

Leprosy Revisited

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Letter to the Editor

Leprosy [1] is a chronic granulomatous disease involves skin peripheral nerves, nasal mucosa affecting tissues and organs. Demonstration of Causative Organism through Slit -Skin smear Examination [2] Mycobacterium leprae / M. leprae (Figure 1) Ziehl-Neelsen stain Acid fast bacilli. Narrative of M. leprae including its characteristics, mode of transmission pathogenesis, and evolution of classification are salient pre-requisite to comprehend leprosy and gender.

Mycobacterium leprae: characteristics

- Appear as straight or curved rods
- Size is 1-8 microns x 0.5 microns.
- Polar bodies present as clubbed forms.
- Lateral buds
- Acid fast but less resistant only 5% H₂SO₄
- Live bacilli, solid uniform structure.
- Dead appear as fragmented with granules.

Investigations for M. Leprae

Bacteriological examination

Slit-Skin smears:

Made by slit and scrape method from the most active looking edge of skin lesion and stained with Ziehl-Neelsen method.

Reading of smears:

- **Bacteriological-index (BI)**

Indicates density of leprosy bacilli (live & dead) in the smears and range from 0 to 6+

- **Morphological-index (MI)**

It is the percentage of presumably living bacilli in relation to total number of bacilli in the smear.

Paucibacillary (PB) leprosy: It is a form of leprosy classified for the purpose of treatment, based on clinical manifestations and slit-skin smear results. Paucibacillary leprosy has fewer than six skin lesions with no causative agent, the mycobacterium leprae on any slit-skin smear testing. It encompasses indeterminate, borderline tuberculoid, and tuberculoid leprosy.

Multibacillary (MB) leprosy: It is a form of leprosy classified for the purpose of treatment, based on clinical manifestations and slit-skin smear results. They have six or more lesions with or without positive slit-skin smear results for the

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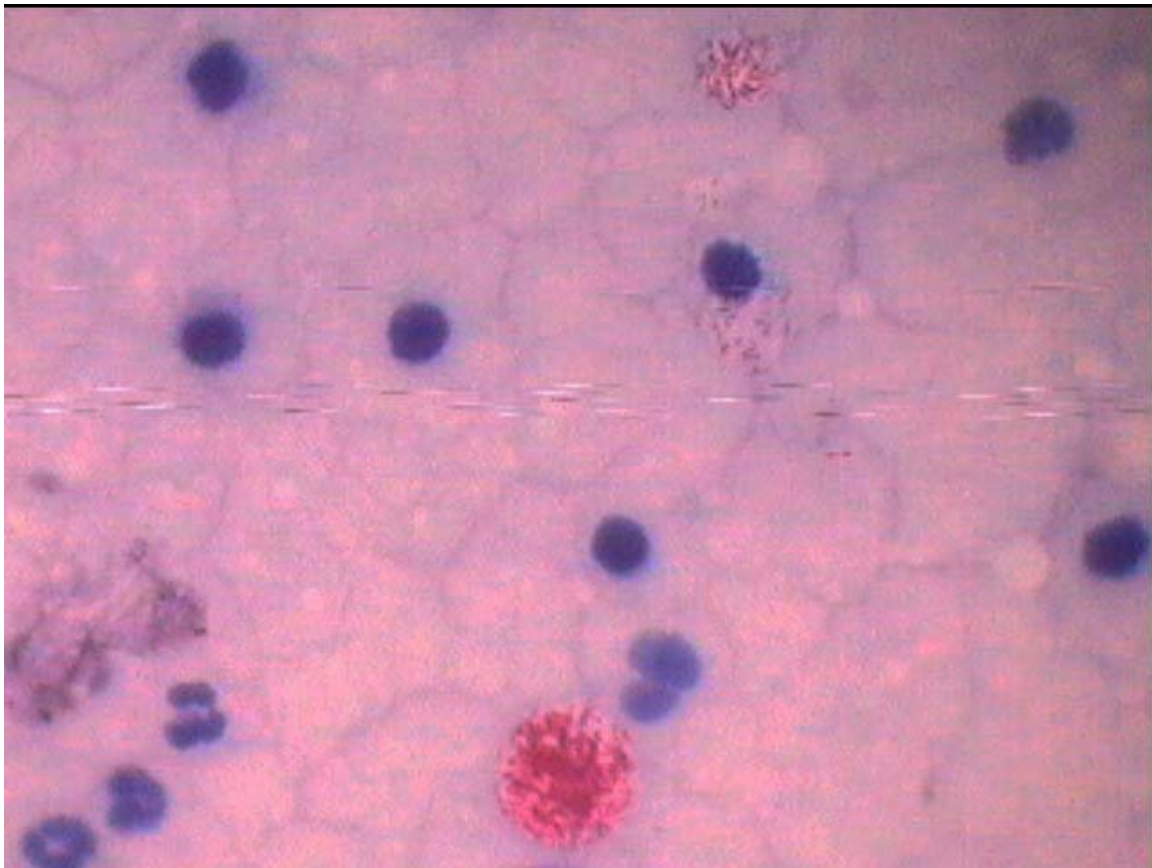


Figure 1: *M. leprae* in slit skin smear.

causative agent *Mycobacterium leprae*. It encompasses borderline lepromatous, midborderline, and lepromatous leprosy [3].

Mode of Transmission

- Air-borne transmission: through inhalation of the bacilli
- Indirect transmission: Clothes and sleeping mates
- Direct prolonged and intimate skin-to-skin contact

Pathogenesis of leprosy

M. leprae genes help to define the minimal gene set necessary for in vivo survival of this mycobacterial pathogen as well as genes potentially required for infection and pathogenesis [4] seen in leprosy.

Furthermore, *M. leprae* has a predilection to invade regenerating and / or degenerating branches of peripheral nerve undergoing inadvertent injury or trauma, seem to be dictated by multiple signaling pathways, playing key regulatory roles during the development of peripheral nervous

system (PNS) and also in neuro regeneration process following nerve degeneration.

Schwann cells, the glial cells of the PNS, by interacting with neuronal (axonal) ligands, mainly neuregulins via Receptor Tyrosine Kinase (RTK) complex, ErbB2/ ErbB3, initiate intracellular signaling pathways to drive proliferation and differentiation of schwann cells, both during development and the process of regeneration and re-myelination after nerve injury. One of the major signaling kinases, extracellular signal-regulated kinase-1/2 (ERK1/2), that is also a downstream signaling pathway of neuregulin-ErbB2/ErbB3 activation, has been identified as a key regulator of Schwann cell proliferation, differentiation, demyelination and nerve regeneration.

Recent studies have provided evidence that the bacterium that causes human leprosy, *Mycobacterium leprae* that has a unique capacity to invade Schwann cells of the adult PNS, utilizes the neuregulin-ErbB2/ErbB3 associated signaling network to the bacterial advantage. *M. leprae* directly bind to ErbB2

on myelinated Schwann cells and activate the RTK by a novel route that bypasses the classical neuregulin/growth factor-induced ErbB2-ErbB3 heterodimerization, and subsequently induce downstream the canonical Erk1/2 signaling, leading to myelin breakdown and subsequent axonal damage.

This initial injury provides a survival advantage for *M. leprae* as it induces de-differentiation and generates myelin-free cells, which are highly susceptible to *M. leprae* invasion and promote bacterial survival. Once invaded *M.*

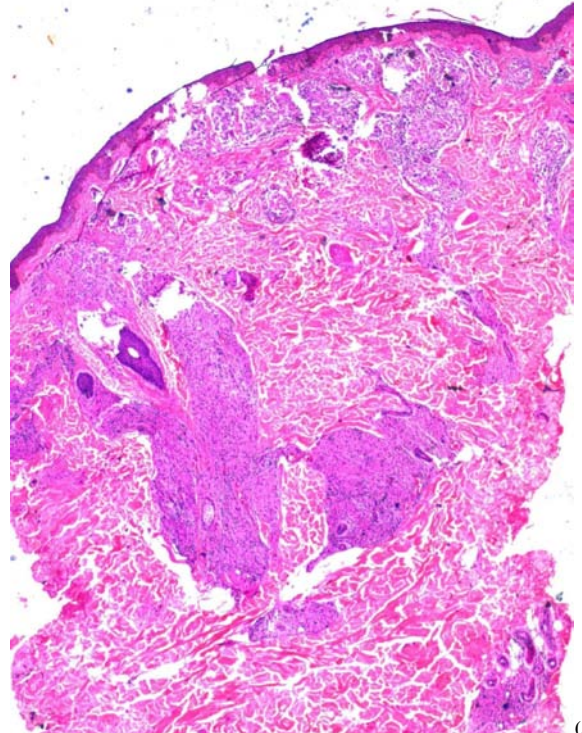


(A)



(B)

Figure 2 (A,B): Borderline borderline (BB) Leprosy, depicting an indurated plaque with serrated / irregular margin affecting the face and back of the trunk in a woman, numerous but countable.



(A)

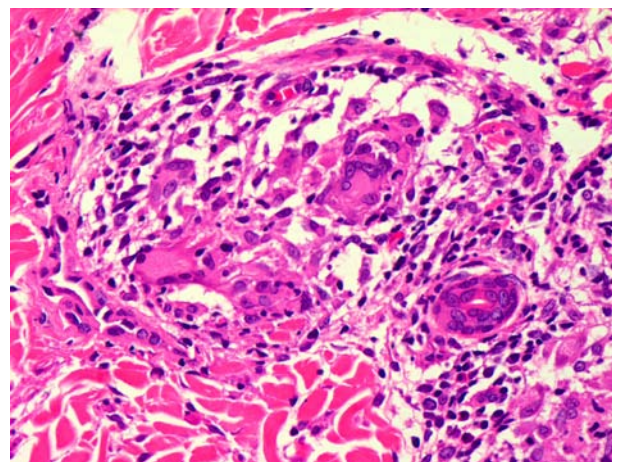


Figure 3 (A,B): The presence ill and well defined granuloma formed by epithelioid and lymphocytes in the dermis AFB are demonstrable in the granuloma of the dermis.

leprae activate Erk1/2 via a non-canonical pathway and subsequently increase the cell proliferation and maintain the infected cells in de-differentiated state, thereby preventing remyelination. Therefore, by subverting major RTKs and signaling pathways in adult schwann cells *M. leprae* appear to propagate the bacterial niche and maintain survival within the PNS [5]. Diagnosis of leprosy is largely clinical [6,7] (Figure 2 (a,b)) histopathology (Figure 3 (a,b)) supplements not supplant [8-10] the diagnosis. Classification is an effective means of understanding and communicating a difficult disease. Leprosy is a disease with various manifestations and, therefore, difficult to understand without comprehensive classification. Accordingly, leprosy possesses a continuous spectrum envisaging five [11] or seven [12] groups.

Recapitulation of groups of leprosy based on the immunological and histopathological form the basis in addition to the clinical and bacteriological findings. The classification divides leprosy into five groups

- Tuberculoid tuberculoid (TT)
- Borderline tuberculoid (BT)
- Borderline borderline/ Midborderline (BB)
- Borderline lepromatous (BL)
- Lepromatous lepromatous (LL)

Seven group classification in addition has indeterminate and polyneuritic Besides, histoid leprosy emanating in consequence to emergence of dapsone resistant strain [13]. Five and seven groups are now being practiced field work, research in institution

Leprosy and Gender

There seems an intractable effect of leprosy vis-a-vis gender, which attracted the focused attention, and are considered worthwhile, for they may add to comprehensive understanding of this so-called factor. It is, therefore, worthwhile, to form a perception keeping in view co-laterals namely [14]

- Biological,
- Socio-cultural / economic and
- Service-related factors

Interestingly, biological factors in the countries such as; Indonesia Nigeria, Nepal and Brazil were found to be

similar irrespective of the male/female ratio; more men than women were registered with multi-bacillary (MB) leprosy, socio-cultural factors explaining why women were under reporting. Yet, accessible, well reputed services augmented female participation and helped to diminish stigma, which in three out of the four societies seemed greater for women than for men. These positive effects could still be higher if the services would enhance community and patient education with active participation of patients and ex-patients themselves. Earlier, Similar gender leaning was observed in the across Indian sub-continent [15,16].

Multi-Drug Therapy [17] (MDT) comprising diaminodiphenyl sulfone (DDs) dapsone, rifampicin and clofazimine in recommended doses in the main stay of treatment for both pauci-multi bacillary leprosy and its elimination[18].

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