CLINICAL AND HISTOPATHOLOGICAL CORRELATION IN HANSEN’S DISEASE

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfilment of the regulations

for the award of the degree of

M.D. ( PATHOLOGY )

BRANCH - III

COIMBATORE MEDICAL COLLEGE
THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

APRIL 2012.
CERTIFICATE

Certified that this dissertation entitled “CLINICAL AND HISTOPATHOLOGICAL CORRELATION IN HANSEN’S DISEASE” is a bonafied work done by Dr. A.MURUGANANTHAM, post graduate student of the Department of Pathology, Coimbatore Medical College, Coimbatore, during the academic year 2009 - 2012. This work has not previously formed the basis for the award of any degree or diploma.

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SPECIAL ACKNOWLEDGMENT

My sincere thanks to

Prof. Dr. R. VIMALA.M.D.,

DEAN,

Coimbatore Medical College & Hospital,

For allowing me to do this

Dissertation and utilize the institutional facilities.
ACKNOWLEDGEMENT

I am gratefully indebted to Prof. Dr. M. Murthy, M.D., Professor and Head, Department of Pathology for his invaluable guidance, motivation and help throughout the study.

I would like to express my sincere and heartfelt gratitude to Dr. C. Lalitha, M.D., Additional Professor and Dr. A. Arjunan, M.D., Additional Professor, Department of Pathology, CMCH, Coimbatore.

I am grateful to Dr. A. Dhanalakshmi, M.D., Associate Professor, Department of Pathology for her invaluable guidance and help.

I express my sincere gratitude to all Assistant Professors, Department of Pathology, for their kind support, suggestions and encouragement.

I express my earnest gratefulness to Dr. Ramaswamy, M.D., D.D., Professor and Head of Department of Dermatology, Venerology and Leprosy, for his benevolent help and support.

My sincere thanks to my colleagues and junior collegues for their support and help.

I duly acknowledge the Paramedical staffs and Lab Technicians for their help and support.
I express my sincere gratitude to my father Late. Mr. N.K. Arunagirinathan, who has empowered me to carry out this work.

I wish to thank my mother, brothers, sisters, my wife and my daughter for their constant support.

Last but not least I am profoundly grateful to all patients for their cooperation and participation in the study.
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| Abbreviation | Definition |
|--------------|------------|
| AFB          | Acid Fast Bacilli. |
| BB           | Borderline Borderline (Midborderline). |
| BI           | Bacterial Index. |
| BL           | Borderline Lepromatous. |
| BT           | Borderline Tuberculoid. |
| DPX          | Destrene Phthalate (dibutyl phthalate) Xylene. |
| ENL          | Erythema Nodosum Leprosum. |
| IL           | Indeterminate Leprosy. |
| LL           | Lepromatous Leprosy. |
| MDT          | Multi Drug Therapy. |
| O.P.D        | Out Patient Department. |
| SSS          | Slit Skin Smear. |
| TT           | Tuberculoid (Polar). |
| WHO          | World Health Organisation. |
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INTRODUCTION

Leprosy, also known as Hansen’s disease, is a chronic infectious disease that primarily affects the skin & the peripheral nerves. Leprosy is one of the oldest diseases of mankind. Even though tremendous progress has been made in the field of leprosy, it still continues to be a global health problem.

Despite an extensive global drug programme for leprosy implemented by the WHO, leprosy is endemic in many countries with approximately 250,000 new cases reported every year.

The overall prevalence of leprosy in India has declined from 5.27/10000 in the year 2000 to 0.7/10000 in the year 2010, but still it continues to be a sizable public health problem. India represents approximately 55% of the global burden.

Leprosy expresses itself in different clinico-pathological forms depending on the immune status of the host. Diagnosis of leprosy is based on different clinical parameters which involves detailed examination of skin lesions and peripheral nerves. Demonstration of acid-fast bacilli in slit skin smears by Ziehl-Neelsen’s staining also aids in the diagnosis of leprosy. A reliable diagnosis hinges around a good histopathological work up and demonstration of bacilli in
histopathological sections. Modified Fite-Faraco procedure has proved most valuable in demonstrating lepra bacilli in tissue sections.

Ridley and Jopling were the first to suggest a subclassification of leprosy based on immunological aspects, as five types: Tuberculoid (TT), Borderline Tuberculoid (BT), Mid borderline (BB), Borderline Lepromatous (BL) and Lepromatous Leprosy (LL). Later, they correlated clinical and bacteriological findings in each group with respective immunological and histological findings.
AIM OF THE STUDY

To assess, classify and adopt apt treatment protocols based on histopathological evaluation of leprosy (Hansen’s) patients.

- To categorize and assess the severity of the disease.
- To provide confirmatory diagnosis for suspected cases which could be missed in clinical practice.
- To exactly type the patients as non-infectious (closed) and infectious (open) cases.
- To provide guidelines for appropriate drug therapy and duration of therapy.
- To study the prevalence of various subtypes in the locality.
NEED FOR THE STUDY

Clinical classification of leprosy is based solely on the gross appearance of the lesions and peripheral nerve involvement, while the parameters used for the histopathological classification are well defined, precise and also take into account, the immunological manifestations.

Histopathology provides confirmatory information for suspected cases which could be missed in clinical practice or epidemiological studies and helps in exact typing. Histology also gives an indication of progression and regression of the disease under treatment.

Elimination of such a complex and destructive infectious disease as leprosy needs tissue biopsy findings, which were earlier not considered relevant for treatment. Tissue biopsy should be given a status in the categorization and assessment of severity of the disease. The significant finding of AFB and histopathology in all types of leprosy should be studied with the help of tissue biopsies and special stain (Fite-Faraco), so that patients could be given the appropriate drug therapy for the stipulated duration warranted.

The present study was done to assess the concordance between clinical and histopathological diagnosis in cases of leprosy using Ridley-Jopling scale.
OBJECTIVE

Meticulous classification of Hansen’s disease (Leprosy) into various subtypes based on histopathology would enable decision making on apt treatment protocols and disease containment in the community. Prevalence of various subtypes of leprosy in the locality could also be evaluated.
REVIEW OF LITERATURE

DEFINITION

Leprosy (Hansen’s Disease) is a chronic disease caused by Mycobacterium leprae, infectious in some cases, and affecting the peripheral nervous system, the skin and certain other tissues\(^1\).

The Seventh WHO Expert Committee on Leprosy defined a case of leprosy as a person having one or more of the following features and who has yet to complete a full course of treatment: hypopigmented or reddish skin lesion(s) with definite loss of sensation; involvement of peripheral nerves (thickening) and skin smear positive for acid fast bacilli\(^2\).

HISTORY OF LEPROSY

Leprosy is a very ancient disease. Leprosy is generally believed to have originated in Asia and the earliest records of leprosy like disease come from China and India as early as 6\(^{\text{th}}\) century BC\(^4\). Leprosy is prevalent for many centuries in India, Africa and China. In China, a disciple of Confucius named Pai-niu suffered from a disease resembling lepromatous leprosy, which was known at that time as lai, li and Ta Feng\(^4\).

Some believe that it first originated in Asia and others believe that it originated in Africa, in Egypt. In India, leprosy was first described in the Susruth Samhita in 600 BC and treatment with chaulmoogra oil was known
at that time. Leprosy in India has been mentioned in the Vedic writing as kusht around 1400 BC.

The disease was probably carried from India to Europe in the 4th century BC by the soldiers and camp followers returning from the Greek wars of conquest in Asia, led by Alexander the Great. The earliest description of a disease which was unmistakably leprosy was by Aretaeus, in Greece, in 150 A.D as elephantiasis.

From Greece, leprosy slowly spread throughout Europe, conveyed by infected soldiers, traders and settlers. In Western and Northern Europe, the disease was most active between the 10th and 15th centuries.

Noble families found Leprosoria, hospitals for leprosy patients in twelfth and thirteenth centuries. Leprosy patients were legally considered as dead during that period.

Moller Christensen’s (1961) work revealed that 80% of the skeleton excavated at Naestved, Denmark, the burial ground of Lazar hospital which existed between 1250 and 1550 A.D., showed pathognomonic changes of leprosy.

Carl William Boeck (1808 – 75) and Daniel Cornelius Danielssen, (1818-94) two of the most renowned leprosy experts of the nineteenth century, believed that leprosy was a congenital disease and not an infectious one.
Gerhard Henrick Armauer Hansen (1841-1912) Danielssen’s son-in-law discovered the causative organism of leprosy, Mycobacterium leprae in 1873.6

EPIDEMIOLOGY

Geographical distribution

The worldwide prevalence of leprosy is less than one per 10000, but it is still a public health problem in 15 countries including India, Brazil, Myanmar and Nepal.7 During the past 12 years, the number of registered cases has fallen by about 85%.2

WHO - report published in August 2010 says that India accounts for about 55% of new leprosy cases reported all over the world. Out of 244,796 cases, 133,717 cases were reported from India.7

Leprosy cases in India have come down from 42/100,000 population in 2001- 02 to 7/100,000 population in 2010- 11.8

In India, Uttar Pradesh, Bihar, Chattishgarh, Jharkhand, Maharastra, Orissa, Andhra Pradesh, West Bengal and four union territories Chandigarh, Dadra Nager Haveli, Delhi and Goa did not reach the goal of elimination (< 1 case/ 10,000 population ).9 The incidence in Tamilnadu is 0.95/10000.
Diagramatic representation of leprosy prevalence in various states of India as per December - 2010.
Predisposing factors\textsuperscript{10}

Over crowding.
Malnutrition.
Poor sanitation.

Factors in transmission of leprosy\textsuperscript{10}

Source of infection.
Modes of transmission.
Susceptibility of host.

Source of infection

The only source of infection is a leprosy patient. Infectious cases or open cases are capable of discharging bacilli from their body and belong to the lepromatous pole. Non-infectious or closed cases are unable to shed bacilli and belong to the tuberculoid pole.

Modes of Transmission

Portal of exit: The two main portals of exit of M. leprae are the skin\textsuperscript{11,12} and nasal mucosa, the latter being the most important one.\textsuperscript{13} Other portals of exit are breast milk and female genital mucosa.\textsuperscript{14}

Portal of entry: Skin and the upper respiratory tract are the two main modes of entry.\textsuperscript{11,12} The organism may also enter through gastrointestinal tract\textsuperscript{14} and transplacental transmission may occur as a rare event.\textsuperscript{1}
Susceptibility of host

The development of the disease and the spectrum are determined by the degree of specific immunity of the infected person against the leprosy bacilli. Children are more susceptible as the immunity is poorly developed.

Duration of contact

Closeness and duration of contact are of importance in determining the dose of infection, but in highly susceptible persons even a casual contact may result in infection. Maximum number of patients acquired the disease in 4-6 years of contact followed by 0-3 years of contact.

Age

Leprosy is known to occur at all ages from infancy to very old age. The incidence is higher in 10-14 years age group and 30-60 years age group. The mean age at onset of leprosy in males is 31.49 years and in females is 29.43 years.

Sex

Leprosy in adults is more prevalent among men than women. In children there is no significant difference in leprosy prevalence between sexes. Most studies have reported a male female ratio that favours males.
Physiological aspects

Puberty, menopause, pregnancy, lactation and malnutrition might predispose to the onset or deterioration of clinical leprosy.\textsuperscript{22}

Incubation period

It may be as short as few months to as long as 20 years or more. On an average it is between 2 - 5 years.\textsuperscript{10,13}

Genetic factors

HLA association

Tuberculoid Leprosy DR3
Lepromatous Leprosy DQ\textsuperscript{1} \textsuperscript{23}

MICROBIOLOGY OF LEPROSY

Taxonomically, Mycobacterium leprae is classified under the order of Actinomycetales and the family mycobacteriaceae. It is a straight or slightly curved rod shaped organism with parallel sides and rounded ends. It is 1-8 µm long and 0.3 µm in diameter. Like other species of mycobacteria, M.leprae divides by binary fission, and is gram positive and strongly acid-fast following staining with carbol-fuchsin, although the staining is irregular in most of the organisms. Characteristically, acid-fastness is lost following extraction with pyridine (pyridine extractability).\textsuperscript{24}
Mycobacterium leprae is an acid-fast obligate intracellular organism that grows very poorly in culture but can be propagated in the armadillo and foot pad of mice.\textsuperscript{25}

M. leprae has a generation time of 12 to 14 days. M. leprae is the only species of mycobacteria to infect peripheral nerves, and Schwann cells.\textsuperscript{26}

M. leprae proliferates best at 32\textdegree{} to 34\textdegree{} C, the temperature of the human skin and the core temperature of armadillos.\textsuperscript{25} M. lepra has not been grown in an artificial culture medium.\textsuperscript{26}

**CLASSIFICATION**

**International classification of Madrid (1953)**\textsuperscript{27}

**Lepromatous Type (L)**

Macular  
Diffuse  
Infiltrated  
Nodular  
Neuritic, pure.

**Tuberculoid Type (T)**

Macular (Tm)  
Minor tuberculoid (Tt)  
Major tuberculoid (TT)  
Neuritic, pure (Tn)
**Intermediate Group (I)**

Indeterminate Group (I)

Macular (Im)

Neuritic, pure (In)

**Borderline (Dimorphous) Group (B)**

Infiltrated

(Others?) .

**Revised Indian Classification (1981)**

Tuberculoid

Borderline

Lepromatous

Indeterminate

Pure neuritic.

**Ridley & Jobling (1962)**

Indeterminate (not a type)

Tuberculoid (TT)

Borderline tuberculoid (BT)

Borderline Borderline (BB)

Borderline lepromatous (BL)

Lepromatous Leprosy (LL).
WHO Classification (1982)

Paucibacillary
Less than 5 skin lesions
No nerve involvement or one nerve involvement
Bacterial index < 2+

Multibacillary
More than 5 skin lesions
More than one nerve involvement
Bacterial index = 2+

(Changed in 1988 to paucibacillary = bacterial index of 0; multibacillary = 1+, WHO Expert committee on leprosy 1988).

Clinical features:

Leprosy may manifest in one of the four ways, cutaneous lesions, neural symptoms, reactional episodes and deformities.

Cardinal signs

1. Hypopigmented or reddish skin lesion(s) with definite loss of sensation;

2. Involvement of peripheral nerves (thickening) and

3. Skin smear positive for acid fast bacilli².
Early signs of leprosy

The early signs mainly affect the skin and to a lesser extent the peripheral nerves. The early signs include:

1. A hypopigmented patch in the skin that is lighter in color than the surrounding area, persists for long, does not irritate or itch, and in which there is partial or total loss of sensation, temperature, pain and light touch.

2. Numbness or feeling of pins and needles or crawling of ants or tingling sensation especially in hands and feet or weakness in fine movements of fingers.

3. Burns resulting from contact with hot articles, which at the time of contact did not cause pain.

4. Appearance of spontaneous blisters and ulcers especially in fingers.

Skin lesions:

Skin lesions may be single or multiple. Approximately 90% of the leprosy patients had skin lesions and 79.5% had skin lesions only. Single skin lesion is more common followed by 2 to 3 and more than 4 is rare. The sites of development of skin lesions of leprosy are predominantly the exposed parts, thighs and buttocks followed by arms, forearms, legs, trunk especially lumbar region, face and neck.
The main diagnostic sign is the loss of superficial sensation within the lesion in the order of temperature, pin prick and light touch, this is a constant feature of tuberculoid and borderline tuberculoid but not a feature of early borderline borderline, borderline lepromatous and lepromatous leprosy. In indeterminate leprosy, pain and temperature are impaired with exception but light touch is not frequently impaired.\textsuperscript{17}

**Nerve involvement**

Leprosy is one of the most important causes of nerve enlargement. Nerve enlargement occurs in approximately about 20.4%. Peripheral nerves commonly enlarged are superficial nerve trunks namely ulnar, lateral popliteal and greater auricular in that order. Other nerves include posterior tibial, median, radial, facial and cutaneous nerves like radial cutaneous, supraclavicular, supraorbital and sural nerve.\textsuperscript{17,29} Apart from the nerve trunks and the cutaneous nerves, there may be enlargement of small superficial nerves supplying the suspicious macule. This is of great diagnostic significance, more common in tuberculoid patch.

**Indeterminate leprosy (I)**

Indeterminate leprosy is an early stage of leprosy evolution where the histological and immunological responses have not yet evolved completely. It is observed only in endemic areas especially during surveys of population or school children. It is characterised by one to three ill-defined hypopigmented macules
ranging in size from 1 to 5 cm. These are commonly seen over the trunk, outer aspect of the extremities and the face. Their surface is smooth. The sensation may be impaired and nerve thickening may be present. Acid fast bacilli are not demonstrable by routine slit skin smears. The lepromin reaction is negative to doubtful.  

**Tuberculoid leprosy (TT)**

The lesions of tuberculoid leprosy may be macules or plaques. Plaques vary in number from 1-3, their size varies from 0.5 cm to as large as 30 cm. They may be located anywhere on the body but the preferred sites are the face, lateral or dorsal aspects of the extremities and the buttocks. They are asymmetrical and usually unilateral. They are slightly to markedly thickened and erythematous. Their edges are sharply defined and infiltrated, but the centre is less infiltrated, giving an annular appearance. The surface is dry, rough and irregular, and the lesions feel firm on palpation. They are anaesthetic and frequently associated with thickened nerve trunks; the nerve to the lesion may also be palpable. Slit skin smear for AFB is negative. The lepromin test is strongly positive (2+ to 3+).
**Borderline tuberculoid leprosy (BT)**

Borderline tuberculoid leprosy is the commonest presenting form of leprosy. The lesions are well-defined infiltrated plaques whose number varies from 3 to 10. The margins may be well defined and raised in a part of the lesion, flat and vague in another. They have a tendency for a break in borders and the development of satellite lesions. The surface is dry and anhidrotic. Lesions may involve large areas of the trunk, limbs or face.

Nerves in the vicinity of plaques are frequently enlarged but less so in the case of macules. Nerve damage leading to anesthesia and paralysis is common. AFB may be found. The lepromin test is weakly positive.

**Midborderline leprosy (BB)**

Midborderline leprosy is a very unstable and uncommon form of leprosy. Upgrading BL or downgrading BT leprosy might pass through this stage. It is characterised by widespread bilateral but asymmetrical erythematous infiltrated plaques with a punched out appearance. The plaque is depressed in the centre and has a sharp inner edge and a sloping outer border. Lesions may take bizarre shapes with irregular borders and a geographic appearance. They vary in number from 10 to 20 but may be even more numerous. They
involve the trunk, face and extremities. The palms, soles, scalp, axilla, groin, midline back and scrotum may be involved. These lesions are hypoesthetic and nerves show asymmetrical thickening.

Nerve damage is variable; it may be asymmetrical or symmetrical depending on its evolution from the BT or the BL spectrum. Peripheral sensory loss is asymmetrical. Slit skin smears for AFB are moderately positive. The lepromin test is doubtful or negative.27

**Borderline lepromatous leprosy (BL)**

Borderline lepromatous leprosy is clinically a mixture of lesions observed in midborderline (BB) and lepromatous leprosy (LL). The lesions tend to be more widespread than BB leprosy, but still not as symmetrical as in lepromatous leprosy. The nodular lesions and diffuse infiltration of the pinna and eyebrows seen in lepromatous leprosy start making their appearance in BL leprosy. The lesions may be macules, annular plaques or even nodules. They are shiny, copper colored, and more infiltrated in the centre than in the periphery. Lesions are of medium size and are numerous (20 and more). Compared to lepromatous leprosy, the macules of BL leprosy are better defined, have variable shapes and are not so perfectly symmetrical.
Nerve involvement is widespread in patients who downgrade from BT leprosy. In patients who evolve as BL leprosy, peripheral nerve involvement is bilateral. The peripheral nerves are thickened though not as symmetrically as in lepromatous leprosy. They are also less tender than those of BT leprosy. Slit skin smears show 3+ or more acid fast bacilli. The lepromin test is usually negative but may be doubtful or positive in up to 20% of patients.²⁷

**Lepromatous leprosy (LL)**

Lepromatous leprosy is a multisystem disease that develops in individuals who are unable to mount a cell mediated immune response against M. leprae. It leads to massive multiplication of M. leprae that infiltrate the skin, nerves, reticuloendothelial system, upper respiratory tract, eye, testes, adrenals and other viscera. It is one of the most infectious forms of leprosy and a large number of bacilli are discharged from the respiratory tract.

In the early stage of lepromatous leprosy, there may be numerous, small, bilaterally symmetrical, smooth, shiny, ill-defined macules that are hypopigmented or less commonly, slightly erythematous in colour. Gradually these macules enlarge and coalesce. Progressive gradual infiltration may lead to formation of papules, nodules and plaques. The lesions are bilaterally symmetrical and smooth surfaced with sloping edges. Sensations of
touch and pain (pin prick) are usually unimpaired but sweating may be diminished. The distribution of lesions is characteristically on the face over the forehead, the zygoma, the chin and the ear lobes, and on the limbs over the cooler dorsal areas, notably the forearms, dorsum of the hands and extensor surfaces of the lower legs. Loss of sensation occurs over the dorsum of the hands, the forearms and the lower legs. Hair is lost over all skin lesions especially over the face. Loss of eyebrows and eyelashes (madarosis) is characteristic.

In advanced stage of the disease, massive infiltration of the face leads to ‘leonine facies’ due to prominent ridges and furrows on the forehead, enlarged and thickened ears and loss of eyebrows.

Sensory fibres are damaged first. The nerves are not palpably enlarged in early stage, but later they become firm, then enlarged, and finally hard at the sites of predilection in a symmetrical fashion. Muscle weakness appears in hands and feet. The digits may shorten due to concentric absorption of the digits.

The presenting features of lepromatous patients may be nasal stuffiness, epistaxis, edema of hands and feet, type 2 lepra reaction with skin lesions, neuritis, iritis and orchitis. Others may present with deformity and ulceration of hands and feet and saddle nose. Slit skin smears for AFB are strongly positive (5+ or 6+).
Pure neuritic leprosy (P)

Wade in 1952 was the first to recognize polyneuritic cases as a separate group. The Indian Classification of Leprosy (1955) and its modified version have recognized it as a distinct group. Primary neuritic leprosy usually present with signs and symptoms of nerve deficit. There may be a gradual weakness in a hand or a sudden foot drop or it may present as anesthesia in an extremity or extremities. On examination, the relevant peripheral nerves and sometimes others are enlarged. If they are in reactional state, the nerves will be tender to palpation or spontaneously painful. The diagnosis is usually made by the presence of definite nerve enlargement. The symptoms caused by the affected nerves include sensory, motor and trophic changes in the area supplied by the nerves. These may result in deformities, neuropathic ulcers and lagophthalmos which may result in severe eye complications. The ulnar, median, common peroneal, the posterior tibial, the greater auricular and rarely radial nerves are involved in the order of frequency. The cranial nerves involved are 5th and 7th. Abscess formation when observed suggests a tuberculoid histology.

Pure neuritic leprosy can be diagnosed on the findings of a thickened nerve and sensory impairment, slit skin smears negative for AFB and absence of skin lesions. About 15-35% of pure neuritic leprosy patients develop skin lesions during follow up.
Rare presentations of lepromatous leprosy

Histoid Leprosy

Histoid leprosy was first described by Wade in 1963. Histoid leprosy appear as cutaneous / sub-cutaneous, firm, translucent, erythematous / coppery, shiny papules, nodules or plaques emanating from an apparently normal skin. The lesions are usually located on the back, buttocks, face and extremities and over bony prominences especially around the elbows and knees.

Histoid leprosy is commoner in men. It may represent relapse and arise in treated cases of lepromatous leprosy. Histoid leprosy is also encountered in untreated patients. It usually follows dapsone monotherapy. Slit skin smears from histoid lesions show abundant AFB occurring in clusters, singly or tightly packed in macrophages.

Lucio’s leprosy

It is a rare form of leprosy usually found in Mexico. It was first described in 1852 by Lucio and Alvarado and later by Latapi and Zomara in 1948. It is a polar form of lepromatous leprosy characterised by thickening of eyelids, giving a sad, sleepy appearance. The first symptom is usually numbness of the hands or feet, nasal congestion, epistaxis, hoarseness of voice or edema of the feet; this may be mistaken for myxedema. The first sign is madarosis. Slit skin smears shows abundant lepra bacilli.
Deformities and disabilities associated with leprosy

Both paresis and established deformities is more common in BT leprosy and established deformity in lepromatous pole. Claw hand is the most common deformity followed by trophic ulcer, foot drop and wrist drop. Other rare deformities includes facial nerve palsy, lagophthalmos, leading to cornea ulcers.

REACTIONS IN LEPROSY

The term reaction is used to describe the appearance of symptoms and signs of acute inflammation in the lesions of patients with leprosy. Clinically there is redness, swelling, pain and tenderness of skin lesions along with swelling, pain and tenderness of nerves, often accompanied by loss of function.

Reactions can be divided into two types on clinical and immunological grounds

Type 1 lepra reaction

It is a delayed hypersensitivity (Coombs and Gell Type 4) reaction due to rapid change in cell-mediated immunity. It is typically seen in borderline patients because of the immunological instability. It may be upgrading (reversal) or downgrading reaction. Upgrading reaction occurs in patients when the immunological status shifts towards tuberculoid spectrum,
usually during the first six months of treatment.\(^\text{39}\) Downgrading reaction occurs when there is deterioration of immune status and the patient shifts towards lepromatous pole.

The most prominent sign is the rapidly developing change in the appearance of some or all the skin lesions; they become erythematous, more prominent, shiny, warm to touch, and resemble erysipelas. The lesions are often tender and painful. Sometimes necrosis supervenes with breakdown and ulceration. Lesions desquamate as they subside. New lesions may appear. Usually the new lesions resemble the pre-existing ones but it may be numerous and small, and in case of downgrading reaction, the new lesions may be more lepromatous in appearance.

Neuritis is the most important part of type I reaction. Neuritis presents as enlargement of one or more nerves with pain and tenderness at the sites of predilection. Anesthesia develops rapidly in the distribution of the affected nerve. More severe motor disturbances like claw hand, foot drop, facial palsy may occur. Rarely nerve abscess may occur. Another associated manifestation is edema of hands, feet, or face; sometimes all three sites are involved, or, rarely, one foot or hand. Constitutional symptoms are rare.

**Type 2 lepra reaction**

Type 2 lepra reaction or Erythema nodosum leprosum (ENL) is an immune complex syndrome (type III hypersensitivity reaction). It occurs almost exclusively in lepromatous leprosy, only occasionally appearing in borderline lepromatous leprosy. There is no change in the appearance of
the leprosy lesions, but there is occurrence of crops of brightly erythematous nodules, which come and go. Systemic disturbance is usual. Unlike upgrading reaction, when it occurs in relation to therapy, it is very unusual for it to occur during the first six months of therapy. It tends to occur later during the course of treatment when the skin lesions appear quiescent and all or most of the bacilli in the skin are granular, however patient may be in reaction when first seen.27

Erythema nodosum leprosum (ENL) lesions are brightly erythematous, raised nodules or plaques, variable in size but usually small, and if multiple, they tend to be distributed bilaterally and symmetrically. They are often tender, warmer than the surrounding skin, blanch with light finger pressure and are evanescent. They commonly occur on the face, arms and thighs; the flexor aspects of the forearms and the medial aspects of the thighs are favoured; rarely on the palms and soles. They fade leaving a blue stain. When ENL lesions are numerous there is likely to be fever and malaise. The fever being intermittent with its fastigium in the evenings, and it is usual to find fresh crops of ENL lesions appearing between 17.00 and 18.00 hours, a time when endogenous cortisol production is at its lowest. They desquamate as they subside.40

In severe Type 2 reaction, ENL lesions may become vesicular and bullous. Type 2 reaction may be associated with nerve pain, periosteal pain, muscle pain, pain and swelling in joints, rhinitis, epistaxis, acute iritis, painful dactylitis, swollen and tender lymph nodes,
acute epididymo-orchitis, acute glomerulonephritis\textsuperscript{41} and proteinuria. The face, hands and feet may become edematous and the spleen may become palpable.

**RELAPSE**

A patient who successfully completes an adequate course of multi drug therapy (MDT) but who subsequently develops new signs and symptoms of disease during the surveillance period or thereafter is considered to have relapsed.\textsuperscript{42} Early relapse is within 3 ½ years and is due to insufficient treatment, insufficient drugs, improper classification and insufficient duration. Late relapse is after 3½ years and is due to bacterial persistence and drug resistance. The features of relapse are extension in area of the existing lesions, thickening, erythema or infiltration of previously subsided lesions, or new lesions; thickening and tenderness of nerves and/or fresh nerve involvement and bacteriological positivity in previously negative sites and/or positivity in fresh lesions.
### Differences between reversal reaction and relapse

| S.No | Reversal reaction | Relapse |
|------|-------------------|---------|
| 1    | Seen in BT, BB, BL and LL types. | Seen in all types subtypes which have been inactive. |
| 2    | Onset is sudden, within 6 months of termination of treatment | Onset insidious, often after 1-5 years of treatment. |
| 3    | Swelling, erythema and scaling of inactive lesions. Rarely, new lesions of same morphology. Tenderness of lesions. Edema of hands and feet. | Old lesions show extension in area with increased signs of activity. New lesions appear. Edema is not a prominent feature. |
| 4    | Previously involved nerves are exquisitely tender with deterioration in sensory and/or motor deficit. Nerve abscess may form. | Fresh nerves involved. Nerves show thickening and tenderness is rare. Sudden onset of paralysis is not seen. |
| 5    | Skin smears usually negative; BI is lowered in BL. | Skin smears usually positive in relapse in BL, LL and negative in tuberculoid. |
| 6    | Response to steroids good; subsidence within 2 months. | Steroid therapy not very effective; disease progressive. |
IMMUNOPATHOLOGIC SPECTRUM OF LEPROSY

The sequence of disease pathogenesis is complex, chronic and depends on host-parasite immunologic response. The leprosy bacillus is nontoxic, and clinicopathologic manifestations are the result of immunopathology and/or the progressive accumulation of infected cells. Leprosy is the best example of a disease showing an immunopathologic spectrum whereby the host immune reaction to the infective agent ranges from apparently none to marked, with a consequent range of clinicopathologic manifestations.\textsuperscript{43,44}

Tuberculoid leprosy indicates a high cellular immune response (T cells and macrophages activation) and few bacilli in tissues; at the opposite pole, lepromatous leprosy indicates an absent cellular immune response to M. leprae antigens, with no macrophage activation and abundant bacilli in tissues. The spectrum of leprosy is a continuum and patients may move in either direction according to host response and treatment.

Tuberculoid (TT) and lepromatous (LL) patients are stable, the former often self-healing and the latter remaining heavily infected unless given appropriate chemotheraphy. The term \textit{borderline} is used to denote patterns that share some features of both tuberculoid and lepromatous leprosy.\textsuperscript{43,45} Patients presenting at the BT point will often downgrade towards BL leprosy in the absence of treatment.
The central point of the spectrum (BB) is the most unstable, with most patients downgrading to LL if not treated. The term *indeterminate* leprosy is used to describe patients presenting with very early leprosy lesions that cannot be categorized definitely along the immunopathologic spectrum.46

**Staining of *Mycobacterium leprae* Bacilli**

The classical method for demonstrating leprosy bacilli in lesions is a modified Ziehl-Neelsen stain, where the degree of acid and alcohol removal of carbol fuchsin is less than in the methods used for identifying other mycobacteria. The Fite methods are the most commonly used.44 Methanamine silver stains are also useful in detecting fragmented acid-fast bacilli. The sensitivity of detection of acid-fast bacilli by histologic means remains poor, because about 1000 bacilli per cubic centimetre of tissue must be present in order to detect 1 bacillus in a section.47

The standard enumeration of leprosy bacilli in lesions -- the bacterial index (BI) follows Ridley’s logarithmic scale (which applies to both skin biopsies and slit skin smears).
Ridley’s logarithmic scale:

| BI  | Description                                      |
|-----|--------------------------------------------------|
| 0   | No bacillus observed                             |
| 1   | 1 to 10 bacilli in 100 oil immersion fields.     |
| 2   | 1 to 10 bacilli in 10 oil immersion fields       |
| 3   | 1 to 10 bacilli in an oil immersion field        |
| 4   | 10 to 100 bacilli in an oil immersion field      |
| 5   | 100 to 1000 bacilli in an oil immersion field    |
| 6   | > 1000 bacilli in an oil immersion field.         |

Solid staining bacilli indicate that the organisms are capable of multiplication. Fragmented (beaded) and granular acid-fast bacilli indicate that they are dead. Patients with no bacilli are termed paucibacillary; those with some or many bacilli are multibacillary (this distinction is important in determining the duration of chemotherapy).\(^{48}\)

Immunocytochemical methods for demonstrating mycobacterial antigens have a limited role. The most frequently used is a polyclonal anti-BCG antibody. Immunohistochemistry does have a role in demonstrating the presence of leprosy antigen after the bacilli have fragmented, been partly digested by macrophage enzymes and lost their acid-fast staining quality.\(^{46}\)
HISTOPATHOLOGY OF LEPROSY

Early, Indeterminate Leprosy

In indeterminate leprosy, there is mild lymphocytic and macrophage accumulation around neurovascular bundles, the superficial and deep dermal vessels, sweat glands, and erector pili muscle; focal lymphocytic invasion into the lower epidermis and into the dermal nerves may be observed. No formed epithelioid cell granuloma are present. Schwann cell hyperplasia may be observed. The diagnosis hinges on finding one or more acid-fast bacilli in the sites of predilection: in nerve, in erector pili muscle, under the epidermis, or in a macrophage about a vessel. Without demonstrating bacilli, the diagnosis can only be presumptive.46

Tuberculoid leprosy

Primary tuberculoid (TT) leprosy has large epithelioid cells arranged in compact granulomas along with neurovascular bundles, with dense peripheral lymphocyte accumulation. Langhans giant cells are typically absent. Dermal nerves may be absent (obliterated) or surrounded and eroded by dense lymphocyte cuffs. Acid-fast bacilli are rarely found, even in nerves.46
**Borderline Tuberculoid Leprosy**

In borderline tuberculoid (BT) leprosy granulomas with peripheral lymphocytes follow the neurovascular bundles and infiltrate sweat glands and erector pili muscles. Langhans giant cells are variable in number and are not large in size. Granulomas along the superficial vascular plexus are frequent, but they do not infiltrate up into the epidermis. Nerve erosion and obliteration are typical. Acid-fast bacilli are scanty (BI ranges from 0 to 2) and most readily found in Schwann cells of nerves.46

**Midborderline Leprosy**

In midborderline (BB) leprosy, macrophages are uniformly activated to epithelioid cells but are not focalized into distinct granulomas, and lymphocytes are scanty. There are no Langhans giant cells. The bacterial index (BI) ranges from 3 to 4. Dermal edema is prominent between the inflammatory cells.46

**Borderline Lepromatous Leprosy**

The important difference between the histology of LL and BL leprosy is that in BL, the lymphocytes are more prominent and there is a tendency for some activation of macrophages to form poorly to moderately defined granulomas. Perineural fibroblast proliferation, forming an “onion skin” in cross-section is typical. Foam cells are not prominent, and globi do not usually accumulate; the BI range from 4 to 5.46
Lepromatous Leprosy

Lepromatous Leprosy (LL), in macular or infiltrative-nodular lesions, exhibits an extensive cellular infiltrate that is almost invariably separated from the flattened epidermis by a narrow grenz zone of normal collagen. The infiltrate causes the destruction of the cutaneous appendages and extends into the subcutaneous fat. In florid early lesions, the macrophages have abundant eosinophilic cytoplasm and contain a mixed population of solid and fragmented bacilli (BI = 5 to 6). The bacilli, on Wade-Fite staining, can be seen to measure about 5.0 by 0.5 µm and if solid may be packed like cigars. Bacilli are commonly observed in endothelial cells as well. There is no macrophage activation to form epithelioid cell granuloma. Lymphocyte infiltration is not prominent, but there may be many plasma cells.46

With antimycobacterial chemotherapy, degenerated bacilli accumulate in the macrophages - the so called lepra cells or Virchow cells - which then have foamy or vacuolated cytoplasm. The Wade-Fite stain reveals that the bacilli are fragmented or granular and, disposed in large clumps called globi. In lepromatous leprosy, in contrast to tuberculoid leprosy, the nerves in the skin may contain a considerable number of leprosy bacilli.46
**Histoid Leprosy**

In histoid leprosy, the macrophage reaction is unusual in that the cells frequently become spindle shaped and oriented in a storiform pattern, similar to those of a fibrohistiocytoma. The epidermis may be stretched over such dermal expansile nodules. Histoid Leprosy shows the highest loads of bacilli (BI is 6), and the majority are solid staining, arranged in clumps like sheaves of wheat.\(^{46}\)

**Lucio Leprosy**

The histopathology of Lucio leprosy is similar to lepromatous leprosy but with a characteristic heavy bacillation of small blood vessels in the skin.\(^{49}\)

**PERIPHERAL NERVES**

In all patterns of leprosy, the major peripheral nerves often undergo parallel pathological changes. The inflammation is similar, and the same classification system is applied. However, the density of acid-fast bacilli is often a logarithm higher than in the nearby skin.\(^{50}\)
HISTOPATHOLOGY OF LEPROSY REACTIONS

Type 1 Reactions

The distinction between upgrading and downgrading reactions is difficult to make and may require serial examinations. Typically, there is edema within and about the granulomas and proliferation of fibrocytes in the dermis.

In upgrading reactions, the granuloma becomes more epithelioid and activated, and Langhans giant cells are larger; there may be erosion of granulomas into the lower epidermis, and there may be fibrinoid necrosis within the granulomas and even within dermal nerves.

In downgrading reactions, necrosis is much less common, and over time the density of bacilli increases. Multibacillary leprosy patients who upgrade on therapy show old foamy macrophages and degenerate bacilli admixed with new epithelioid cell granuloma.

Type 2 Reaction: Erythema Nodosum Leprosum (ENL)

In ENL, the lesions are foci of acute inflammation superimposed on chronic multibacillary leprosy. Polymorph neutrophils may be scanty or so abundant as to form a dermal abscess with ulceration. Whereas foamy macrophages containing fragmented bacilli are usual, in some patients no bacilli remain and macrophages have a granular pink hue on Wade-Fite staining, indicating mycobacterial debris. A necrotizing vasculitis affecting arterioles, venules
and capillaries occurs in some cases of ENL and these patients may have superficial ulceration.\textsuperscript{46}

\textbf{Lucio Reaction}\textsuperscript{52}

In the Lucio reaction, vascular changes are critical.\textsuperscript{44} Endothelial proliferation leading to luminal obliteration is observed in association with thrombosis in the medium sized vessels of the dermis and subcutis. There is a sparse, largely mononuclear infiltrate. Dense aggregates of acid-fast bacilli are found in the walls and the endothelium of normal appearing vessels as well as in vessels with proliferative changes. Ischemic necrosis, brought on by the vascular occlusion, leads to hemorrhagic infarcts and results in crusted erosions or frank ulcers.\textsuperscript{46}
MATERIALS AND METHODS

The study was conducted on the skin biopsies of patients newly registered at the Department of Dermatology, Venerology & Leprosy and subsequently reported to the histopathology section of the Department of Pathology, Coimbatore Medical College & Hospital, Coimbatore.

STUDY PERIOD:

From May 2010 to October 2011 for a period of 18 months.

INCLUSION CRITERIA:

- Patients aged between 15 to 65 years.
- New cases presenting with hypopigmented patches & loss of sensation.

EXCLUSION CRITERIA:

- Patients younger than 15 years and older than 65 years.
- Old treated cases.
- Patients who where started on MDT (Multi Drug Therapy).
COLLECTION OF DATA:

Patients aged between 15 to 65 years attending the Department of Dermatology, Venerology & Leprosy O.P.D with hypopigmented & anaesthetic patches were enrolled.

History of presenting complaints, duration of illness and socioeconomic status were taken from the patients.

General examination and dermatological examination regarding the morphology, number, size, site, colour, anaesthesia, margins, surface, satellite lesion and central clearing of skin lesions as well as the involvement of peripheral truncal nerves and cutaneous nerves was done. Reactions and deformities were also noted.

Skin biopsy was done from the margin of the skin lesion and fixed in 10% formalin. The specimen was processed routinely in the histopathology lab and sections were stained with haematoxylin and eosin.

Haematoxylin and eosin stained sections of the skin biopsies of all cases of leprosy included in the study were examined for:

- a) Epidermal atrophy, epithelioid granulomas, number and distribution of lymphocytes, histioocytes & foam cells.
- b) Infiltration of nerves, blood vessels and adnexa.
- c) Grenz zone.
Sections stained with Fite-Faraco stain were examined for lepra bacilli.

**FITE-FARACO STAIN FOR LEPRA BACILLI:**

FIXATION: 10% formalin.

SECTIONS: 4 microns thick.

SOLUTIONS:

Xylene : Oil (Liquid paraffin) = 3 : 2

Xylene - 15 ml.

Oil (Liquid paraffin) - 10 ml.

CARBOL FUCHSIN SOLUTION:

Phenol crystals melted - 5 ml.

Basic fuchsin - 1 gm.

Absolute ethyl alcohol - 10 ml.

Distilled water - 100 ml.

The basic fuchsin is dissolved in alcohol and phenol in water. The two solutions are mixed and filtered before use.

5% $\text{H}_2\text{SO}_4$:

Con. $\text{H}_2\text{SO}_4$ - 5 ml.

Distilled water - 95 ml.
DEPARAFFINISATION:

- Incubator (62°C) – dewax for 10 to 20 minutes.
- Xylene : Oil (Liquid paraffin) mixture - 15 ml : 10 ml.

PROCEDURE:

1. The slides are kept in xylene: oil mixture - 40 minutes.
2. Drained, blotted dry, wiped around sections.
3. Rinsed in water - for 1 minute. (no alcohol step).
4. Wiped around sections.
5. Carbol fuchin - 40 minutes. (no heat).
6. Rinsed in water - 1 minute.
7. Decolourised with 5% sulphuric acid - 5 minutes.
   (Microscopic control till the sections are pale pink).
8. Washed in water - rinse.
9. Counter stained with haematoxylin - 3 minutes.
10. Washed in water - 10 minutes.
11. Air dried, mounted in DPX.

RESULTS:

Mycobacterium - Red.

Background - Blue.

Based on Ridley’s logarithmic scale, bacterial index (BI) was done. Histopathological findings were graded into tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous
(BL) and lepromatous leprosy (LL) according to Ridley & Jopling scale. Sections showing scattered non-specific lympho-histiocytic infiltration with cellular reaction within the dermal nerve or presence of bacilli in arrector pilorum muscle/dermal nerve were classified as indeterminate leprosy and also included for purpose of analysis.

Clinical diagnosis of leprosy cases (as provided by Department of Dermatology, Venerology & Leprosy) using Ridley & Jopling scale was correlated with the results of histopathologic examination of their respective biopsies.
OBSERVATION AND RESULTS

During the study period of 18 months from May 2010 to October 2011, 35 skin biopsy specimens of clinically diagnosed untreated cases of leprosy were studied, which included 23 males and 36 females aged between 15 to 65 years.

TABLE 1. AGE & SEX CORRELATION

| SEX     | AGE GROUP | TOTAL |
|---------|-----------|-------|
|         | 15 - 30 yrs | 31 - 50 yrs | 51 - 65 yrs | n = 35 |
| MALE    | 6          | 11      | 6           | 23     |
| FEMALE  | 5          | 5       | 2           | 12     |
| TOTAL   | 11         | 16      | 8           | 35     |

Most number of cases were in the age group of 31 - 50 years (ie) 16 cases (45.7%)

Number of males = 23 (65.7%).

Number of females = 12 (34.3%).

Male : Female ratio = 1.92 : 1.
Histopathological examination of the skin biopsies of 35 patients revealed the following: the distribution of histopathological spectrum was IL - 12 (34.28%), TT - 8 (22.86%), Histoid - 6 (17.15%), BL - 3 (8.58%), BT, BB, LL - 2 cases each (5.71% each). The maximum histopathological cases were seen in IL (Indeterminate) type followed by TT and Histoid type. Maximum number of cases were seen in the polar spectrum i.e). TT & LL (including its variant Histoid) and indeterminate type.
TABLE.3. AGE AND HPE CLASSIFICATION.

| CLASSIFICATION | 15 - 30 YEARS | 31 - 50 YEARS | 51 - 65 YEARS |
|----------------|--------------|--------------|--------------|
| TT             | 3            | 3            | 1            |
| BT             | 1            | 1            | -            |
| BB             | -            | 2            | -            |
| BL             | 2            | -            | 1            |
| LL             | -            | 1            | 1            |
| HISTOID        | -            | 6            | -            |
| IL             | 5            | 4            | 4            |

The most commonly seen spectrum was polar leprosy ie) TT and LL (with its variant Histoid) followed by indeterminate type. Maximum number of cases were seen in the age group of 31-50 years.
Of the 35 cases studied 23 (67.72%) were males and 12 (34.28%) were females (M:F = 1.92:1). Among the female patients IL (indeterminate) was the commonest spectrum - 8 cases (22.87%). Among males LL and its variant Histoid was the commonest - 7 cases (2 + 5) (5.71% + 14.29%), followed by TT - 6 cases (17.15%).

**TABLE. 4. CORRELATION OF SEX & HPE SPECTRUM**

| HPE SPECTRUM | MALE | PERCENTAGE | FEMALE | PERCENTAGE |
|--------------|------|------------|--------|------------|
| TT           | 6    | 17.15%     | 2      | 5.71%      |
| BT           | 2    | 5.71%      | -      | -          |
| BB           | 1    | 2.85%      | 1      | 2.85%      |
| BL           | 3    | 8.58%      | -      | -          |
| LL           | 2    | 5.71%      | -      | -          |
| HISTOID      | 5    | 14.29%     | 1      | 2.85%      |
| IL           | 4    | 11.43%     | 8      | 22.87%     |
| TOTAL        | 23   | 65.72%     | 12     | 34.28%     |
TABLE. 5. CORRELATION OF HPE DIAGNOSIS AND BACTERIOLOGICAL INDEX (FITE FARACO STAIN).

| HPE DIAGNOSIS | BACTERIOLOGICAL INDEX (BI) |
|---------------|---------------------------|
| TT            | 0                         |
| BT            | 1+                        |
| BB            | 2+/3+                     |
| BL            | 3+/4+                     |
| LL            | 5+                        |
| HISTOID       | 5+/6+                     |
| IL            | 0/1+                      |

Based on the Ridley & Jopling logarithmic scale, bacteriological index (BI) was studied on Fite Faraco stained slides. BI observed was 0 (zero) in case of TT and 5+/6+ in cases of LL and its variant Histoid leprosy.
The distribution of 35 cases on clinical leprosy spectrum based on Ridley & Jopling scale revealed maximum cases in polar spectrum: TT - 14 cases (40%), LL and its variant Histoid - 9 cases (3 + 6) (25.72%), borderline (BT + BB + BL) - 10 cases (28.57%) and the least in IL - 2 cases (5.71%). Complete agreement of clinical and histological diagnosis was seen in Histoid Hansen’s (variant of LL) (100%) and IL (100%) followed by LL (66.66%) & TT (57.14%). Least agreement of clinical and histopathological diagnosis was observed in borderline spectrum (BT, BB, BL). Most number of cases which had disparity between clinical and histopathological diagnosis showed histological features of IL (9 cases) due to the absence of granuloma.
TABLE 7. COMPLETE AGREEMENT - CLINICAL DIAGNOSIS & HISTOPATHOLOGY

| TYPES   | CLINICAL CASES | COMPLETE PARITY (HPE) |
|---------|----------------|-----------------------|
|         | NUMBER         | NUMBER                | PERCENTAGE |
| TT      | 14             | 8                     | 57.14%     |
| BT      | 4              | 1                     | 25%        |
| BB      | 2              | 1                     | 50%        |
| BL      | 4              | 2                     | 50%        |
| LL      | 3              | 2                     | 66.66%     |
| HISTOID | 6              | 6                     | 100%       |
| IL      | 2              | 2                     | 100%       |
| TOTAL   | 35             | 22                    | 62.85%     |

In the present study the histopathological characteristics were consistent with the clinical diagnosis in 22 cases out of 35 cases. Complete agreement between clinical diagnosis and histopathology was observed in 62.85% and disagreement was seen in 37.15% cases.
Fig. 1. Correlation of sex and age. Y-axis denotes the number of patients.

Fig. 2. Percentage of various histological types of leprosy in the present study.
Fig. 3. Clinico–Histopathological correlation of various types of leprosy.
Y-axis denotes the number of patients.

Fig. 4. Percentage of complete agreement of histopathological diagnosis with clinical diagnosis and percentage of disagreement.
Fig. 5. Tuberculoid leprosy: A well defined hypopigmented anaesthetic plaque with slightly raised borders.

Fig. 6. Tuberculoid leprosy: Lesion showing pandermal perineurovascular and peri appendageal granulomas and lymphocytes.
Fig. 7. Tuberculoid leprosy: Typical epithelioid cell granuloma.

Fig. 8. Tuberculoid leprosy: Fite-Faraco stain. Bacterial Index (BI) = 0
Fig. 9. Borderline tuberculoid leprosy: A large well defined hypopigmented annular plaque over elbow with satellite lesion.

Fig. 10. Borderline tuberculoid leprosy: Granulomas with lymphocytes follow the neurovascular bundle and infiltrate the hair follicle.
Fig.11. Borderline tuberculoid leprosy: Granulomas surrounded by lymphocytes.

Fig.12. Borderline tuberculoid leprosy: Fite-Faraco stain.
Bacterial Index (BI) = 1+
Fig. 13. Borderline border line leprosy: Wide spread bilateral but asymmetrical hypopigmented anaesthetic patches.
Fig.14. Borderline leprosy: Activated macrophages with sparse lymphocytes with a clear subepidermal grenz zone.

Fig.15. BB leprosy: Fite – Faraco stain. Bacterial Index (BI) = 3 +
Fig. 16. Borderline lepromatous leprosy. Multiple bilateral more or less symmetrical copper coloured shiny anaesthetic patches.
Fig. 17. Borderline lepromatous leprosy: Atrophic epidermis, clear subepidermal grenz zone, collection of macrophages and lymphocytes.

Fig. 18. BL leprosy. Fite-Faraco stain. Bacterial Index (BI) = 4+
LEPROMATOUS LEPROSY

Fig. 19. Lepromatous leprosy: Hypopigmented patches with diffuse skin infiltration - waxy appearance.

Fig. 20. Lepromatous leprosy: Ear lobe infiltration and madarosis.
Fig. 21. Lepromatous leprosy: Atrophic epidermis with collection of foamy macrophages in dermis with clear subepidermal grenz zone.

Fig. 22. LL leprosy. Fite- Faraco stain. Clumps of bacilli in macrophages (Globi). Bacterial Index (BI) = 6+
HISTOID LEPROSY

Fig. 23. Histoid leprosy (variant of LL): Shiny succulent skin coloured nodules over chest and abdomen.

Fig. 24. Numerous, thin, spindle shaped histiocytes arranged in whorls in the dermis with clear subepidermal grenz zone.
Fig. 25. Histoid leprosy. Fite–Faraco stain. Bacterial Index (BI) = 6+.

Fig. 26. Fite-Faraco stain showing lepra bacilli in a magnified view.
INDETERMINATE LEPROSY

Fig. 27. Indeterminate leprosy: Ill defined hypopigmented macule over the face.

Fig. 28. IL leprosy: perineurovascular & periannexal lymphocytic infiltration.
Fig. 29. High power view showing perineural lymphocytic infiltrate in IL leprosy.

DEFORMITIES ASSOCIATED WITH LEPROSY

Fig. 30. Autoamputation & resorption of fingers in a case of lepromatous leprosy.
Fig. 31. Resorption of toes in a case of lepromatous leprosy.

Fig. 32. Small muscle wasting of hand & destruction of little finger in a case of BT Hansen’s.
DISCUSSION

A chronic disease like leprosy needs appropriate classification because of its varied manifestations. The most commonly accepted classification by research workers is that of Ridley & Jopling\(^{43}\) which is primarily based on immunity but has been correlated with clinical, histopathological and bacteriological findings.

Despite having such an accurate classification, there are diversities between the clinical and histopathological features. Clinical spectrum of leprosy in the present study revealed maximum cases in polar spectrum - TT (40%), followed by LL and its variant Histoid (25.72%), borderline (ie) BT, BB, BL (28.57%) and IL (5.71%). Similar predominance of cases in polar spectrum was observed by Kalyani mitra et al\(^{53}\). In the present study the histopathological characteristics were consistent with the clinical diagnosis in 22 cases out of 35 cases (62.85%). Lepromatous cases (including its variant Histoid) seem to present the least problem in classification. Similar highest percentage of agreement between clinical and histopathological diagnosis of lepromatous leprosy cases was also observed by Shenoi & Sidappa\(^{54}\), Pandey & Tailor\(^{55}\), Bhatia et al\(^{56}\), Kalla et al\(^{57}\) and Shanker Naryan et al\(^{58}\) in their respective studies.

Least agreement was seen in cases of borderline spectrum (BT, BB, BL) in this study, which is in concordance with observations recorded by Shenoi & Siddappa\(^{54}\), Nadkarni & Rege\(^{59}\), Bhatia et al\(^{56}\) and Singhi et al\(^{60}\). Maximum discordance (37.15%) between clinical
and histopathological diagnosis was observed in borderline spectrum (BT, BB, BL) cases of present study and the same was also noted by Singhi et al\textsuperscript{60}. Borderline spectrum particularly midborderline leprosy is immunologically the least stable and a variety of clinical lesions of different morphology may be found in the same patient. It is therefore necessary to relate the histological features with the clinical characteristics presented by the particular morphological lesion subjected to biopsy. If this is done carefully, it may be possible to achieve a better correlation of clinical with the histological changes.

Tuberculoid and borderline tuberculoid leprosy often overlap clinically, histologically and immunologically but differ only in degree and the same is true for borderline lepromatous and lepromatous leprosy.

In the present, study, 12 cases (43.28\%) were diagnosed as indeterminate leprosy histologically as against 2 cases (5.71\%) clinically. Nadkarni & Rege\textsuperscript{59} and Kalyani Mitra et al\textsuperscript{53} had also diagnosed a sizeable proportion of the cases as indeterminate histopathologically, who were clinically classified as cases of TT, BT, BL or BL leprosy. Indeterminate lesion is one which cannot be classified within the Ridley & Jopling spectrum due to lack of distinguishing features and this happens more often histologically (due to failure to find a granuloma) than clinically. In the present study, the high percentage of indeterminate leprosy noted histologically in clinical TT, BT & BB groups could have been due to immunological differences in host responses.
The disparity between clinical and histological observation was anticipated because the parameters used for the histopathologic classification are well-defined, precise and also take into account the immunologic response of the tissue, while the clinical classification gives recognition only to the gross appearances of the lesions which is due to the underlying pathological change. Moreover, a sizable proportion of leprosy cases (BT, BB, BL) are in a continuously changing immunological spectrum and histological classification gives a better indication for any recent shift of a case position in the spectrum.

In some early cases, clinical signs and symptoms may precede the presently known characteristic tissue changes, or vice versa. If a biopsy is taken at an early stage, there is likely to be discordance between the clinical and histopathologic observation. As disparity depends upon the lesion biopsied at the time of study, biopsy from the lesion which is morphologically suggestive of clinical diagnosis, serial biopsies from the same lesion, or from paired lesions should be studied for better clinico-pathological correlation.
SUMMARY

From the present study it was observed that:

- The commonest age group affected by leprosy was 31 - 50 years.
- Males are 2 times more commonly affected by leprosy than females. (M : F = 1.9 : 1).
- The most commonest clinically diagnosed spectrum was tuberculoid leprosy (TT).
- The commonest histopathologically diagnosed spectrum was IL, followed by TT & histoid leprosy.
- It was observed that there was complete agreement between clinical diagnosis and histopathological diagnosis in 62.85% cases.
- Disagreement between histopathological diagnosis and clinical diagnosis was observed in 37.15% cases.
- If there is discrepancy between clinical and histopathological classification, both the findings should be reviewed by independent experienced observers.
- In case of confirmed discrepancy, the more advanced findings (i.e., towards the lepromatous pole) should be given greater weightage and the case is to be classified and treated accordingly.
In all cases of leprosy, in order to type the exact spectrum of disease for appropriate treatment, skin biopsy of the lesions with histopathological examination followed by special stain (Fite-Faraco) is recommended.
CONCLUSION

In clinical practice a case of leprosy is to be classified as per clinical criteria. Skin biopsy has to be taken from the most active site of the lesion. This will help in confirmation of diagnosis and classification. If there is discrepancy between clinical and histopathological classification both the findings should be reviewed by independent experienced observers. In case of confirmed discrepancy the more advanced findings (i.e. towards the lepromatous pole) should be given greater weightage and the case is to be classified and treated accordingly. This will prevent inadequate treatment of a particular case.

According to the present WHO guidelines, any patient with bacterial index (BI) of 1+ is classified as multibacillary and hence they are treated with multibacillary regimen (MDT) for 12 months. Hence for all leprosy cases, skin biopsy must be done and histopathological examination done along with Fite-Faraco stain to evaluate the bacterial Index (BI) according to Ridley & Jopling logarithmic scale and treated accordingly.
APPENDIX - I : ( PROFOMA )

Name :        Date :

Age :        Registration Number:

Sex :        Hospital Number:

Occupation :

Address :

COMPLAINTS :

HISTORY OF PRESENT ILLNESS :

PAST HISTORY :

FAMILY HISTORY :

TREATMENT HISTORY :

GENERAL EXAMINATION :

SYSTEMIC EXAMINATION :

DERMATOLOGICAL EXAMINATION : ( As provided by Department Of Dermatology ).

SKIN LESIONS:

PERIPHERAL NERVES :

DEFORMITIES:

CLINICAL DIAGNOSIS :
SKIN BIOPSY:

SITE:

PUNCH BIOPSY SIZE:

FIXATION: 10% Formalin.

GROSS EXAMINATION:

HISTOPATHOLOGICAL EXAMINATION:

SPECIAL STAIN (FITE - FARACO):

Bacterial Index:

HISTOPATHOLOGICAL DIAGNOSIS:
## APPENDIX - II (CLINICAL CRITERIA - RIDLEY & JOPLING)

| S.No | CRITERIA                           | TT              | BT             | BB             | BL             | LL             |
|------|------------------------------------|-----------------|----------------|----------------|----------------|----------------|
| 1.   | Number of lesions                  | 1 - 3 Multiple (3-20) | Multiple       | Multiple       | Generalised    |                |
| 2.   | Size                               | Variable        | Variable       | Variable       | Small          |                |
| 3.   | Margins                            | Well defined    | Mostly well defined | Well - ill defined | Well - ill defined | ill defined |
| 4.   | Surface                            | Very dry        | Dry, rough     | Smooth, soft slightly shiny | Smooth, shiny, soft | Smooth, shiny, soft |
| 5.   | Central healing                    | Anaesthesia in the central healing area | +/- - | +/- - | +/- - | +/- - |
| 6.   | Satellite lesion                   | None            | +/- -          | +/- -          | +/- -          | -              |
| 7.   | Sensation in lesions               | Absent          | Moderately - markedly diminished | Slightly - Moderately diminished | Slightly diminished | Not affected |
| 8.   | Loss of hair over the lesions      | Absent          | Markedly diminished | Moderately diminished | Slightly diminished | Not affected |
| 9.   | Loss of sweat                      | +               | +/- -          | +/- -          | +/- -          | +/- -         |
| S.No | CRITERIA                          | TT   | BT   | BB   | BL   | LL   |
|------|-----------------------------------|------|------|------|------|------|
| 10.  | Symmetry                          | -    | -    | -    | +/-  | +    |
| 11.  | Nerve involvement                 | Nerves close to the skin lesion may be affected | Multiple nerves affected | Multiple nerves affected | Multiple nerves affected | Multiple nerves affected |
| 12.  | Nerve damage                      | Nil  | Common | Common | Common | Common in advanced stages |
| 13.  | Other Systems:                    |      |      |      |      |      |
|      | Nose                              | -    | -    | -    | Mild | Severe |
|      | Larynx                            | -    | -    | -    | +/-  | +    |
|      | Eyes                               | -    | -    | -    | +/-  | +    |
|      | Testis                             | -    | -    | -    | +/-  | +    |
|      | Gynaecomastia                      | -    | -    | -    | -    | +    |
| 14.  | Bacteriological                    | -    | + from lesion | +    | ++  | +++  |
| 15.  | Immunological - Lepromin test     | +++  | +    | -    | -    | -    |
## APPENDIX - III

**HISTOLOGICAL & IMMUNOLOGICAL CHARACTERISTICS OF THE LEPROSY SPECTRUM - RIDLEY & JOPLING CLASSIFICATION**

| S.No | CHARACTERISTICS                              | TT  | BT  | BB  | BL  | LL  |
|------|---------------------------------------------|-----|-----|-----|-----|-----|
| 1.   | Epithelioid cells.                          | ++  | +   | -   | -   | -   |
| 2.   | Langhans giant cells.                       | ++  | +/- | -   | -   | -   |
| 3.   | Macrophages                                 | -   | -   | +/- | ++  | ++  |
| 4.   | Lymphocytes                                 | +++ | ++  | ±   | +/± | ±   |
| 5.   | Clear subepidermal grenz zone               | ±/- | +/- | ++  | ++  | ++  |
| 6.   | Erosion of epidermis                        | ++/-| +/- | -   | -   | -   |
| 7.   | Bacterial Index                             | 0   | 1+  | 2+/3+| 3+/4+| 5+/6+|
| 8.   | Lepromin - Fernandez reaction               | +++ | ++  | +/- | -   | -   |
| 9.   | Lepromin - Mitsuda reaction                 | +++ | ++  | -   | -   | -   |
| 10.  | Immunological stability                     | +++ | +   | -   | +   | +++ |
| 11.  | Erythema nodosum leprosum                   | -   | -   | -   | +/- | ++  |
# APPENDIX - IV (MASTER CHART)

| SERIAL NO: | HPE NO:  | AGE  | SEX | ASSOCIATED ILLNESS | CLINICAL DIAGNOSIS | HISTOPATHOLOGICAL DIAGNOSIS | BACTERIOLOGICAL INDEX (BI)- FITE FARACO STAIN. |
|------------|----------|------|-----|---------------------|---------------------|-----------------------------|-----------------------------------------------|
| 1.         | 404/10   | 50 yrs M | -   | Histoid             | Histoid             | Histoid Hansen’s            | 6+                                           |
| 2.         | 527/10   | 62 yrs F | Hypertension | TT | Indeterminate      |                                  | 0                                            |
| 3.         | 1709/10  | 25 yrs M | -   | LL                  | Borderline lepromatous | 4+                           |                                              |
| 4.         | 2056/10  | 50 yrs M | -   | TT                  | Indeterminate      | 0                           |                                              |
| 5.         | 2085/10  | 18 yrs M | -   | TT                  | Tuberculoid        | 0                           |                                              |
| 6.         | 2093/10  | 16 yrs M | -   | TT                  | Tuberculoid        | 0                           |                                              |
| 7.         | 2426/10  | 65 yrs M | Mesothelioma | TT | Tuberculoid        | 0                           |                                              |
| 8.         | 30/11    | 50 yrs M | D. M | LL                  | Lepromatous leprosy | 5+                          |                                              |
| 9.         | 519/11   | 23 yrs M | -   | BL                  | Borderline Tuberculoid | 1+                          |                                              |
| 10.        | 617/11   | 45 yrs F | -   | BT                  | Indeterminate      | 0                           |                                              |
| SERIAL NO: | HPE NO: | AGE | SEX | ASSOCIATED ILLNESS | CLINICAL DIAGNOSIS | HISTOPATHOLOGICAL DIAGNOSIS | BACTERIOLOGICAL INDEX (BI)- FITE FARACO STAIN. |
|-----------|---------|-----|-----|-------------------|-------------------|-----------------------------|--------------------------------------------|
| 11.       | 624/11  | 55 yrs | M   | -                | BB                | Indeterminate               | 1+                                         |
| 12.       | 899/10  | 50 yrs | F   | Hypertension     | TT                | Tuberculoid                 | 0                                          |
| 13.       | 1362/10 | 55 yrs | M   | Tuberculosis     | TT                | Indeterminate               | 0                                          |
| 14.       | 1364/10 | 32 yrs | F   | -                | BL                | Indeterminate               | 0                                          |
| 15.       | 1426/10 | 35 yrs | M   | -                | Histoid           | Histoid Hansen’s           | 6+                                         |
| 16.       | 1693/10 | 28 yrs | M   | -                | BL                | Borderline Lepromatous      | 4+                                         |
| 17.       | 1663/10 | 15 yrs | F   | -                | IL                | Indeterminate               | 0                                          |
| 18.       | 2539/10 | 31 yrs | F   | -                | BB                | Mid Borderline              | 2+                                         |
| 19.       | 2317/10 | 33 yrs | M   | HIV Positive     | Histoid           | Histoid Hansen’s           | 6+                                         |
| 20.       | 1888/10 | 52 yrs | M   | -                | LL                | Lepromatous Leprosy         | 6+                                         |
| SERIAL NO: | HPE NO: | AGE | SEX | ASSOCIATED ILLNESS | CLINICAL DIAGNOSIS | HISTOPATHOLOGICAL DIAGNOSIS | BACTERIOLOGICAL INDEX (BI)- FITE FARACO STAIN. |
|-----------|---------|-----|-----|--------------------|--------------------|-----------------------------|-----------------------------------------------|
| 21.       | 715/11  | 52 yrs | F   | D.M               | BT                 | Indeterminate               | 1+                                             |
| 22.       | 790/11  | 18 yrs | F   | -                 | TT                 | Tuberculoid                 | 0                                             |
| 23.       | 862/11  | 50 yrs | M   | -                 | IL                 | Indeterminate               | 0                                             |
| 24.       | 911/11  | 25 yrs | F   | -                 | TT                 | Indeterminate               | 0                                             |
| 25.       | 1042/11 | 32 yrs | F   | -                 | Histoid            | Histoid Hansen’s           | 6+                                             |
| 26.       | 1071/11 | 22 yrs | F   | -                 | TT                 | Indeterminate               | 0                                             |
| 27.       | 1211/11 | 48 yrs | M   | -                 | TT                 | Tuberculoid                 | 0                                             |
| 28.       | 1379/11 | 52 yrs | M   | D.M               | BT                 | Borderline Tuberculoid      | 1+                                             |
| 29.       | 1577/11 | 35 yrs | M   | -                 | BT                 | Mid Borderline              | 3+                                             |
| 30.       | 1680/11 | 21 yrs | F   | Lip vitiligo      | TT                 | Indeterminate               | 0                                             |
| SERIAL NO: | HPE NO: | AGE   | SEX | ASSOCIATED ILLNESS | CLINICAL DIAGNOSIS | HISTOPATHOLOGICAL DIAGNOSIS | BACTERIOLOGICAL INDEX (BI)- FITE FARACO STAIN. |
|-----------|---------|-------|-----|-------------------|-------------------|-----------------------------|----------------------------------|
| 31.       | 883/11  | 42 yrs| M   | -                 | Histoid           | Histoid Hansen’s            | 6+                               |
| 32.       | 1834/11 | 50 yrs| M   | -                 | TT                | Tuberculoid                 | 0                                |
| 33.       | 2117/11 | 64 yrs| M   | Hypertension      | BL                | Borderline Lepromatous       | 4+                               |
| 34.       | 2437/11 | 45 yrs| M   | -                 | Histoid           | Histoid Hansen’s            | 6+                               |
| 35.       | 2449/11 | 29 yrs| M   | -                 | TT                | Tuberculoid                 | 0                                |
BIBLIOGRAPHY

1. Jopling WH, McDougall. Definition, Epidemiology and World Distribution Handbook of Leprosy, Fifth edition. CBS Publishers and Distributors 1996: 1.

2. Gupte M.D, Leprosy : Epidemiology, Chapter 65, IADVL Textbook of Dermatology Vol 2, Second Edition. Bhalani Publishing House: 2003, 1543.

3. Lowe J. Comments on the history of leprosy. Leprosy Review 1947; 18: 54 – 63.

4. Jopling WH, McDougall Definition, Epidemiology and World Distribution Handbook of Leprosy, Fifth edition. CBS Publishers and Distributors 1996: 6 – 7.

5. Stephen R Ell, Leprosy in history. In Hastings RC, ed. Leprosy, second edition, Edinburgh: Churchil livingstone, 1994: 3 – 4.

6. John R. Trautman, The history of leprosy. In Hastings RC, ed. Leprosy, second edition, Edinburgh: Churchil livingstone, 1994: 20 – 21.

7. WHO - Report by WHO Regional office of South East Asia 2011.

8. Minister of Health and Family Welfare, Govt of India in written reply to Parliament of India on September 02. 2011.

9. Rao CK. Leprosy elimination in India – so near. Indian journal of leprosy; 77(3) 2005: 207 – 211

10. Dharmendra, Ganapati R. Leprosy in children. Studies on leprosy by Bombay leprosy project; 1976 – 1986: 10- 31.
11. Girdhar BK. Skin to skin transmission of leprosy. Indian Journal of Dermatology, Venereology and Leprology 2005; 71(4): 223 – 225.

12. Jasmita Satapathy, Bikash Ranjan Kar, Job CK. Presence of Mycobacterium leprae in epidermal cells of lepromatous skin and its significance. Indian Journal of Dermatology, Venereology and Leprology 2005; 711(4): 267 – 269.

13. Noordeen SK. The epidemiology of leprosy. In Hastings RC, ed. Leprosy, second edition, Edinburgh: Churchil livingstone, 1994: 29 – 44.

14. Prasad PVS. Epidemiology. In All about leprosy, First edition, Jaypee Brothers, Medical publishers (P) Ltd, New Delhi 2005: 41 – 43.

15. Swain JP, Mishra S, Jena S, Prevalence of leprosy among household contacts of leprosy cases in western Orissa. Indian journal of leprosy 2004; 76 (1): 19 –27.

16. Sehgal VN, Koranne RV, Sharma AK, Misra S, Jain RK. Age-at-onset of Leprosy. Leprosy in India 1982; 54(2): 332 – 337.

17. Noussitou FM, Sansarricq H, Walter J. Leprosy in children. Geneva: World Health Organisation, 1976.

18. Norman G, Joseph GA, Udayasuriyan P, Samuel P & Venugopal M. Leprosy case detection using school children. Leprosy Review 2004; 75: 34 – 39. 26.

19. Kabir Sardana. A Study of Leprosy in Children, From a Tertiary Pediatric Hospital in India. Leprosy Review 2006; 77: 160 – 162.
20. Renu Roy, Kalla G. Pattern of leprosy in Children in Jodhpur. Indian Journal of Leprosy 1997; 69(2): 199 – 200.

21. Virendra N Sehgal, Anup K Chaudhry. Leprosy in Children; A prospective study. International journal of Dermatology 1993; 32: 194 – 197.

22. Badger LF. Epidemiology. In : Cochrane RG, Davey TF. Leprosy in theory and practice. 2nd ed. Bristol: John Wright and Sons; 1964. p.69-97.

23. Rene RP de Vries & Tom HM Ottenhoff. Immunogenetics of Leprosy. In Hastings RC, ed. Leprosy, second edition, Edinburgh: Churchil livingstone, 1994 : 115. 32.

24. R.J.W.Rees, D.B.Young. The microbiology of leprosy . Text book of Leprosy edited by Robert C. Hastings, Diltor V.A. Opromolla. Second Edition. Churchill Livingstone: 1994, 51-52.

25. Alexander J.McAdam, Arlene H.Sharpe. Infectious Diseases. Robbins and Cotran Pathologic Basis Of Disease. Eigth Edition. Kumar, Abbas, Fausto, Aster. Elsevier: 2010, 372.

26. M.D.Gupte. Chapter 65, Leprosy : Epidemiology, IADVL Textbook of Dermatology Vol 2, Second Edition. Bhalani Publishing House :2003,1545-1546.

27. Vinod Kumar Sharma. Chapter 69, Leprosy : Clasification and clinical features, , IADVL Textbook of Dermatology Vol 2, Second Edition. Bhalani Publishing House :2003,1578-1591.

28. Abraham Selvasekar, Joseph Geetha, Kurian Nisha, Manimozhi N, Jesudasan K and Rao PSS. Childhood leprosy in an endemic area. Leprosy review 1999; 70(1): 21 – 27.
29. Jain S, Reddy RG, Osmani SN, Lockwood DNJ, Suneetha S. Childhood leprosy in an urban clinic, Hyderabad, India: clinical presentation and the role of household contacts. Leprosy review 2002; 73: 248 – 253.

30. Pfaltzgraff RE, Bryceson A. Clinical leprosy. In: Hastings RC, Convit J, editors. Leprosy. Edinburgh : Churchill Livingstone ; 1985, 153-162.

31. All India Leprosy Workers Conference. Classification of leprosy adopted by the Indian Association of Leprologists. Lepr India 1955 ; 27: 93-95.

32. Wade HW, Rodriguez JN. Borderline tuberculoid leprosy. Int J Lepr 1940; 8: 307.

33. Gridhar BK. Neuritic leprosy. Ind J Lepr 1996; 68: 35-42.

34. Sujai Suneetha, Arunthathi Sigamani, Nisha Kurian, Chinoy JG Chacko. The development of cutaneous lesions during follow up of patients with primary neuritic leprosy. International Journal of Dermatology 2005; 44: 224 – 229.

35. Wade H.W. ( 1963 ). The histoid variety of lepromatous leprosy. International Journal of Leprosy ; 31 : 129-142.

36. Bhutani L.K, Bedi T.R, Malhotra Y.K, Kandhari K.C, Deo M.G. histoid leprosy in North India. International Journal of Leprosy ; 42:174-81.

37. Virendra N. Sehgal, Ashok Aggarwal, Govind Srivastava, Neelima Sharma, Sonal Sharma. Evolution of histoid leprosy (de novo) in lepromatous (multibacillary) leprosy. International Journal of Dermatology 2005; 44: 576 -578.
38. Latapi F, Zamora A.C. The ‘spotted’ leprosy of Lucio; an introduction to its clinical and histological study. International Journal of Leprosy; 16 : 421-430.

39. Naafs B, Wheate H.W. the time interval between the start of anti-leprosy treatment and the development of reactions in borderline patients. Leprosy Review ; 49 :153-157.

40. Rea T.H., Levan N.E. Erythema nodosum leprosum in a general hospital. Archives of Dermatology ; 111 :1575- 80.

41. Drutz D.J., Gurman R.A. Renal manifestations of leprosy : glomerulonephritis, a complication of erythema nodosum leprosum. American Journal of Tropical Medicine & Hygiene ; 22 :496- 502.

42. WHO : A guide to leprosy control. 2nd Edition. Geneva : World Health Organisation ; 1988. p.40.

43. Ridley DS, Jopling WH. Classification of leprosy accroding to immunity: a five-group ystem. Int J Lepr 1966; 34: 255.

44. Ridley DS. Histological classification and the immunological spectrum of leprosy. World Health Organisation 1974 ; 51: 451.

45. Brittton WJ, Lockwood DNJ. Leprosy. Lancet 2004; 363 : 1209- 1219.

46. Sebastian Lucas. Bacterial Diseases. Lever’s Histopathology of the Skin. Tenth Edition, Edited by David E. Elder, Rosalie Elenitsas, George F. Murphy, Berrett L.Johnson,Jr., Xiaowei Xu. Wolters Kluwer/ Lippincott Williams & Wilkins 2009; 21 :558- 567.
47. Lowy L. Processing of biopsies for leprosy bacilli. J Med Lab Technol 1956; 13: 558.

48. Van Brakel WH, de Soldenhoff R, McDugall AC. The allocation of leprosy patients into paucibacillary and multibacillary groups for multidrug therapy, taking into account the number of body areas affected by skin, or skin and nerve lesions. Lepr Rev 1992; 63: 231.

49. Rea TH, Ridley DS. Lucio’s phenomenon: a comparative histological study. Int J Lepr 1979; 47: 161.

50. Ridley DS, Ridley MJ. The classification of nerves is modified by delayed recognition of M. leprae. Int J Lepr 1986; 54: 596.

51. Hussain R, Lucas SB, Kifayet A, et al. Clinical and histological discrepancies in diagnosis of ENL reactions classified by assessment of acute phase proteins SAA and CRP. Int J Lepr 1995; 63: 222.

52. Ridley DS. Pathogenesis of Leprosy and Related Diseases. London: Wright; 1988.

53. Kalyani Mitra, Surajit Biswas et al. Correlation between clinical and histopathological criteria for the classification of leprosy. Indian J Dermatol 2001; 46 (3): 135-137.

54. Shenoi SD, Siddappa K. Correlation of clinical and histopathologic features in untreated macular lesions of leprosy - a study of 100 cases. Ind J Lepr 1988; 60: 202-06.

55. Pandy AN, Tailor HJ. Clinicohistopathological correlation of leprosy. Ind J Dermatol Venereol Lep 2008; 74: 74-76.
56. Bhatia AS, Katoch K et al. Clinical and histopathological correlation in the classification of leprosy. Ind J Lepr 1993; 61: 433-438.

57. Kalla G, Salodkar A, Kachhawwa D. Clinical and histopathological correlation in leprosy. Ind J Lepr 2000; 68: 184-185.

58. Shakker Narayan NP, Ramu G et al. Correlation of clinical, histological and immunological features across the leprosy spectrum. Ind J Lepr 2001; 73: 329-42.

59. Nadkarni NS, Rege VL. Significance of histopathological classification in leprosy. Ind J Lepr 1999; 7: 325-32.

60. Singhi MK, Kachhawa D, Ghiya BC. A retrospective study of clinic-histological correlation in leprosy. Ind J Pathol Microbiol 2003; 46: 47-48.