

LEPROSY-AN UPDATE

Pages with reference to book, From 72 To 76

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Synonymous: Hansen's disease. There are an estimated 10-15 million leprosy patients in the world. Of these 96% are in the Asian and African continents¹.

AETIOLOGY

Mycobacterium leprae- an acid fast rod similar to *M. tuberculosis* but less acid and alcohol fast is the causative agent. The best animal for its inoculation is the nine banded armadillo which provides leprosy bacilli for research. Cultivation in vitro and efforts to infect volunteers with this organism have failed². Naturally infected armadillos have been found, but widespread extrabuman reservoir from where leprosy possibly originated remain to be identified³.

EPIDEMIOLOGY

Infants and children are most susceptible to the infection. With a leper in the family, children have 14 times higher prevalence, compared to no such contact in family, due to their immature immune system. If one parent is infected 60% children are at risk. Adults are relatively non-susceptible, and the chances of getting infection from a marriage partner is about 5%. Infectivity rate lower than 5% in spouse has been reported by some authors^{4,5}. Prolonged contact is required for adults but a single contact may infect the infant. The age at onset is usually 5-14 years but the youngest patient reported was 2 months old. The average incubation period is 3-5 years but could be as short as 1 1/2 years and even shorter. Infection is more likely if the contacts are multiple and have lepromatous leprosy. In adults the disease is much more common in males and in children, a similar sex difference has been observed recently⁶. Droplet infection is the most important mode of infection, Penetration through abrasions, ulcers, pyodermas, mosquito bites and inoculation through syringes, vaccination and tattooing is possible⁷. Transplacental transmission has been reported but is rare. Indigenous leprosy in armadillos and transmission to armadillo handlers has been reported⁸.

CLASSIFICATION

Based on immunity, Ridley and Jopling^{9,10} have classified determinate leprosy into 5 types forming a spectrum (Table). Tuberculoid leprosy (TT) occurs in people with high degree of immunity. The immunity decreases as we go from the tuberculoid leprosy towards lepromatous leprosy (LL). Apart from the two polar forms (TT and LL) the borderline forms are unstable. With treatment they may upgrade to subpolar tuberculoid (TTs) and without treatment they may downgrade to subpolar lepromatous (LLs) (Table).

HISTOPATHOLOGY

Histologically, the tuberculoid leprosy shows an elongated, perineural and periadnexal tuberculoid granuloma mainly consisting of epithelioid cells with mild to moderate mononuclear infiltrate and an

occasional giant cell¹¹. The granuloma is not separated from epidermis unlike lepromatous leprosy. Lepra bacilli are usually absent. Nerve remnants may be demonstrated with special stains. The lepromatous leprosy shows extensive cellular infiltrate which is separated from epidermis by a narrow grenz zone. The infiltrate is around nerves and appendages and consists mainly of histiocyte macrophages containing abundant foaming cytoplasm like the xanthoma cells. These cells called lepra cells exhibit, numerous lepra bacilli with acid fast stains. The bacilli may lie in clumps called globi^{11,12}. The borderline leprosy shows a variable histologic picture depending whether it is true border line (BB), borderline tuberculoid (BT) or borderline lepromatous (BL). A granulomatous infiltrate containing both foamy macrophages and epithelioid cells is seen. Acid fast bacilli can usually be demonstrated inside the macrophages^{2,11,12}. Histological differentiation with tuberculosis and other granulomas has been briefed by Kakakhel and Fritsh¹³.

IMMUNOLOGY

Lepromatous leprosy demonstrates impairment of cell mediated immunity as demonstrated by depressed dinitrochlorobenzene (DNCB) sensitization and little or (MIF)¹⁴⁻¹⁶. Low counts of T-lymphocytes and a decreased T-helper: T-suppressor ratio is reported in peripheral blood of nonreactive lepromatous leprosy¹⁷. Enhanced cellular immunity is seen towards tuberculoid spectrum. Increased amount of immunoglobulins and equal distribution of IgG IgM and IgA in both TT and LL has been reported¹⁸. Their actual role in immunity is not clear. Type I lepra reaction is an expression of delayed hypersensitivity representing type IV hypersensitivity reaction of Coombs and Gel classification¹⁴. It occurs as a result of interaction of T-lymphocytes with antigens liberated from disintegrating *M. leprae*, associated with a rapid change in cell mediated immunity. The immunologically unstable borderline group of leprosy primarily exhibits type I lepra reactions¹⁴. Type II lepra reaction (Erythema nodosum leprosum) is a reflection of augmented humoral responses, mediated through antigen (*M. leprae*), antibodies and complement, which interact to form circulating and tissue immune complexes. It thus represents type III hypersensitivity reaction of Coombs and Gel's classification. It occurs primarily in lepromatous leprosy, mainly LLp, LLs and occasionally BL^{14,19}.

CLINICAL FEATURES

Indeterminate leprosy

This is characterized by single or multiple, hypopigmented dull or slightly erythematous maculae, which may be dry and mildly scaly. They may resemble pityriasis alba³. No infiltration, plaque formation or nodules are seen²⁰. Sensory impairment may be slight or absent. Histology is nonspecific but histamine test may be helpful.

Tuberculoid leprosy

The purely neural form of TT shows no skin lesions. The nerve involved is painful, swollen and is followed by anaesthesia and muscle wasting^{6,21}. The typical tuberculoid lesion is an erythematous or purple plaque with raised edges and flattened, hypopigmented centre. The surface is dry, insensitive, hairless and sometimes scaly. A thickened nerve may be palpable at the periphery of the lesion (Figure 1).

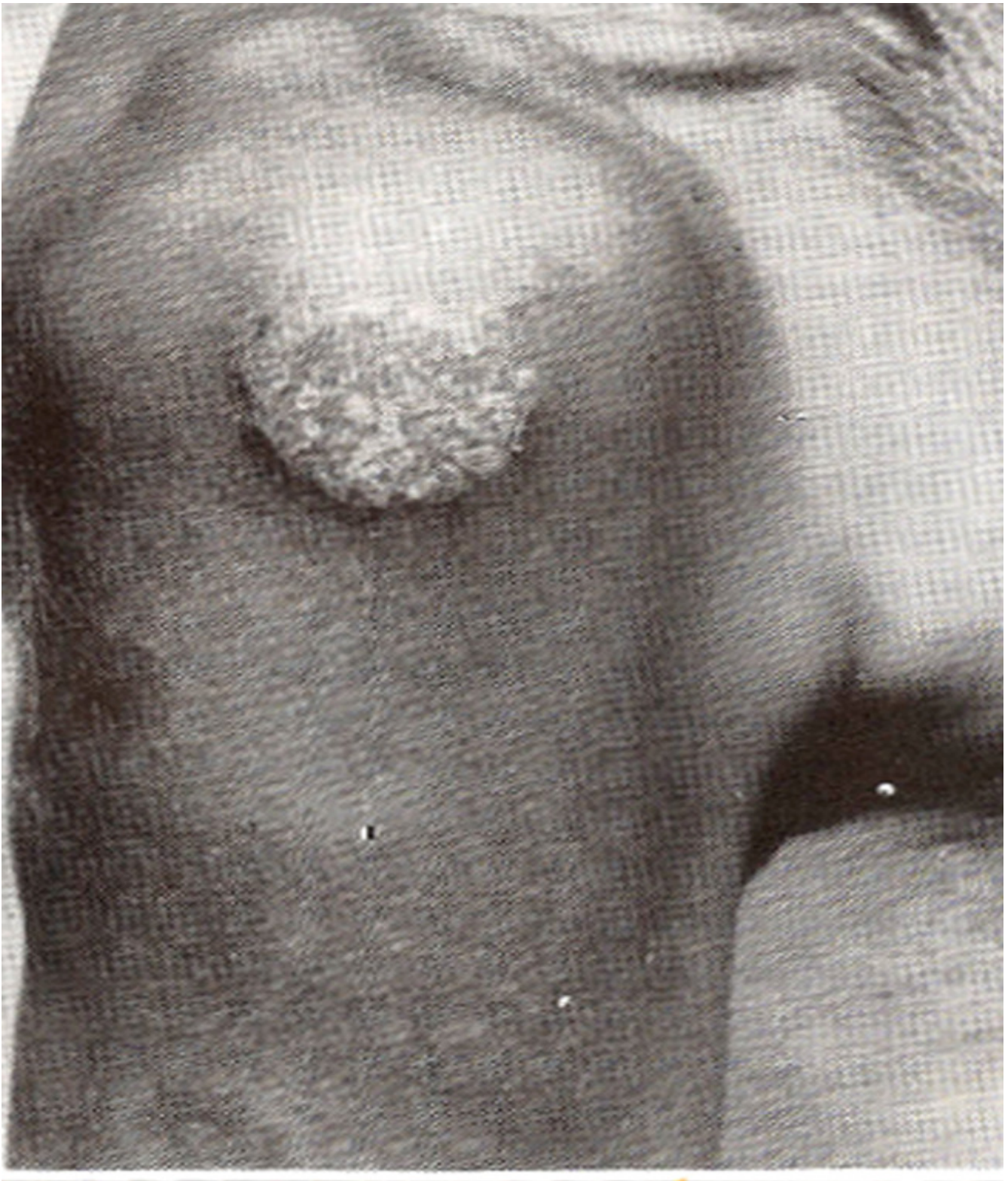


Figure 1. Tuberculoid leprosy (TF).

The maculoanaesthetic type shows an erythematous or hypopigmented macule which is dry, hairless and insensitive. Eye damage²² atrophic changes and bone damage may be seen (Figure 2).



Figure 2. Later stages of tuberculoid leprosy (TT) showing extensive damage to fingers.

Lepromatous leprosy

Nasal stuffiness, discharge and epistaxis are usually the early symptoms. Oedema legs and ankles due to increased capillary permeability may occur. Early dermal lesions include skin coloured, erythematous or faintly hypopigmented maculae with vague edges and shiny surface which are not

anaesthetic (Figure 3).



Figure 3. Early lepromatous leprosy (LL).

Later, skin coloured papules, nodules and plaques occur commonly on face, arms, legs and buttocks. Areas of skin with highest temperature like scalp, axillae, groins and perineum are not preferred. Mucous membrane lesions may occur. There is no toxæmia inspite of presence of millions of organisms. Still untreated, the skin thickens and eyebrows and eyelashes are lost (leonine facies). The nose is misshapen with septal perforation and collapse. Fibrosis of nerves leads to “glove and stocking anaesthesia leading to painless ulcers and shortening of fingers and toes. Eye changes, bone changes and testicular atrophy, may occur. The ocular complications of leprosy have been investigated by Mohammad and Kakakhel²². The most common cause of death in leprosy is renal failure. Histoid leprosy can be defined as a variant of nodular lepromatous leprosy characterized by cutaneous and/or subcutaneous nodules and plaques present over an apparently normal skin²³. Lucio type is a diffuse type of lepromatous leprosy which is found commonly in Mexico, also elsewhere. Here loss or sensation in hands and feet is followed by diffuse scleroderma like thickening of the skin²⁴.

Borderline leprosy

It is the commonest type of leprosy especially in children^{6,25}. Infiltrated plaques with punched out appearance is the characteristic presentation (Figure 4).



Figure 4. Borderline tuberculoid leprosy (BT).

Borderline tuberculoid leprosy will show skin lesions like tuberculoid leprosy and with nerve

thickening. The plaques are infiltrated, dusky red and with some tendency to limitation, but not as sharp as in TT³. When borderline leprosy downgrades to subpolar lepromatous leprosy (LLs), one sees typical lepromatous skin lesions but also tuberculoid lesions and thickened nerves.

AIDS IN DIAGNOSIS

Skin smear

The lesion is held between thumb and index finger to render it free of blood. A 5mm long and 3mm deep cut is given with a scalpel. Without relaxing the fingers, scrape with the same blade, dry over flame and stain with modified Ziehl-Neelsen²⁰. Normally LL, BL and BB are positive, BT may be positive and TT is negative.

Nasal scrape and biopsy

Scrape from the inferior turbinate or posterior nasal septum with a curette will show potential open cases. Skin biopsy should be deep to include subcutis and sent to lab in Ridley's fixative² or 10% formalin.

Nerve Biopsy

In pure neural TT or BT, a portion of thickened peripheral nerve may be removed and sent for histology.

Histamine test

It is a helpful test in early and indeterminate lesions. A drop of 1:1000 histamine is placed on suspected area and on a control area and a superficial needle prick is made. A bright flare develops in 1-2 minutes in normal skin or nonleprosy lesions. The flare is delayed, faint or absent in leprosy.

Lepromin test

It is not a diagnostic test but is used to classify leprosy. 0.1ml of Dharmendra or Mitsuda antigen is injected intradermally and read after 48 hours or 3-5 weeks respectively. Both are delayed hypersensitivity reactions. The test is strongly positive in TT, weekly positive in BT and negative in BB BL and LL. It is unpredictable in indeterminate leprosy².

Reactions in leprosy

In type 1 lepra reaction the leprosy lesions become red, swell and may ulcerate. The affected nerves are tender, painful swollen and the swelling may become fluctuant. Nerve palsies may occur²⁶. Oedema of face, hands and feet with tenderness of palms and soles may occur. Constitutional symptoms are unusual. Type 1 reaction is upgrading under treatment and occurs within the first 6 months of the chemotherapy or in puerperium²⁷. In type 2 reaction or erythema nodosum leprosum, crops of new lesions appear. The actual leprosy lesions are unaffected. The new lesions are bright red, tender nodules or plaques of varying sizes and occur on face, thighs and arms. Lesions last only a few days. Severe constitutional symptoms, epididymo-orchitis, proteinuria and mental depression may occur²⁸. This reaction occurs when majority of bacilli are fragmented. Immune complexes are present in circulation and are deposited in tissues. Reactions are precipitated by effective treatment, physical and emotional stress, infection and operation, etc. Lucio reaction occurring in diffuse lepromatous leprosy are type 2 reactions^{28,29}. Here erythematous and purpuric maculae may become bullous and ulcerated. It occurs in untreated patients and face is not affected unlike in erythema nodosum leprosum.

PREVENTION

An area is hyperendemic if leprosy prevalence is 10 or more per thousand people. All school age children should be examined when the prevalence is 5 or more per thousand. Children should be tested with lepromin and fluorescent leprosy antibody absorption (FLA-Abs) test³⁰. Indeterminate cases with

positive lepromin test should be followed up but not treated. Individuals with negative lepromin test but positive FLA-Abs test should be treated as they are at risk to develop multibacillary leprosy. A family with a leper should be regularly checked. Infective cases should be segregated till they are noninfective³¹. BCG vaccination reduces the risk. WHO is trying to develop a leprosy vaccine using bacilli from armadillo³². The value of dapsone prophylaxis in children, who are contacts of lepers, is doubtful and not recommended.

TREATMENT

Multibacillary type (Negative lepromin test and skin smear readily positive for bacilli i.e. LL, BL and BB): Rifampicin 600mg once monthly supervised, dapsone 100mg (1- 2mg/kg) daily, self administered and clofazimine 300mg once monthly supervised and 50mg daily self administered is the recommended regimen³⁰. Treatment is continued for at least 2 years and later if smear is not negative. Clofazimine may be replaced by ethionamide or prothionamide 250-375 mg/day if skin pigmentation (in white people) is not acceptable. Paucibacillary leprosy (Scanty or absent bacilli in skin smear and positive lepromin i.e. BT and TT): Rifampicin 600mg once a month, supervised and dapsone 100mg (1- 2mg/ kg) daily self administered is recommended. The duration of treatment is 6 months and this applies to all newly diagnosed paucibacillary cases, all dapsone alone treated paucibacillary patients who relapse, and all paucibacillary patients currently on dapsone monotherapy but who have not completed 2 years treatment yet³⁰.

Treatment of reactions

Multiple drug treatment should be continued in full doses. Prednisolone 20-40 mg/day for both type 1 and type 2 reaction should be started. For severe type 2 reactions higher doses may be needed²⁶. If required add clofazimine 300mg or thalidomide 300 mg per day. Beware of the teratogenicity of thalidomide. They may also be needed for weaning of the steroids. Thalidomide is not effective in type 1 reaction and clofazimine is doubtful but type 1 reaction can usually be managed with steroids alone. Thalidomide is also not effective in Lucio reaction. Chloroquine 200mg three times daily and colchicine 1.5-2mg daily can be used instead of thalidomide and clofazimine if they are contraindicated^{33,34}.

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