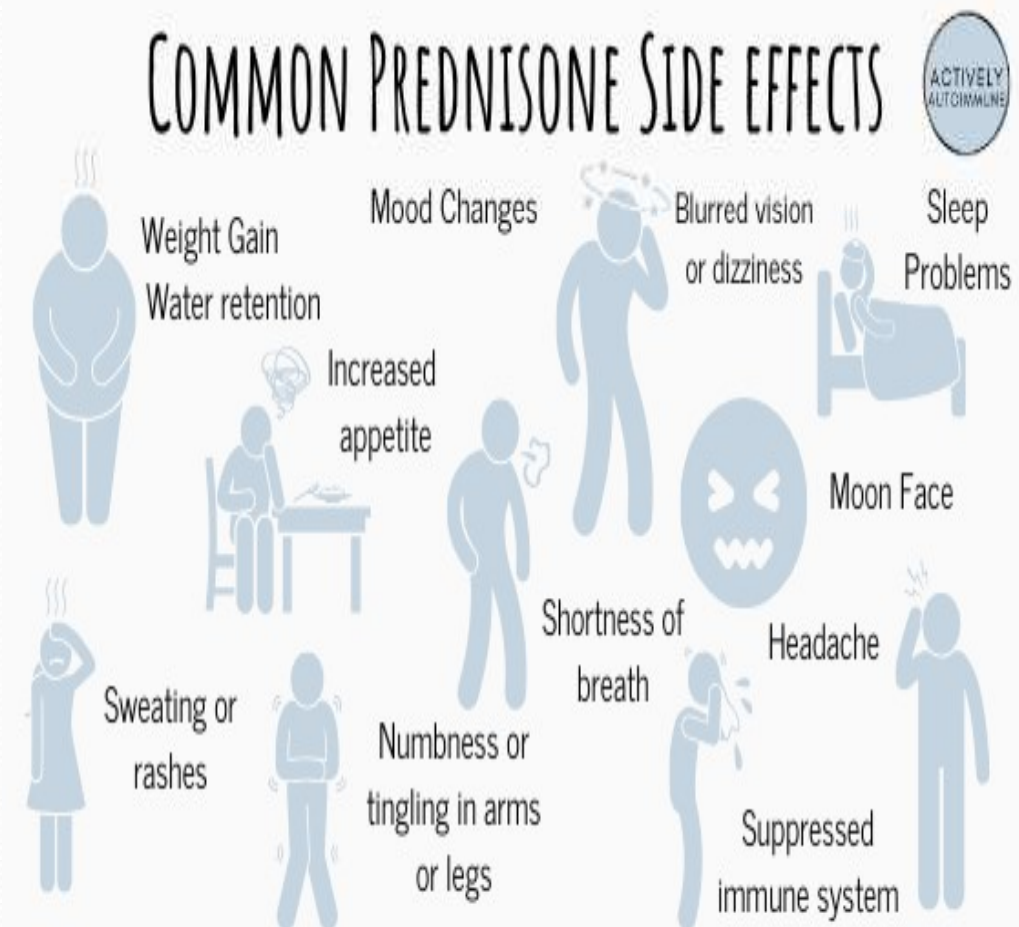
Prednisolone regimen

40 mg O.D. for first 2 weeks
30 mg O.D. for weeks 3 & 4

20 mg O.D. for weeks 5 & 6
15 mg O.D. for weeks 7 & 8

10 mg O.D. for weeks 9 & 10
5 mg O.D. for weeks 11 & 12

- S/E of steroids:
- Fluid Retention, MOON FACE
- Cataract,
- Diabetes,
- Osteoporosis,
- Acid Peptic Disease,
- Steroid dependency,
- Cushingoid Syndrome



Clofazamine

- ❑ Less potent than corticosteroids
 - ❑ Takes 4-6 weeks to develop its full effect
 - ❑ Extremely useful in reducing or withdrawing steroids in dependent persons
 - ❑ Therapy should not exceed >12 months
-
- One capsule (100mg) 3 times a day x 12 weeks
One capsule (100mg) 2 times a day x next 12 weeks
 - One capsule (100mg) once a day x next 12 wks

S/E : Pigmentation

Hepatitis

Pseudo intestinal obstruction



THALIDOMIDE

very effective in moderate to severe EN₂

- It has rapid onset of action unlike CLF
- It reduces the prednisolone requirement

MOA: TNF alpha blocking property

- Dose
- 400mg once or 100mg 4 times a day 3 to 7 days
- 100mg morning + 200mg evening for 4 weeks
- 200mg evening for 4 weeks
- 100mg evening for 4 weeks
- 50mg daily evening or
- 100mg alternate day for 8-12 weeks



S/E : Peripheral Neuropathy

Pruritus (increase in AEC)

Arrhythmia, Venous thrombo embolism

Hypotension

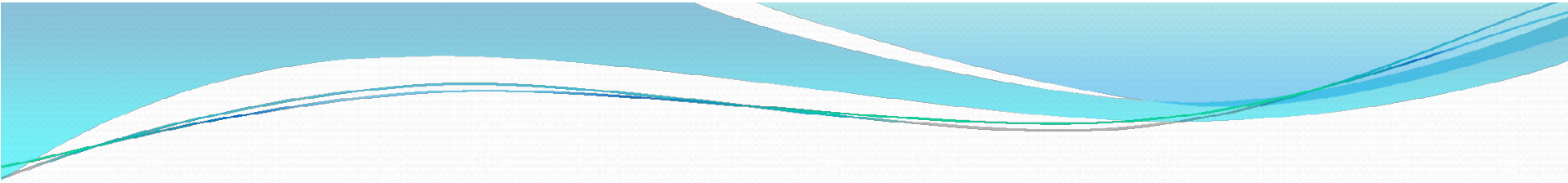
Teratogenicity

C/I : Women In Reproductive Age Group



ROLE OF OTHER DRUGS

- AZATHIOPRINE
- METHOTREXATE
- ORAL ZINC
- INFLIXIMAB
- METFORMIN - managing moderate to severe ENL reactions
maximal inhibition of TNF alpha



Thank You