LEPRA REACTION

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Leprosy Reactions

Reactions are immunologically mediated episodes of acute or sub- acute inflammatory conditions which can occur at any stage of the disease (before, during or after treatment).

They are accompanied by tissue damage (e.g. nerve damage)

Why reaction occurs?

Reactions occur due to abrupt change in immunological response of the body against M. leprae.

Severity of reaction depends on Presence of bacterial load in PAL and Strength of immunological response of the PAL

When reaction occurs ?

- Occurs before & during the first 2-3 years after diagnosis.
- Introduction of MDT.
- *Release from treatment (RFT).*
- Few occurs very late (>5yrs after RFT)

How reaction appears?

- Sudden appearance of symptoms
- Inflammation of existing skin lesions (type-1 reaction)
- Painful /tender nodules (type-2 reaction).
- Inflammation of nerves
- Involvement of ocular tissue
- Swelling of hands, feet and pain in small joints

Why early diagnosis of reaction is essential ?

- Promptly diagnosis of reactions and treatment is essential to prevent disabilities and deformities in leprosy
- All new diagnosed Patients (Borderline group) should be warned about the possibility of reactions
- Education patient for early diagnosis of Reaction.

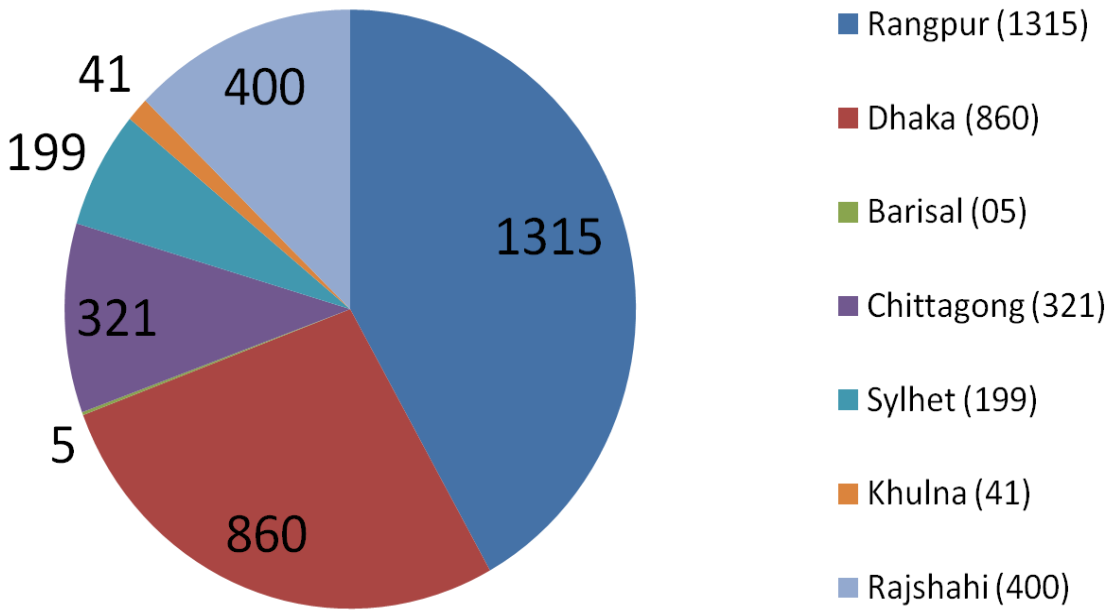
Global Situation
(New Leprosy Case Detection)

Region	Yr 2009	Yr 2012
Africa	28,935	
America	40,474	
South East Asia	***1, 66,115***	***1, 66, 445***
Eastern Mediterranean	4,029	
Western pacific	5,243	
Total	**2,44,796**	**2, 32, 857**

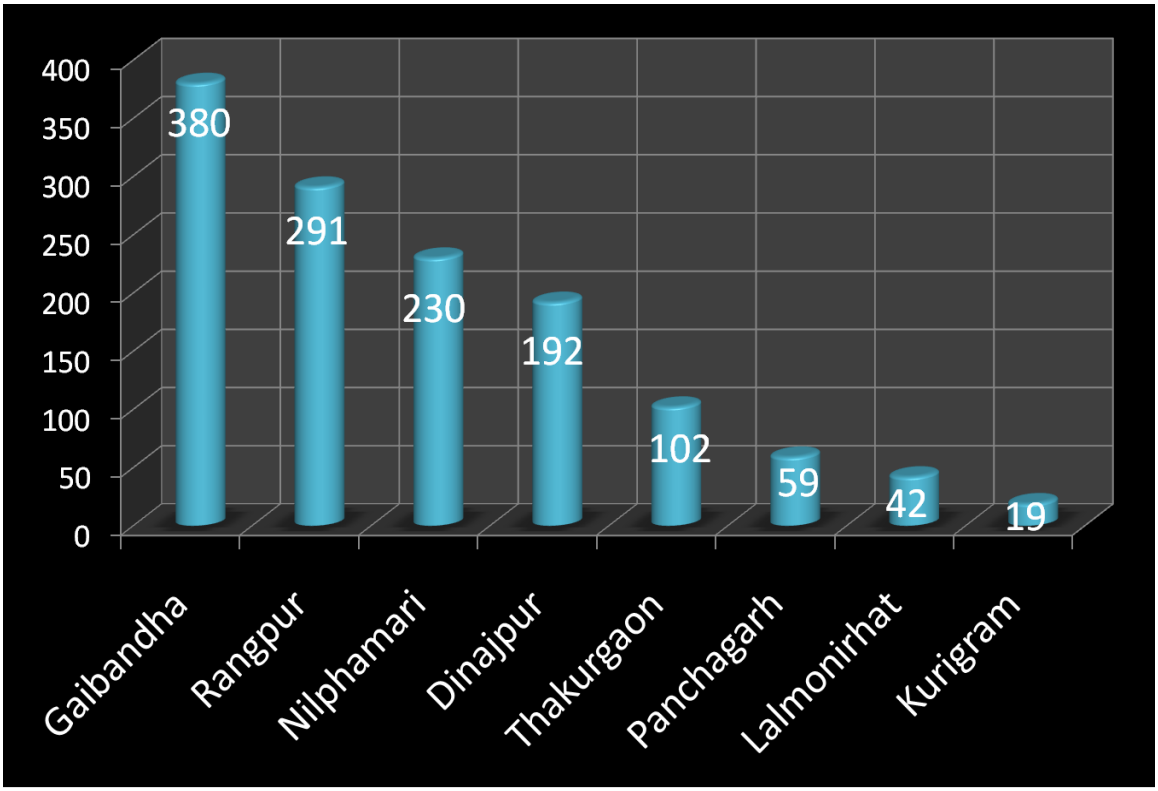
High Endemic countries

- WHO listed 91 countries in which HD is endemic.
- High endemic in Brazil Indonesia,Mozambique, Madagascar, Tanzania and Nepal.
- India, Burma, and Nepal contained 70% of cases. India over 50% of the world's leprosy cases.
- In Bangladesh: At December 31, 2004 the national prevalence rate was 0.5 per 10,000 population.
- New cases detected: 3,754.
- Under treatment: 3,431 cases
- Nearly 150,000 people have completed multidrug therapy (MDT) in Bangladesh from 1985 until the end of 2004
- At December 31, 2004 the national prevalence rate was 0.5 per 10,000 population and the case detection rate for the same year was 6.1 per 100,000, down from 9.8 in 1996, and the lowest level since widespread expansion of the leprosy elimination programme.

New case in 2013 in BD: 3141



New case in Rangpur division in 2013



According to WHO statistics, 3,000 to 4,000 **new leprosy cases** were detected every year from 2011-2017 in **Bangladesh**, while disabilities among detected **cases** are 7 to 11 percent

Types of Reaction

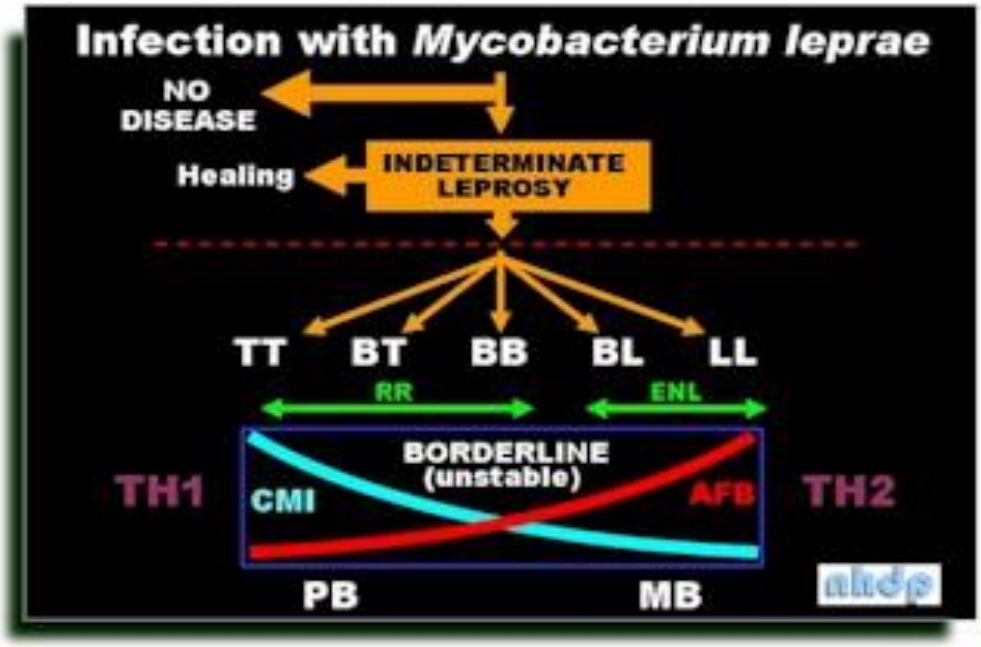
- Reversal Reaction (RR) or Type I Reactio
- Erythema Nodusum Leprosum (ENL) Reaction or Type II Reaction

Factors Precipitating Reactions:

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

What are the Risk for developing reactions?

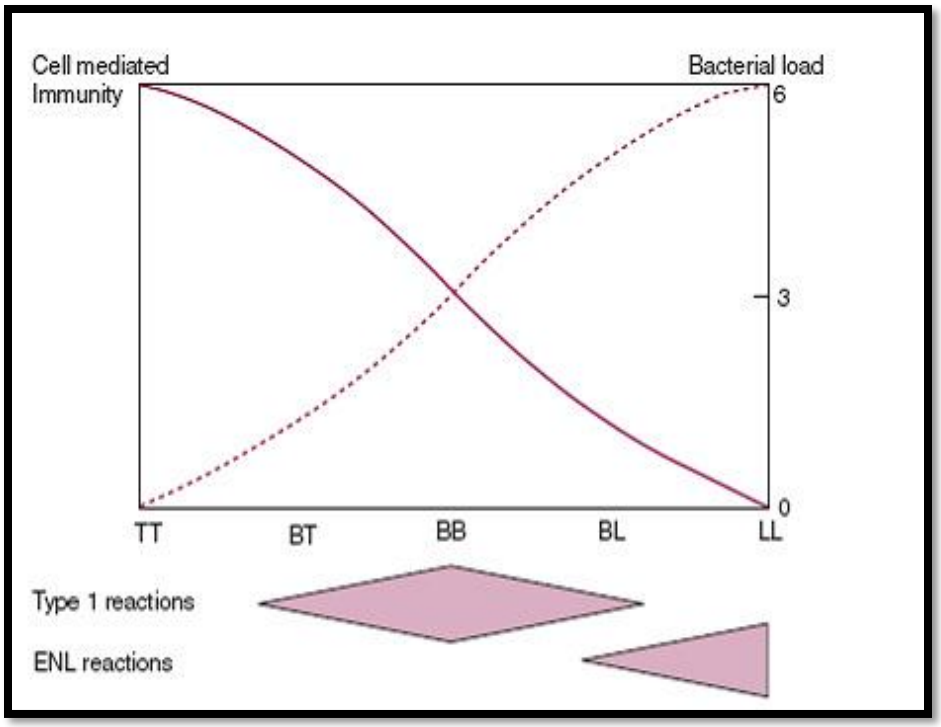
- Any PAL can develop reaction, some are more prone/ predisposed. People having few skin lesions and no nerve enlargement are at low risk of developing reactions.
- Type of Leprosy: BL
- Multiple lesions, Close to the peripheral nerve, Lesions on the face
- Thickened Nerve



Type- I Lepra Reaction

- "Gell and Coombs type IV" hypersensitivity reaction.
- T-cell mediated (delayed) hypersensitivity reaction.
- Upgrading or reversal reaction following an increase in CMI resulting in a shift toward tuberculoid pole.
- Downgrading is applied to reaction associated with a decrease in CMI, shift towards lapromatous pole.
- Occurs in BT, BB, BL during first 6 months of treatment.

The Ridley-Jopling classification and the relationship with host immunity



Type 1 reactions

- Occur both in PB and MB leprosy.
- Increased activity of CMI response to fight against M. Leprae or remnants of dead bacilli.
- Reaction may be the first presenting sign of the disease.
- Signs of inflammation are seen in skin lesion.
- Skin lesions are not painful but felt some discomfort.
- New skin lesions appear.
- General condition: satisfactory.

Classification

A. According to infectivity: **i)** Infectious ii) Non infectious

B. According to symptoms:

i) Asymptomatic – Infectious (MB, BL, LL)

ii) Symptomatic – Noninfectious (PB,TT, BB)

C. WHO classification:

i) Paucibacillary (smear negative) – 80 – 85% patients , non-infectious

ii) Multibacillary (smear positive) – 15-20% patients, infectious

D. Immunological classification:

- True tuberculoid (TT)
- Borderline Tuberculoid (BT)
- Borderline Borderline (BB)
- Borderline Lepromatous (BL)
- Lapromatous Lapromatous (LL)

E. Another classification:

i) Pure neural leprosy ii) Indeterminate leprosy

Classification

- Traditionally been classified into two major types:

  Tuberculoid and Lepromatous.
- T*uberculoid* leprosy: limited disease and few bacteria in the skin and nerves.
- *Lepromatous* leprosy: widespread disease and large numbers of bacteria.
- **Also intermediate subtypes:** between two extremes, borderline leprosy.
- Subtypes are: borderline tuberculoid, midborderline and borderline lepromatous leprosy
- ***Indeterminate leprosy:*** *E*arly form of leprosy with single skin lesion. It will usually progress to one of the major types of leprosy.

Immunological classification

Redly & Joplings classification:

- Indeterminate leprosy (I)
- True tuberculoid (TT)
- Borderline Tuberculoid (BT)
- Borderline Borderline (BB)
- Borderline Lepromatous (BL)
- Lapromatous Lapromatous (LL)
- **Another classification:**

i) Pure neural leprosy **ii)** Indeterminate leprosy

Clinical Features of RR:

Exacerbation of skin lesion & Neuritis.

Skin:

- Lesions: inflammation; Erythema and swelling.
- Appear new lesions.
- Ulcer in the lesions

Nerve:

- Inflammation in affected nerve.
- Nerve Tenderness/pain.
- Loss of nerve function (S M A)

General:

- Fever
- Oedema: hands, feet and face

Single raised Patch on face red in color Such patches overlying major nerve trunk are a sign of risk of neuritis

Reversal Reaction of face patch

Type II Lepra Reaction

- "Gell and Coombs Type III" hypersensitivity (allergic) reaction.
- Erythema nodosum leprosum (ENL) is humoral hypersensitivity.
- Immune complex mediated reaction.
- Occurs in LL and BL patients.
- Occur during the course of treatment.

Clinical Feature of ENL

- Crops of tender nodules, sudden appearance , ulcerated.
- Painful / tender nerve, loss of function.
- Iridocyclitis,
- Epididymo-orchitis,
- Myositis,
- Lymphadenopathy, arthralagia/arthritis, periostitis
- Nephritis
- Fever, general malaise, edema, proteinurea

Type II (ENL)Reaction

Pathology of ENL

- Deposition of antigen-antibody complexes in tissue, with activation of compliment and development of local inflammation and local release of tissue-damage enzyme"
- **When M. Lerae are killed and release antigens. These antigens provoke Coombs and Gell type III hypersensitivity and produce antigen antibody immune complex reaction in the presence of complement system.**
- **Immune complexes are precipitated in: Skin, eyes, joints, lymph nodes, kidneys, liver, spleen,**

Difference between RR and ENL

1 (RR)	2 (ENL)
• Occurs mainly in borderline disease (BT, BB, BL); also occur with TT and pure neural leprosy •Redness and swelling skin lesions, and sometimes ulcerate; Hands, feet, and face edema •Pain or tenderness in one or more nerves, with or without NFI. new nerve damage manifesting as numbness or muscle weakness in the hands, feet, or face	• Occurs in BL and LL • Crops of painful and tender red papules or nodules, occur in limbs trunk and face. Ulceration of nodules may occur; edema of the hands, feet, or face. •Numbness or muscle weakness in the hands, feet, or face; pain or tenderness in one or more nerves

Rural Health Program - TLMIB, Notkhana, Nilphamari

Reaction statistics last 5 years

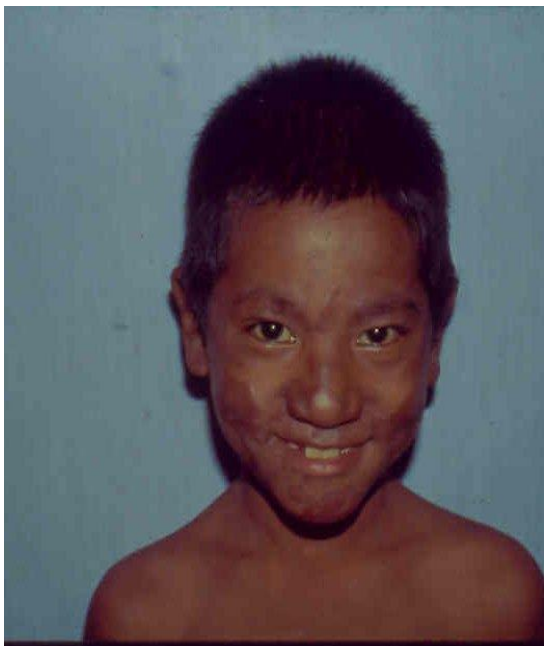
Year	New cases register	Reaction occurred in new cases	Reaction occurred among on treatment patient	Reaction occurred among RFT patients	Total	Type I	Type 2	Neuri-tis
2014	761	90	119	119	328	107	25	96
2015	801	89	89	132	310	85	42	183
2016	666	54	75	91	220	58	32	130
2017	862	68	51	89	208	64	47	97
2018	967	70	76	62	208	68	33	107

Single raised Patch on face
Mild red in color
Such patches overlying major nerve trunk are a sign of risk of neuritis

Severe Reversal Reaction

Before

After steroid



Severe Reversal Reaction

Post Reversal Reaction

REVERSAL REACTION

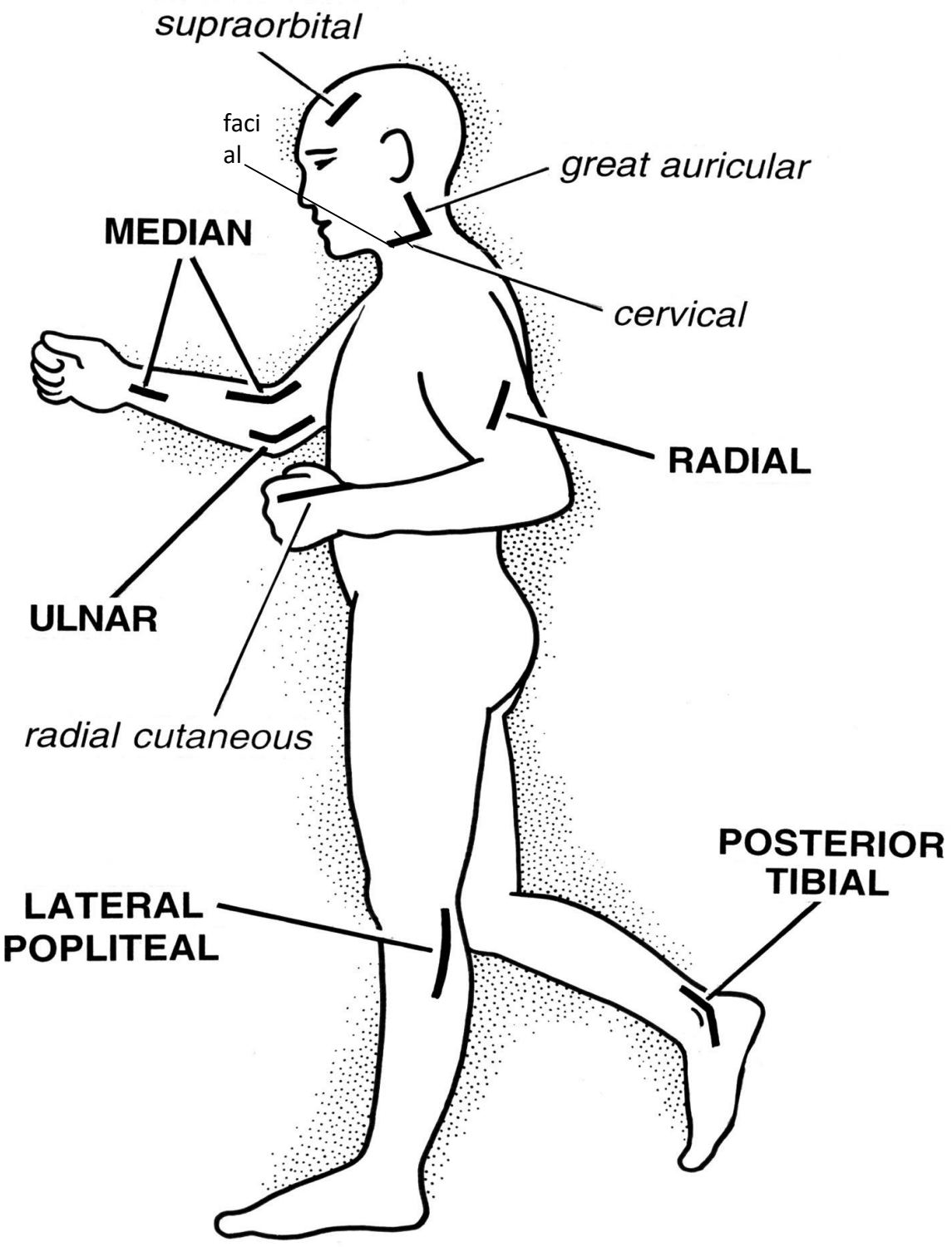
Neuritis

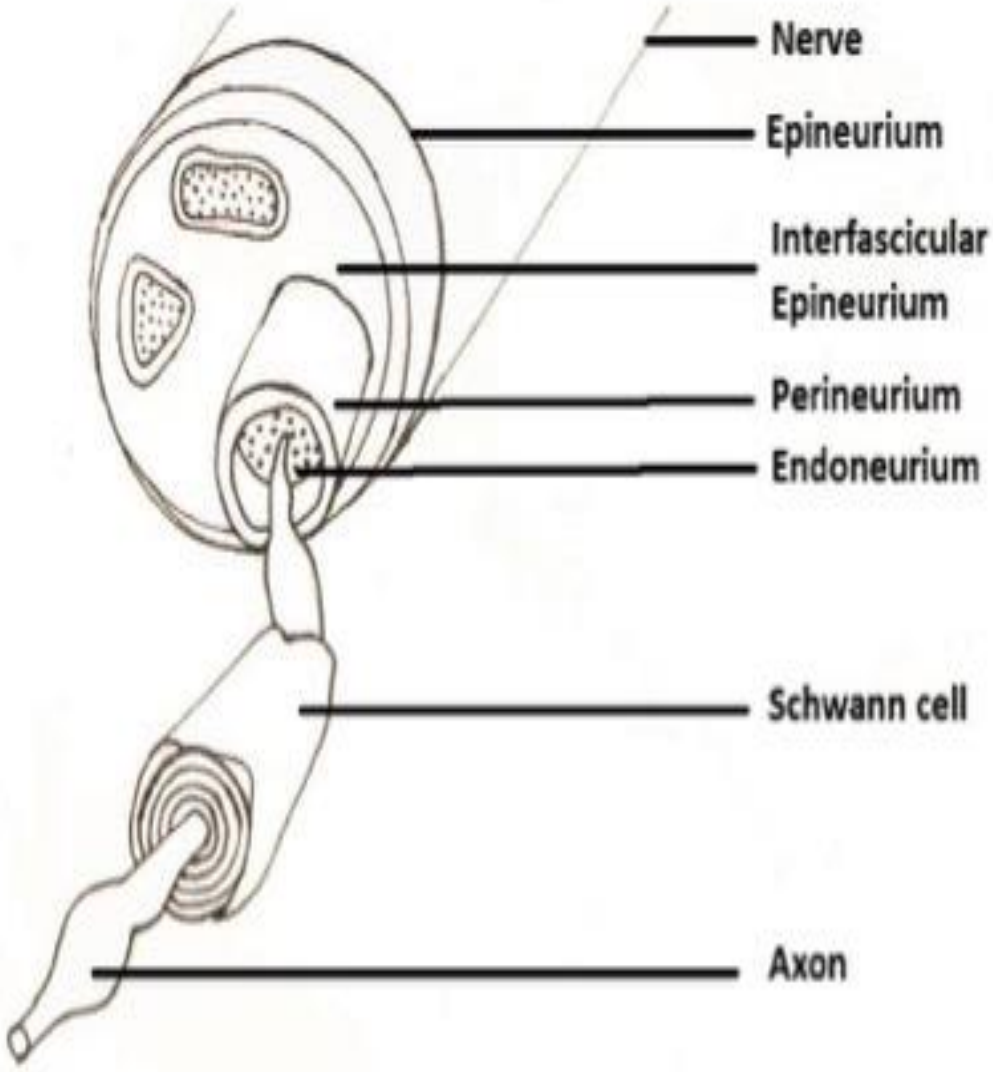
- Inflammation inside nerve sheath causes increase in pressure (influx of lymphocytes plus fluid) ⟹ direct damage to fibres plus ischaemia.
- Result: temporary (physiological) impairment of nerve conduction or more permanent impairment ⟹ degeneration of distal axons

Presentation of neuritis

- “Acute neuritis” with pain and swelling of nerve at specific sites. May be sudden.
- May occur with or without other signs of reaction.
- “Silent neuritis” seen as loss of nerve function.
- Subclinical loss of function/ huge reserve of nerve fibres/ spontaneous recovery.
- Nerve abscess, emergency.

Nerve involvement





Structure of a nerve

Nerves frequently affect in type 1 reaction

- Acute Neuritis: SMA functions affect.

  Nerves get enlarged, painful.
- Pain due to increased intraneural pressure because of edema and cellular reaction of inflammatory process. Pain aggravates when swollen nerve trunk becomes entrapped in bony or fascial tunnel.
- Only nerve involvement may be feature of reaction.
- Silent neuropathy: Sometimes, nerve function may get affected without any pain or tenderness. Early identification and treatment is needed.

Severe changes in nerves in tuberculoid leprosy

•Borderline tuberculoid leprosy: Infiltration of epithelioid cells and Langhan's type of giant cells, surrounded by a large number of lymphocytes, are seen both within and around the involved nerve fascicles.

•Destruction of the nerve parenchyma, including the perineurium and the protective barrier, is apparent in the heavily infiltrated fascicles. These changes are seen in leprosy patients with good cell-mediated immune (CMI) responses.

Nerve abscess

- Abscess formation is most common in tuberculoid leprosy. Rarely in other types.
- *Mycobacterium leprae* dissemination hematogenous or by spread from skin.
- The Schwann cell and ensheathed axon becomes involved and form a granuloma. Invasion of the endoneurium and the whole endoneurial zone occupied by epitheloid cells with or without the presence of bacilli.
- Caseation necrosis occurs within the granulomas, or areas of necrosis may coalesce, forming a cold abscess.

Median Nerve abscess

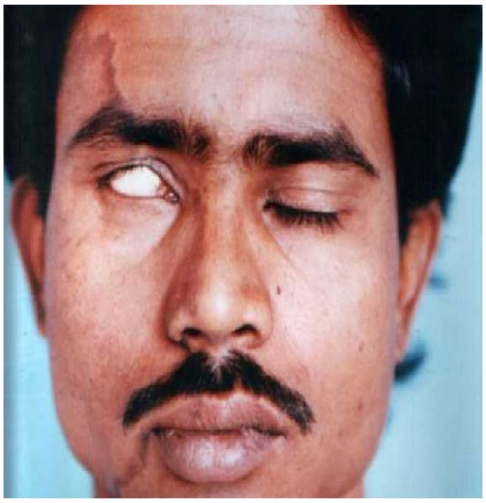
Nerve lesions in lepromatous leprosy (LL):

- Multiplication of bacteria, in the Schwann cells due to lack of efficient CMI.
- Diffuse involvement of nerves in BL-LL leprosy. General architecture of the nerves remains better preserved despite a heavy bacterial presence, with the very low toxicity of the pathogen and the symbiotic relationship it enjoys with the host.

Rt. Foot drop

Rt. Claw hand

Lagophthalmos



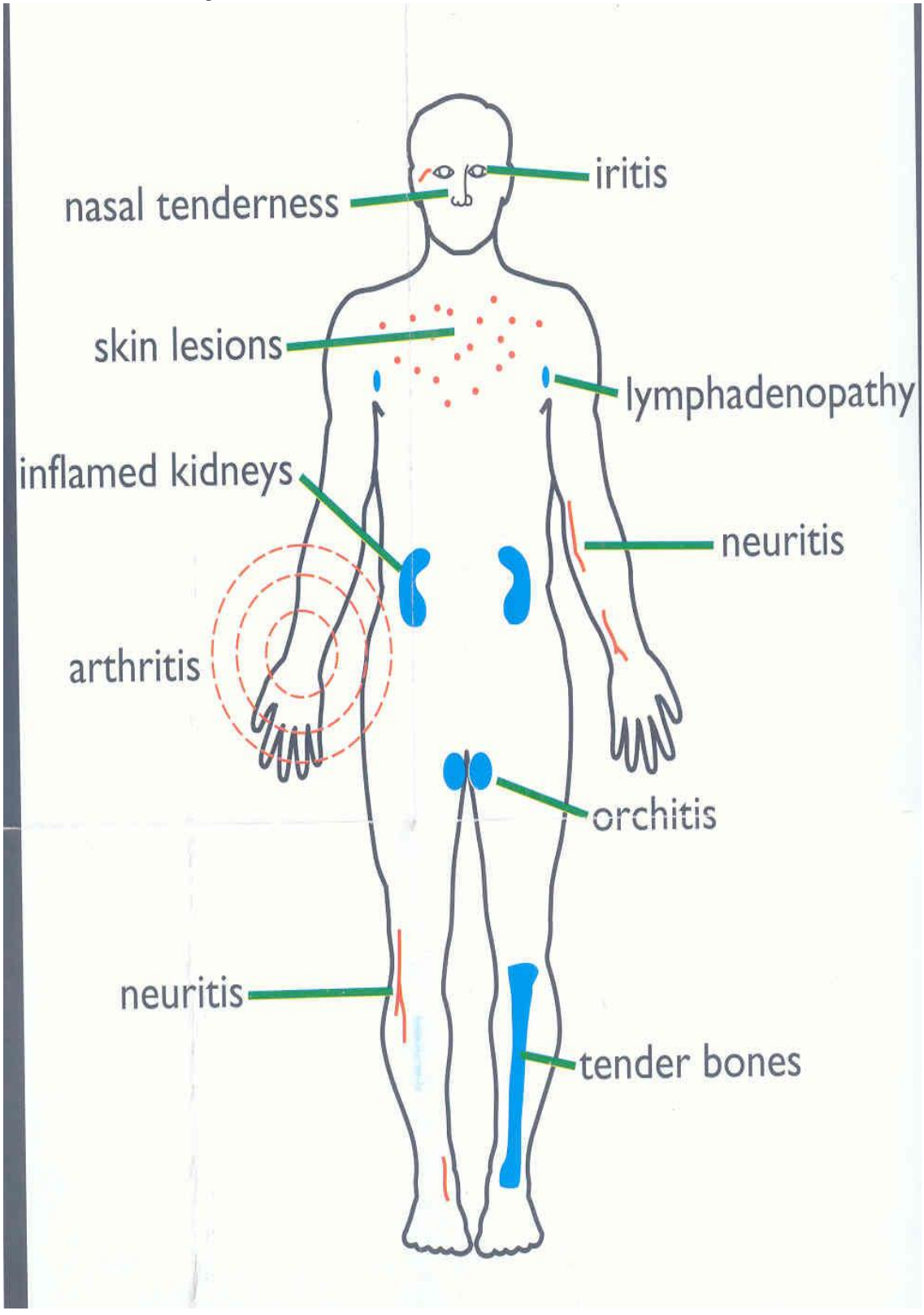
Ulnar Nerve abscess

Reversal Reaction

Before Treatment

After Treatment 2 Weeks

Complication in ENL Reaction



Type II Reaction

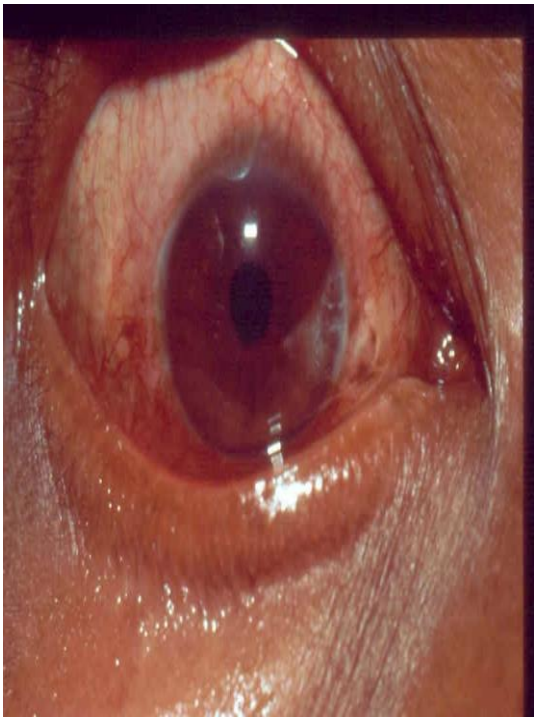
Before Treatment

After Treatment of 4 weeks

ENL Reaction

Ulcerate ENLs





Acute Iritis

- Decreased visual acuity
- Watering
- Photophobia
- Hazy cornea
- Irregular pupil
- Circum corneal congestion.

Mild ENL Reaction

- Multiple Erythematous Nodules
- May be low fever, but patient able to carry out activities of daily living

Severe ENL Reaction

- Multiple Red, Subcutaneous, Nodules
- Some nodules are ulcerated (pus will be “sterile” on routine culture”)

Severe Ulcerated ENL (gentian violet applied as antiseptic)

Management of RR

Mild

- Rest, reassurance, MDT
- Aspirin 600 mg TID for 2 weeks

Severe

- Rest, Analgesic, MDT
- Prednisolone in Tapering Dose from 40mg, 30mg, 20mg, 15mg, 10mg & 5
- Splint to Inflamed nerve for rest or elevation for oedema

Management of ENL Reaction (Severe)

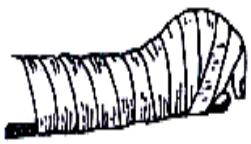
- Rest and reassurance
- Analgesic
- Continuation of MDT if needed
- Prednisolone in Tapering Dose
- Warm bandage/Splint to Inflamed nerve if needed (Physical Management)
- Good nursing care: nutrition, fluid balance, hygeine etc

Managing reactions

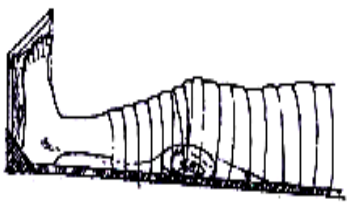
Splinting & Support to give rest for inflammed nerve/for oedema

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°

CHRONIC ENL and RECURRENT ENL

- Rule out co-existing illness!
- Consider adverse effects of steroids
- Alternative drugs which might be used: Clofazimine, Thalidomide, other immuno-suppressive drugs
- Maintain patient`s psychological support, and nutrition etc

CLOFAZIMINE **(1)**

- HIGH DOSE CLOFAZIMINE effective to suppress ENL reaction but onset is slow
- Drug is deposited in fat so stored long time and effect continues after stop intake
- NO GOOD FOR REVERSAL REACTION
- Most useful if chronic /recurrent ENL

CLOFAZIMINE (2)

- Adjust dose according to body weight and history/severity of condition
- Usual regimen: 100mg tdsx1m then 1oomg bd x 1m then 100mg od x 1m
- Can give for 6months
- Adverse effects: nausea, diarrhoea, malabsorbtion, pigmentation of skin, **acute abdominal pain**

Thalidomide

- In-patient use only under strict supervision
- Quick effect (unlike HDC) but soon wears off
- Teratogenic but otherwise adverse effects not a big problem
- Generally only use in men and not in children <12yrs old

Other immuno-suppressives

- Azathioprine
- Cyclosporin
- Methotrexate
- Interferon gamma antagonists etc

  So far none proven sufficiently safe and effective for routine use.

General

- One of the leading causes of permanent physical disability in the world
- Afflicts individuals in their most productive stage of life
- Multi-drug therapy (MDT) can eliminate leprosy as a public health problem (prevalence < 1/10,000)
- MDT can also bring about cure without disability

Thank You all for patience hearing