Chapter 16
Tropical Diseases in Women

Swetalina Pradhan, Abhisek Mishra, and Kananbala Sahu

16.1 Introduction

With debates, actions, and investments gathering steam around the world, the new year has brought a renewed vigour for the realization of the "Health for Everyone" agenda [1]. To fulfil this vision, the wellbeing of women must be positioned at the forefront of our discourse. Although substantial progress has been made in mitigating maternal mortality, adolescent reproductive health services, and high-quality contraception, the missing link is the tropical disease burden in highly populous portion of the world like South east Asia. To a significant degree, tropical diseases are poverty-borne ailments that are frequently ignored. In addition, some of tropical diseases can result in affecting the patient socially, economically, and psychologically. Studies suggest that these diseases are extremely troublesome for young women because of their effects on the chances of marriage, education, and self-esteem [2, 3].

Billions of people in the world are affected by these neglected tropical diseases. While caused by numerous etiological agents, due to their geographical distribution and their overlooked status, NTDs are classified as a separate category. It must be noted that, while the disease is curable in all its aspects, the challenge in its confrontation is not contained in the biological domain, but in the social and cultural sphere,

S. Pradhan (✉)
Department of Dermatology Venereology and Leprology, All India Institute of Medical Sciences, Patna, Patna, Bihar, India

A. Mishra
Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Bhubaneswar, Bhubaneswar, Odisha, India

K. Sahu
Department of Dermatology Venereology and Leprology, Sri Jagannath Medical College and Hospital, Puri, Odisha, India

R. Sarkar, S. Sinha (eds.), *Skin Diseases in Females*,
https://doi.org/10.1007/978-981-16-6065-8_16

which, after all, affects the world's poorest regions, a reality which demonstrates its relationship with social disparities. By categorizing NTD as a group can facilitate their control and care in a coordinated and integrated way [4–6].

WHO has estimated that half a billion of people are suffering from tropical diseases in developing countries which include schistosomiasis, trypanosomiasis, chagas disease, leishmaniasis, and leprosy.

The skin-related tropical diseases include tuberculosis, cutaneous leishmaniasis, post-kala-azar dermal leishmaniasis, leprosy, lymphatic filariasis, mycetoma, onchocerciasis, scabies, and yaws [7–9].

16.2 Leprosy

16.2.1 Epidemiology

Leprosy is the earliest recognized human illness. As per literature around 600 BC, the first recorded documents from India had documented genuine leprosy cases. This neglected tropical disease is caused by Mycobacterium leprae. The current prevalence is estimated as 0.2/10,000 population globally as per World Health Organization. Globally, India accounts for 60 pc of all new cases reported annually, with approximately a million new cases between 2016 and 2020, according to the National Leprosy Eradication Programme (NLEP). In India, there are 44,877 new cases reported in 2019 which are females and it is highest in the world [10–13].

16.2.2 Leprosy Transmission

The incubation period may vary from months up to 5 years. The bacilli are transmitted from one individual to other through aerosol inhalation. The main route of transmission is the nasal mucosa [14–16]. Less commonly, transmission can occur by skin erosions [16, 17]. It can be also transmitted through blood, placenta, breast milk, and insect bites [18–20].

16.2.2.1 Role of Women in Leprosy Transmission

Female is closely associated with her children and all the family members. When female becomes an index in the family, chance of transmitting infection to other family members including her children is much more. The child of leprosy affected mother will transmit the infection to community once infected with lepra bacillus. Hence a female affected with leprosy not only increases the disease burden in the family but also in the community.

16.2.2.2 Leprosy Spectrum

Leprosy mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract and the eyes. The most widely accepted Ridley and Jopling classification (1966) has divided leprosy into five groups: tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT), mid-borderline leprosy (BB), borderline lepromatous leprosy (BL), and lepromatous leprosy (LL) [21]. Later, the leprosy was reclassified with the addition of pure neuritic leprosy and indeterminate leprosy. TT, BT, and indeterminate leprosy are considered PB leprosy, and BB, BL, and LL Hansen's are classified as MB leprosy. Pure neuritic leprosy can fall on both spectrums depending on the number of nerves involved and the bacillary load. The cellular immunity goes down as one moves from the tuberculoid pole to lepromatous pole. The number of skin lesions increase, and size of skin lesions gradually decreases from TT pole to LL pole. Asymmetrical distribution of skin lesions is found in tuberculoid pole and as one downgrades to lepromatous pole the lesions become symmetrically distributed. Due to good immunity, the nerve trunks are usually enlarged in tuberculoid forms of leprosy. Due to damage to the nerve trunks and feeder nerves along with the denervation of skin appendages in tuberculoid forms the skin lesions look dry because of absence of sweating with relative loss of hair on the affected areas [21].

Indeterminate leprosy is first sign in 20–80% leprosy patients and usually presents as hypopigmented patch with loss of tactile or thermal sensation [22].

The lesion of tuberculoid leprosy (TT) is characterized by anaesthetic hypopigmented plaques with raised border that slopes inward (Fig. 16.1). The surface of the plaque looks dry with loss of hair and absence of sweating, and the feeder nerve may be thickened. Borderline tuberculoid leprosy (BT) is characterized by hypopigmented anaesthetic patch with regular to irregular margin. Pseudopodial extensions from margin and satellite lesions are characteristically present in BT patches (Fig. 16.2). The superficial peripheral nerves are likely to be enlarged in an asymmetrical pattern [23].

Mid-borderline leprosy (BB) is an unstable form and it exhibits characteristics of TT and LL pole. The skin lesions are asymmetrically distributed and there is moderate nerve impairment. Annular lesions with a well-defined, punched-out inner edge and an ill-defined outer-sloping edge that give the appearance of Swiss cheese/foveal spot form the classical morphology of BB. Borderline Lepromatous form (BL) is characterized by slightly infiltrated, round to oval macules of 2–3 cm in diameter that are distributed in asymmetrical patterns with areas of normal skin in between. However, papules, nodules, and plaques may develop with slope-like margins merging into the surrounding skin as the disease progresses. Peripheral nerve involvement is asymmetrical [23, 24].

There occurs continuous bacillary multiplication and systemic spread in LL due to absence of cellular immunity. In lepromatous leprosy (LL), the skin lesions tend to be multiple, symmetric and located in colder areas of body. The types of skin lesion include hypopigmented macules, erythematous to brownish nodules and papules, and diffuse and infiltrated skin (Fig. 16.3). Compared to BL the macules in LL

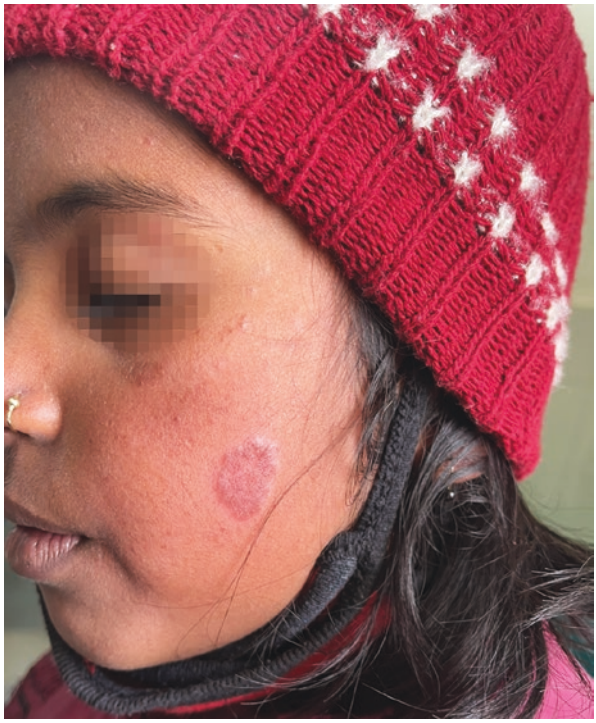

Fig. 16.1 Well-defined erythematous plaque over face with hypoesthesia suggestive of tuberculoid leprosy

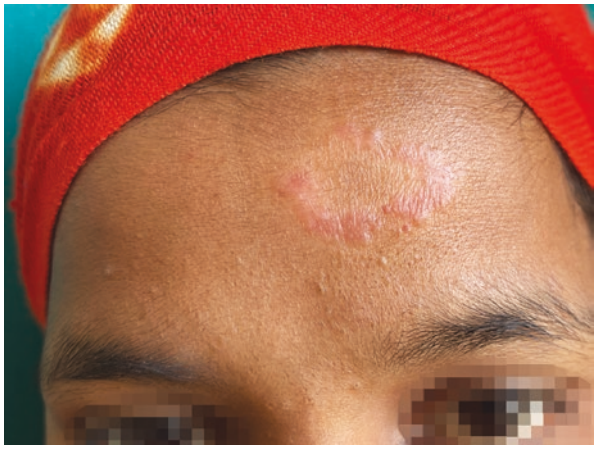

Fig. 16.2 Hypopigmented hypoanaesthetic patch with regular to irregular border with infiltrations at periphery in a female suggestive of borderline tuberculoid leprosy

are smaller, have indistinct edge, shiny surface, and are symmetrical in distribution. The patients of diffuse LL have shiny and thickened skin. The nodular is the advanced stage of LL characterized by presence of nodules over the ear lobes, face, trunk, joints, and extremities. Oedema of legs and feet is commonly found in LL patients. In the advanced stages of LL, the patient has a peculiar appearance

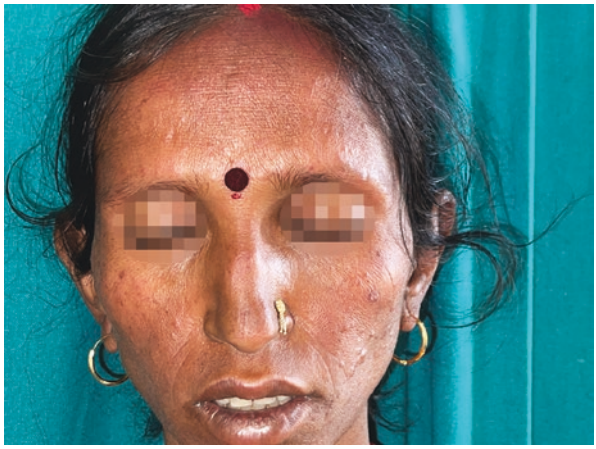

Fig. 16.3 Multiple papules and nodules over face with bilateral madarosis in a lepromatous leprosy female patient

(leonine facies) and madarosis (loss of lateral one-third of eyebrow hairs and eyelashes). Mucous membranes, eyes, bones, joints, lymph nodes, blood vessels, upper airways, teeth, and internal organs may be affected. The nerve trunks are rarely involved. Dermal nerve twigs are infiltrated by bacilli which give rise to symmetrical loss of sensation leading to glove and stocking type anaesthesia [21–24].

16.2.3 Pure Neuritic Leprosy

Pure neuritic leprosy presents with hypoesthesia/anaesthesia in absence of any skin lesions of leprosy but with involvement of nerves supplying the affected areas [25, 26]. It can be mononeuritic and polyneuritic basing upon the number of nerves involved [26].

16.2.4 Histoid Leprosy

Histoid leprosy is a rare variant of lepromatous leprosy characterized by painless discrete, smooth, dome-shaped skin coloured to yellow brown papules or subcutaneous nodules with apparently normal skin surrounding it. Lesions are usually found on the posterior and lateral aspects of the arms, buttocks, thighs, dorsum of the hands, lower part of the back, and over the bony prominences, especially over elbows and knees [27]. The acid-fast bacilli in histoid lesions are found in clusters, singles or tightly packed in macrophages in slit skin smear and appear longer with tapering ends compared to the ordinary lepra bacilli [27].

16.2.5 Lucio Leprosy

Lucio leprosy (LuLp) otherwise called lepra bonita or beautiful leprosy is a pure, primitive, and diffuse form of LL, commonly seen in Mexico and Costa Rica. The skin appears infiltrated waxy and shiny, so that natural wrinkles are obliterated and the person's face appears moist and myxoedematous complexion imparting healthy and beautiful appearance [28].

16.2.6 Lepra Reaction

Leprosy reactions occur due to alteration in the immune balance between the host and *M. leprae*. Such reactions are acute episodes that primarily affect the skin, nerves, mucous membranes, and other sites and change the uneventful course of the chronic disease. They can occur before institution of treatment, during treatment or after treatment. They are classified into two types: type 1 reaction and type 2 reaction [29, 30].

16.2.6.1 Type 1 Lepra Reaction

Type 1 Lepra reaction is a delayed hypersensitivity reaction. It mostly occurs in borderline leprosy. Female gender carries a higher risk than men [31]. This could be due to hormonal fluctuations [32]. Pregnancy and delivery carry an increased risk which is found to be the highest in the first 6 months after delivery (post-partum). These reactions are related to the cellular immune response against mycobacterial antigens and can result in improvement (reversal reaction, pseudo-exacerbation reaction, or upgrading reaction) or worsening (downgrading reaction) of the disease. In majority of situations, the downgrading of untreated patients from tuberculoid forms to lepromatous form occurs during type 1 reaction. In Type 1 reaction, there may be appearance of new lesion and the pre-existing lesions may become erythematous, oedematous, and hyperaesthetic (Fig. 16.4). In severe cases, the skin lesions may get ulcerated. Acral oedema is usually found in type 1 reaction. Neuritis is a prominent feature of type 1 reaction which is the major cause of disability and deformity in a leprosy patient [29, 30].

16.2.6.2 Type 2 Lepra Reaction

Type 2 reaction or erythema nodosum leprosum (ENL) is a type 3 hypersensitivity reaction occurring mostly in LL and sometimes in BL leprosy patients having high bacillary load. It occurs due to body's reaction to release of substances by

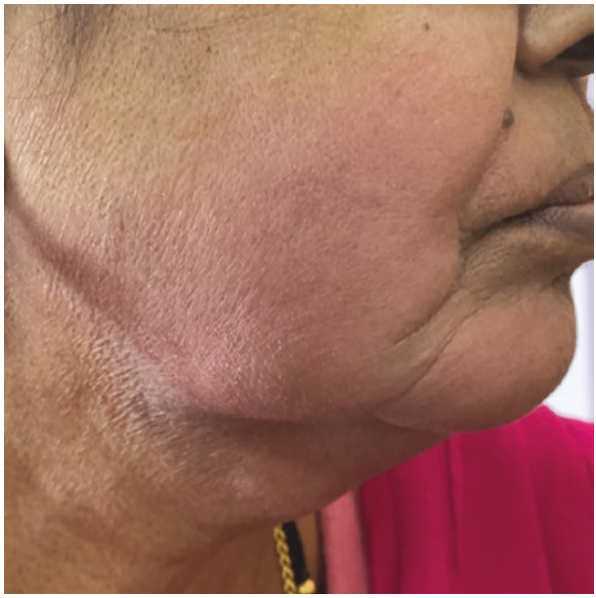

Fig. 16.4 Borderline tuberculoid leprosy with erythema and oedema on the plaque because of type 1 lepra reaction

destruction of bacilli and deposition of immune complex in different parts of body. Commonly ENL presents as sudden onset of erythematous, evanescent, tender nodules in crops over body associated with constitutional symptoms like fever, malaise, myalgia, oedema, and arthralgia. Other morphological presentations include papules, plaques, bullae, erythema multiforme like target lesions, PLEVA like lesions, ulcerated form or ENL necroticans (Fig. 16.5). As immune complex deposition occurs almost in all organs, ENL can present with varied systemic manifestations like lymphadenitis, iridocyclitis, uveitis, hepatosplenomegaly, rhinitis, laryngitis, epididymo-orchitis, myositis, arthritis, painful dactylitis, synovitis, nephritis, proteinuria, and renal failure. Neuritis is less common T2R as compared to T1R and in some patients of severe T2R neuritis may be found [29, 30].

16.2.7 Lazarine Leprosy

Lazarine leprosy is otherwise called ulcerating type 1 reaction which occurs in BT leprosy patients due to exaggerated delayed type hypersensitivity reaction. There occurs spontaneous ulceration of skin lesions [33]. Systemic corticosteroids are necessary for the treatment in addition to anti-leprosy drugs.

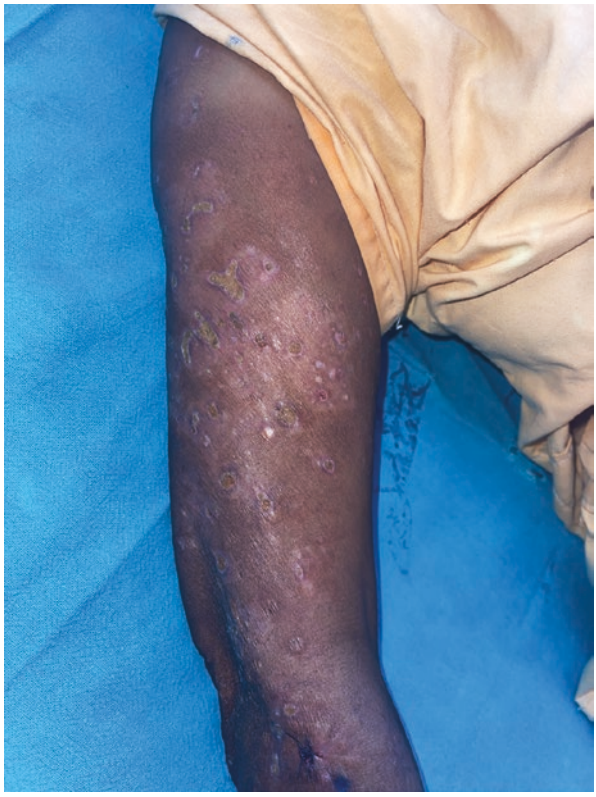

Fig. 16.5 Lepromatous leprosy female patient with necrotic erythema nodosum leprosum and healed scars

16.2.8 Lucio Phenomenon

Lucio phenomenon is a vasculo-necrotic reaction found in untreated or inadequately treated, well-established, diffuse, nonnodular form of leprosy known as Lucio leprosy [34, 35]. It also has been reported in the classic nodular form of lepromatous and borderline leprosy [36]. It usually starts as painful purpuric lesions which progress into well-defined, multi-angulated, jagged ulcers with a geometric shape in descending order of frequency, i.e. the feet, legs, hands, forearms, thighs, arms, and rarely, the trunk and face. Healing of ulcers occurs in about 2–8 weeks, leaving curvilinear jagged atrophic hypochromic scars with a surrounding halo of hyperpigmentation. There is no fever, constitutional symptoms, and systemic involvement and neuritis [37]. It is believed that LP occurs due to uninhibited multiplication of lepra bacilli resulting in diffuse infiltration of the integument in an anergic background and enhanced exposure of mycobacterial antigen to circulating antibodies, resulting in vasculitis. Lucio phenomenon may mimic vasculo-necrotic erythema nodosum leprosum. In ENL, presence of constitutional symptoms with neuritis differentiates it from Lucio phenomenon. Lucio phenomenon requires no specific treatment other than multibacillary multidrug therapy for leprosy. Whereas, necrotic ENL responds to systemic corticosteroid and thalidomide [37].

16.2.9 Leprosy and Pregnancy

Leprosy and pregnancy shape the course of one another. The change in body hormones during pregnancy led to change in immune status of the patient that may cause first appearance of leprosy, reactivation of the disease and relapse in cured patients which is more marked in the third trimester of pregnancy [38, 39]. Leprosy reactions occur during pregnancy because of the alteration in cell-mediated and humoral immunity [39]. A type 1 reaction (reversal reaction) occurs during postpartum phase, whereas a type 2 reaction (erythema nodosum leprosum) peaks during late pregnancy. Both forms of reaction can continue into lactation phase for a long time. Therefore, both leprosy and lepra reaction during pregnancy and postpartum time along with their sequelae make the infected women more vulnerable to several complications [23].

16.2.10 Effect of Leprosy on Fertility Status and Menstrual Cycle

There have been conflicting findings regarding gonadal involvement in female leprosy patients from several parts of the world. The Indian study found that primary infertility rate is higher in females affected with leprosy compared to the India's general population [40, 41]. Fifty four percent of female patients with leprosy were sterile in the study of Fleger et al., and the females reported gross menstrual abnormalities in the study of King and Marks [42, 43]. Bogush concluded in his study that in patients with leprosy, menstrual dysfunction could be avoided by the early start of therapy [44]. The Indian study by Khanna et al. found a significantly larger number of female patients with MB leprosy had irregular periods postdating the onset of leprosy than patients with PB leprosy [45]. The same study also found that gonadotropic hormone levels were elevated in slightly more MB leprosy patients relative to PB leprosy patients, and the mean levels of these hormones demonstrated a rising pattern from controls to PB patients to MB leprosy patients.

16.2.11 Diagnosis of Leprosy

The diagnosis of leprosy is mostly clinical and based upon the WHO criteria.

a. Hypopigmented hypoanaesthetic/anaesthetic skin lesions.
b. Peripheral nerves enlarged/or tender.
c. Slit skin smear for AFB should be positive.

Only one criterion is required for diagnosis of leprosy.

16.2.12 Investigations

16.2.12.1 Slit Skin Smear and Ziehl–Neelsen Staining

Slit skin smear is a simple technique which is very useful in diagnosis and prognosis of disease. Initially smears were obtained from multiple sites which included both ear lobes, both cheeks, forehead, chin, both buttocks, and additional six suspicious sites. Presently four sites are chosen for the test: (1) right earlobe, (2) forehead, (3) chin, and (4) left buttock in men and left upper thigh in women [46]. However, the smear can be taken from other active or doubtful lesions in PB leprosy. The BI is calculated by adding the values from all the skin sites examined (usually four) and then dividing the total by the number of sites examined (Table 16.1). The BI in TT is usually 0, BT 1+ to 2+, 2+ to 4+ in BB, more than 4+ to 5+ in BL, and 6+ in LL.

16.2.12.2 Morphological Index (MI)

Morphological index represents percentage of live bacilli. It is calculated as percentage of solid stained bacilli after examining 200 bacilli lying singly. The live bacilli/solid staining bacilli are uniformly stained, rounded at both the ends and have length of five times the width and parallel sides.

16.2.12.3 Histopathology of Skin and Nerve

In case of indeterminate leprosy, middle of the lesion should be considered for biopsy [47]. When multiple lesions are present, the most active lesion should be identified for biopsy. Always choose the active infiltrated edge for biopsy for better results. In the scenario of multiple skin lesions with different morphology, more than one biopsy is required for proper evaluation. Histopathology of nerve is more useful in diagnosis of pure neuritic Hansen. Histopathology of various types of leprosy and reactional states has been elaborated in Table 16.2.

Table 16.1 Calculation of bacillary index in slit skin smear

Examination by oil immersion field	Number of AFB	Bacillary Index (BI)
One field	>1000 bacilli in every field	6+
One field	100–1000 bacilli in every field	5+
One field	10–100 bacilli in every field	4+
One field	1–10 bacilli in every field	3+
10 fields	1–10 bacilli/10 fields	2+
100 fields	1–10 bacilli/100 fields	1+
100 fields	No bacilli/100 fields	0

Table 16.2 Histopathological findings of skin lesions of leprosy

Leprosy spectrum	Histopathology of skin lesions
Indeterminate leprosy	Early stage: occasional AFB in the non-inflamed nerve, erector pilorum, or subepidermal zone Late stage: lymphocyte and nonspecific histiocytic infiltration in the perineurium or nerve parenchyma suggestive of neural inflammation along with schwann cell proliferation
Tuberculoid leprosy	The tuberculoid granuloma is compact and well organized comprised of epithelioid cells surrounded by a mantle of lymphocytes. Langhans giant cells are found. The granuloma usually effaces the epidermis obliterating the subepidermal clear zone. The nerves damaged and replaced by the infiltrating epithelioid cells. AFB are usually not detected
Borderline tuberculoid leprosy	The epithelioid cell granuloma shows some admixture of macrophages and lymphocytes, relatively loose and follows the neurovascular bundles in branching pattern. Lymphocytes are relatively less in number compared to TT and the giant cells are often foreign body type. Neural infiltration with few AFB is seen (BI 1+ to 2+). Clear SEZ is always found
Mid-borderline leprosy	Granuloma of mid-borderline is not compact and shows almost equal numbers of epithelioid cells and macrophages. Lymphocytes are scattered and lesser in number. Clear SEZ is seen. Nerves are not completely destroyed and show cut-onion appearance on transverse section [48]. AFB may be frequent (BI 2+ to 4+)
Borderline lepromatous leprosy	Macrophage granuloma is found with isolated clumps of epithelioid cells. Lymphocytes are sparse and scattered. Nerves are not destroyed completely unlike TT and BT. Concentric perineural cell proliferation gives a cut-onion appearance. SEZ is free. Bacilli are always plenty
Lepromatous leprosy	Macrophage granuloma is a distinct feature of lepromatous leprosy (LL). Epidermis is thinned out and flattened due to expansion of granuloma. There is a clear subepidermal zone demarcating the granuloma and epidermis. Lymphocytes are rarely present. Histiocytes are abundant and have foamy appearance. The foamy macrophages contain plenty of AFB (BI 4–6)
Histoid leprosy	Epidermal atrophy is found because of dermal expansion of the underlying leproma and a grenz zone located immediately below the epidermis. Granuloma consists of fusiform histiocytes arranged in a whorled, criss-cross, or storiform pattern. The histiocytes resemble fibroblasts. Within the histiocytes, an abundance of acid-fast bacilli can be seen
Type 1 lepra reaction	There is increased infiltration of lymphocytes, macrophages, and neutrophils. Granulomas are disorganized due to increase oedema in dermis. The foreign body giant cells number is more and the Langhans giant cells also become larger and increased in number [49]. There is erosion of the epidermis with necrosis in case of severe type 1 reaction [50]
Type 2 lepra reaction	There is dense neutrophilic infiltration of dermis and granulomas. Vasculitis may cause full necrosis of the epidermis and erosion. Vasculitis is though not universally seen [51]
Lucio phenomenon	There is proliferation of endothelial cells in medium-sized vessels of mid-dermis along with colonization of the endothelial cells by acid-fast bacilli. In addition, neutrophilic infiltration, ischemic epidermal necrosis, and necrotizing vasculitis of the small vessels of the superficial dermis are seen [52]

16.2.12.4 FNAC of Skin Lesions and Nerve

FNAC nerve is more useful in diagnosis of pure neuritic leprosy and the cytological features can help in identifying the leprosy spectrum like histopathology. However, it is an invasive procedure and requires skill and expertise of an individual.

16.2.13 Advanced Diagnostic Methods

16.2.13.1 Serological Assay

Antibody-Based Immunological Tests

a. Phenolic glycolipid-1 (PGL-1) antibody assay ELISA (kit format): PGL-1 is a major glycolipid cell wall antigen of the bacterium. Hence PGL-1 assay can be used as a confirmatory marker for disease, as a predictor of disease outcome, an indicator of nerve damage and exacerbation and as a tool for preclinical intervention. PGL-1 antibody levels have been found to correlate with the bacterial load and the levels decline after adequate chemotherapy and hence can be useful to monitor leprosy patients under treatment [53].
b. MLflow test: ML flow test is an immunochromatographic assay which detects *M. leprae* specific anti PGL-1 IgM antibodies. It is easy to perform and can be used at primary health care centres [54].
c. 35-kD-based serology: 35 kDa protein is found in the membrane of M. leprae. 35 kDa assay using monoclonal antibody (MLO4) has been utilized for serological studies. The number of anaesthetic patches in patients found to positively correlate with the level of antibody. Also, the antibody levels correlate positively with the number of nerves involved in primary neuritic leprosy. After chemotherapy, the levels decline suggesting the role in monitoring the leprosy patients [55, 56].
d. LID-1 Assay (designated leprosy IDRI diagnostic): Two fusion proteins ML0405 and ML2331 (LID-1 designated leprosy IDRI diagnostic) have been tested for their antibody reactivity. The test was found to be more sensitive than PGL-1. Antibody level to LID-1 showed more rapid decline after MDT regimen compared to that of PGL-1 antibody level [57–59].

Cytokine Profile

Studies on cytokines have revealed involvement of Th1 cytokines like interleukin-2 and IFN-γ in TT leprosy and Th2 type cytokine like IL-4, IL-5, and IL-10 in LL patients. Th-1 and Th-2 cytokines are involved in type 1 and type 2 lepra reaction, respectively [60].

16.2.14 Polymerase Chain Reaction (PCR)

PCR is able to detect *M. leprae* DNA from even 10–30 fg of *M. leprae* component which is equivalent to 2.8–8.3 bacilli [59]. The samples for PCR could be taken from skin biopsy, skin smears, nerves, oral or nasal swabs, blood, ocular lesions,

and urine. PCR is helpful in early identification of difficult to diagnose cases. By this method, pure neural leprosy, indeterminate leprosy, and household contacts are detected early by PCR. PCR is confirmatory in cases of clinical and histopathological dispute [61].

16.2.14.1 Nerve Conduction Study

Electrophysiological study or NCS can detect changes in both sensory and motor components. For the motor nerves, parameters like distal motor latency, compound muscle action potential, and conduction velocity are recorded while for sensory nerves sensory nerve action potential (SNAP), onset latency, and conduction velocity are recorded. In the preclinical stage of the leprosy, where there are no signs and symptoms suggestive of nerve damage NCS can detect changes in sensory and motor fibres [62, 63].

16.2.15 High Resolution Ultrasonography (HRUS)

High-resolution ultrasonography is a non-invasive modality which can study the structural changes in nerve sites from which histopathology is difficult to obtain. Peripheral nerves can be visualized with reasonable precision by USG with broadband frequency of 10–14 MHz, CD frequency of 6–13 MHz and linear array transducer. One can idea regarding location and degree of nerve enlargement, nerve morphological alterations, echo texture, and fascicular pattern by HRUS [64]. Colour Doppler USG is being done to look for absence or presence of blood flow signals in the perineural plexus and interfascicular vessels of nerve trunks. Normal healthy nerve is hypo-vascular with neither the fascicles nor the epineurium showing CD signals. Detection of blood flow signal in colour doppler USG suggests hypervascularity and ongoing neural inflammation and nerve damage [64].

16.2.16 Management of Leprosy

Multidrug therapy (MDT) instituted by the Word Health Organization in 1981 has been considered the gold standard treatment for leprosy. The regimen has undergone different modifications regarding duration of therapy and doses. However, the currently recommended duration is 6 months for PB and 12 months for MB (Tables 16.3 and 16.4).

Table 16.3 Multidrug therapy (MDT) regime in leprosy

Feature	MB[a]	PB
Skin lesions	>5	1–5
Smear for AFB	Positive	Negative
MDT (adults)	Rifampicin: 600 mg MS Clofazimine: 300 mg MS; 50 mg daily Dapsone: 100 mg daily	Same as MB
MDT (children)	10–14 years Rifampicin 450 mg MS Clofazimine 150 mg MS, 50 mg daily Dapsone 50 mg daily <10 years or <40 kg Rifampicin 10 mg/kg MS Clofazimine 6 mg/kg MS and 1 mg/kg daily Dapsone 2 mg/kg daily	Same as MB
Duration	12 months course completed in 18 months period	6 months course completed in 9 months period

MB multibacillary, *PB* paucibacillary, *MDT* multidrug therapy, *MS* monthly supervised, *AFB* acid-fast bacilli
[a]As per NLEP 2009: patient with more than one thickened nerve is also classified as MB

Table 16.4 Treatment of Leprosy in special situation

Sl. No.	Clinical scenarios	Treatment modification/adjustment
1.	Co-existent tuberculosis and leprosy	Start treatment of tuberculosis first -Make the necessary additions or adjustments in the anti-leprosy treatment such that during the treatment course, patient is on at least three anti-leprosy drugs in case of MB leprosy and at least two anti-leprosy drugs in case of PB leprosy
2.	Non-acceptance of clofazimine	Ofloxacin 400 mg daily, or minocycline 100 mg daily as substitutes for clofazimine or Monthly ROM for 24 months
3.	Pregnancy	First time diagnosed: Start MDT irrespective of the trimester Already on MDT: continue MDT
4.	Severe dapsone toxicity	Stop dapsone immediately For MB leprosy, no further modification is required For PB leprosy, clofazimine may be substituted for dapsone for a period of 6 months

16.2.17 Treatment of Type 1 Lepra Reaction

Mild reaction should be treated with analgesics, such as acetylsalicylic acid or paracetamol. If there is nerve involvement, type 1 reactions should be treated with analgesics and corticosteroids, such as oral prednisolone.

16.2.17.1 Dose of Steroid in T1R Recommended as per WHO for the Field Purpose

Dose of prednisolone	Weeks of treatment
40 mg daily	1st and 2nd week
30 mg daily	3rd and 4th week
20 mg daily	5th and 6th week
15 mg daily	7th and 8th week
10 mg daily	9th and 10th week
5 mg daily	11th and 12th week

16.2.17.2 Dose of Steroid in T1R at Referral Centres

Start dose: 40–60 mg daily (up to a maximum of 1 mg/kg).

Tapering: reduced by 5 mg weekly or fortnightly after improvement of skin lesions and nerve tenderness subsides.

Maintenance dose: 15–20 mg for several months, then reduced by 5 mg for every 2–4 months.

Duration: BT—4–9 months, BB—6–12 months, BL—6–24 months.

16.2.18 Treatment of Type 2 Lepra Reaction

16.2.18.1 Severity Grading of T2R (Table 16.5)

Mild T2R
Only few ENL lesions with no other organ involvement
Severe T2R

1. High fever, body pain, myalgia
2. Extensive ENL with or without pustular/necrotic lesion

Table 16.5 Treatment of T2R

Type 2 reaction	Mild reaction	Severe reaction
First episode	1. Aspirin 2. Cholchicine 3. Paracetamol	Option 1: prednisolone (1 mg/kg BW till clinical improvement, then taper by 5–10 mg over 6–8 weeks. Maintenance dose of 20–40 mg needed for several weeks to prevent recurrence Or prednisolone with clofazimine-not responding corticosteroid or whom corticosteroids are contraindicated Option 2: Thalidomide 200 mg BD for 3–7 days or till reaction is under control, followed by tapering within 3–4 weeks or slow tapering
Recurrent ENL Or Chronic ENL		Combination treatment is preferred Option 1: clofazimine + prednisolone Option 2: Thalidomide + prednisolone

3. Pain/tenderness of one or more nerve or loss of function
4. Recent NFI (nerve function impairment)
5. Painful swelling of testes (orchitis)
6. Marked arthritis or lymphadenitis

16.2.18.2 Deformities in Leprosy in Females

Deformities in leprosy occur due to neuritis and inadequate care of anaesthetic parts. Females outnumbered males in having particular deformities in a study from Southeast Nigeria and the difference time of diagnosis from onset of problem was double in females as compared to males [65]. In developing countries, a significant proportion of females are homemaker and engaged in cooking and other domestic services and hence are vulnerable to repeated trauma, ulceration, and other grave deformities.

16.2.18.3 WHO Grading of Deformities in Leprosy [66]

Hands and feet

Grade 0 No anaesthesia, no visible deformity or damage

Grade 1 Anaesthesia present, but no visible deformity or damage

Grade 2 Visible deformity or damage present

Eyes

Grade 0 No eye problem due to leprosy; no evidence of visual loss

Grade 1 Eye problems due to leprosy present, but vision not severely affected as a result (vision: 6/60 or better; can count fingers at 6 metres).

Grade 2 Severe visual impairment (vision worse than 6/60; inability to count fingers at 6 metres); also includes lagophthalmos, iridocyclitis, and corneal opacities.

16.2.18.4 Leprosy and Stigma in Female

Stigma may be defined as "a social process, which is experienced or anticipated, characterized by exclusion, rejection, blame or devaluation that results from experience, perception or reasonable anticipation of an adverse social judgment about a person or group" [67]. From 1988 to 1997, a study of leprosy patients in South East Nigeria showed that the condition affected women more than men. Not only in the medical context, but even in socio cultural and economic ways, infections can have a different effect on women. Gender disparities will play a much larger part in labelling women as offenders because of their effects on body appearance and the social shame associated with them [68]. A survey in India showed that 18% of women surveyed mask their symptoms, and another Indian research found that women appear more than men to mask the signs and complications [69]. In sub-Saharan Africa, women afflicted by leprosy mask their health-seeking behaviour and are

unable to speak about their disease and are expecting its fearful implications for marriage and sexual life. Owing to the lack of schooling, knowledge, and value in the home, women with disease are forced to conceal their symptoms as long as possible in developing countries such as India. The responsibility of household care and home isolation also contributes to late detection and treatment of leprosy in women. For women failing to carry out domestic tasks, childcare, active sexual life because of leprosy, have been abandoned by husbands and companions. In addition, leprosy deformities and disability make the condition noticeable, adding much to women's social isolation. This leads to social breakdown, psychiatric disorder, and a feeling of being deprived of their basic characteristics as a capable female afflicted by leprosy.

16.3 Cutaneous Tuberculosis

Tuberculosis (TB) is a major public health issue all over the world with Southeast Asia being burdened with 10.4 million (45%) infective Tuberculosis cases [70]. In India, tuberculosis accounts for 0.1–0.9% of the total dermatology out-patients in India [71]. The estimated extrapulmonary tuberculosis is about 2% and it is about 14% of all tuberculosis cases in different study [72] (Table 16.6).

16.3.1 Tuberculosis Verrucosa Cutis (TVC)

TVC also known as warty TB, is the most common form of exogenous TB in adult. It results from direct inoculation of *M. tuberculosis* in individuals with moderate to high immunity. The lesion appears as painless, erythematous, isolated papule or

Table 16.6 Classification of cutaneous tuberculosis [73, 74]

Based on route of infection	
1. Exogenous route	Tuberculous chancre, LV, TVC
2. Endogenous route	
Contiguous spread	Scrofuloderma, Orificial TB
Hematogenous spread	Acute miliary TB, metastatic tuberculous Abscess (gummatous TB), tuberculids and LV
Lymphatic spread	LV
3. Tuberculids	
Micropapular	Lichen scrofulosorum
Papular	Papulonecrotic tuberculid
Nodular	Erythema induratum
Based on bacillary load	
1. Multibacillary	Tuberculous chancre, Scrofuloderma, Orificial TB, acute miliary TB, gummatous TB
2. Paucibacillary	TVC, LV, and tuberculids

LV Lupus vulgaris, *TVC* tuberculosis verrucose cutis, *TB* tuberculosis

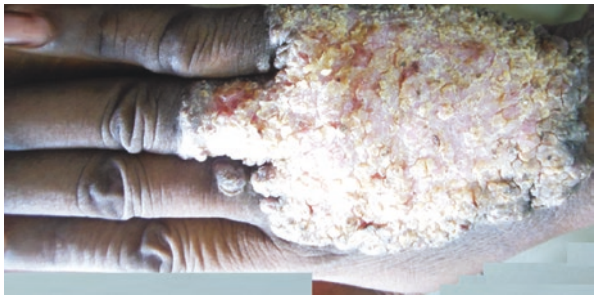

Fig. 16.6 Tuberculosis verrucosa cutis presenting as verrucous plaque on dorsum of hand

plaque with verrucous surface (Fig. 16.6). Rarely multiple lesions can be seen. There is always a predilection for trauma prone sites like extremity. The plaque is surrounded by a purplish inflammatory halo that evolves to asymptomatic verrucous plaques, with 1–5 cm in diameter [75]. The verrucous plaque may enlarge through peripheral extensions, accompanied by central atrophy [76]. Rarely ulceration may occur with extrusion of pus from the fissures or clefts [77]. Lymphadenopathy is rarely found. Sometimes secondary bacterial infection and elephantiasis can occur in case of extensive lesions affecting extremities [76].

16.3.2 Lupus Vulgaris (LV)

Lupus vulgaris is the most common form of cutaneous tuberculosis (CTB) all over the world. Women are commonly affected than men [78]. It occurs in patients with high degree of immunity against *Mycobacterium tuberculosis*. Inoculation of bacillus occurs endogenously by lymphohematogenous spread or by continuity, and rarely via exogenous routes like draining sinus of scrofuloderma, scar of TVC, scrofuloderma, or BCG vaccination [79]. Morphologically LV presents a well-demarcated skin coloured to erythematous, nodule or plaque which rarely ulcerate. The nodular lesion evolves slowly with occurrence of new lesions in the adjoining areas which may coalesce to form a plaque. The plaque grows peripherally, with serpiginous or verrucous borders, may reach a size over 10 cm in diameter with central atrophy and skip areas (Fig. 16.7). The ulcerative and atrophic forms rarely occur. Types include flat, hypertrophic, ulcerated, vegetative, and mutilating type. On diascopy of the lesion may give "*apple jelly nodules*" look in fair individual; however, it is rarely seen in dark complexed. Regional lymphadenopathy is found commonly in lupus vulgaris [79].

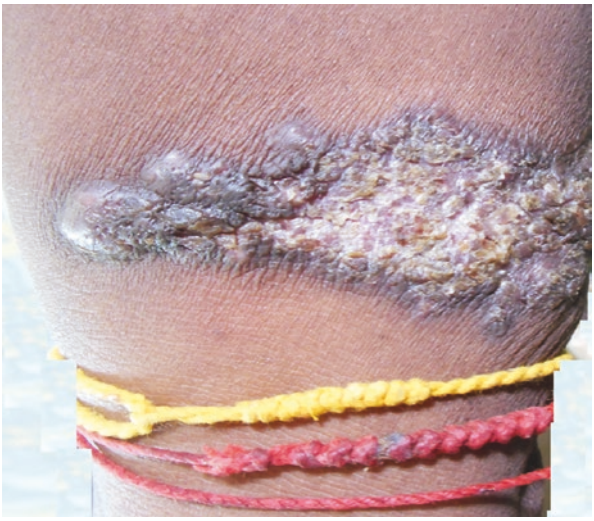

Fig. 16.7 Lupus vulgaris presenting as reddish-brown well-defined plaque with central atrophy and scarring

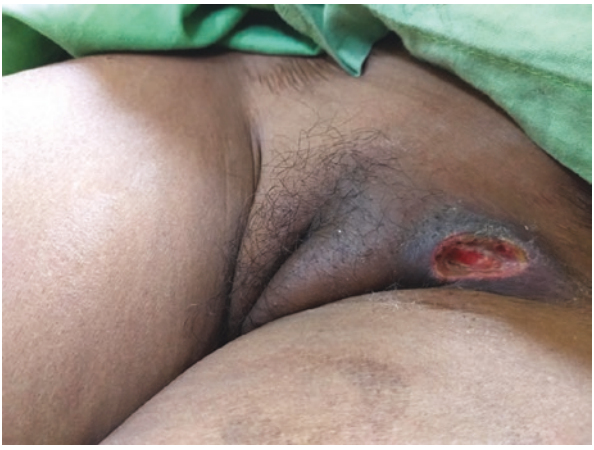

Fig. 16.8 Scrofuloderma presenting a subcutaneous swelling with sinus formation in inguinal area

16.3.3 Scrofuloderma

Scrofuloderma, also known as *tuberculosis colli quativa cutis* is a common form of cutaneous tuberculosis in developing countries like Brazil and India. The inoculation of bacillus occurs from direct extension of endogenous tubercular infection to lymph node, bone, joints, or testicles neck, axillae, groin, and cervical lymph nodes. Lesions may be single or multiple. Lesions start as painless subcutaneous skin coloured nodules which gradually progress to form cold abscesses and later rupture to sinuses with seropurulent discharges (Fig. 16.8). The skin overlying the abscess looks pigmented suggesting chronic inflammation [76]. Spontaneous involution may occur leaving puckered scar with retractions [78].

16.3.4 Tuberculous Chancre

Tubercular chancre also known as primary tubercular chancre is a rare form of cutaneous TB. The mycobacterial inoculation occurs directly into the skin following local trauma. It affects previously un-sensitized individuals, especially children, who have not been vaccinated or had no contact with environmental *M. tuberculosis*. Exposed areas like face and extremities are often affected. It starts as a firm, painless nodule that enlarges and ruptures to form shallow ulceration with undermined edge and covered with thick crust. The borders of the ulcer are undermined. A painful regional lymphadenopathy occurs after 2 weeks. Spontaneous regression with scarring and calcification of regional lymph node may occur [73].

16.3.5 Tuberculous Gumma

Tuberculous gumma, also called metastatic tuberculous abscess occurs following a hematogenous spread of bacilli in an individual with immunosuppression especially those with HIV/AIDS and malnourished children. Commonly widespread distribution of lesions is found because of hematogenous dissemination of bacilli all over the body. The commonest sites involved include trunk and extremities. The lesions start as subcutaneous nodule which in due course of time becomes fluctuant like abscess and subsequently rupture to form ulcer or sinus with serous or seropurulent discharge resembling scrofuloderma [77]. The edge of the ulcer is undermined with bluish discolouration at the border. Regional adenopathy is usually absent. The prognosis is relatively poor in these patients. If not treated the lesions may persist for years or spontaneous resolution can occur sometimes [77].

16.3.6 Orificial Tuberculosis

Orificial tuberculosis, or *tuberculosis cutis orificialis* occurs commonly at mucocutaneous junctions, around the orifices (mouth, anus, urethra, and palate). The infection occurs by self-inoculation of mycobacteria by the individual herself with an active focus of infection like in lung, intestine, and urogenital system under the state of immunosuppression. Skin lesions are friable, painful, erythematous papules or nodules with severe underlying visceral disease [77].

16.3.7 Acute Miliary Tuberculosis

It is a rare and severe form of tuberculosis which occurs in individuals with impaired cellular immunity, anergic child with negative PPD, and HIV patients with CD4 count below 100 cells/μL. Skin involvement occurs because of acute bacteraemia

with primary focus of infection in the lungs. The lesions are widespread and occur in the form of erythematous macules, papules, papulo-vesicles and central umbilication, ulceration or crusting [77]. Rarely exanthematous rash is seen. The lesions tend to regress in 1–4 weeks, leaving depressed and hypopigmented scars. There is associated systemic symptoms like fever, anorexia, asthenia, and weight loss.

16.3.7.1 Histopathological Findings of Different Types of Cutaneous Tuberculosis

Basing upon location and type of granuloma along with presence or absence of necrosis, various types of cutaneous TB are differentiated in histopathology (Table 16.7) [80].

a. Well-formed granulomas with absence of caseous necrosis—LV, Lichen scrofulosorum
b. Intermediate forms-granuloma with caseous necrosis—TVC, primary cutaneous TB, acute miliary TB, Tuberculosis orificialis
c. Poorly formed granuloma with intense caseous necrosis—Scrofuloderma, metastatic abscess, and gumma

Table 16.7 Histopathology of cutaneous TB [80]

Clinical types	Epidermis	Dermis	Types of cell	AFB status
Lupus vulgaris	Atrophic or hypertrophic Acanthosis, papillomatosis	Well-formed epithelioid granuloma Small foci of caseous necrosis rarely Lymphocytic infiltrate is dense	1. Langerhans type 2. Foreign body like 3. Sarcoidosis-like	Infrequent
Lichen scrofulosorum	Discrete rectification of epidermis	Well-formed epithelioid granuloma surrounded by lymphocytes in more superficial dermis No caseous necrosis	Giant cells absent	Absent
TVC	Hyperkeratosis, acanthosis, papillomatosis	Caseous necrosis of moderate intensity	Tuberculous granuloma	Can be found
Primary cutaneous TB	Normal	Recent lesion—necrotizing neutrophilic infiltrate	Late lesion—organization of granuloma	Numerous in recent lesions, gradually decreases

(continued)

Table 16.7 (continued)

Clinical types	Epidermis	Dermis	Types of cell	AFB status
Acute miliary tuberculosis	Normal	Nonspecific inflammatory infiltrate and focal caseous necrosis with microabscess	Infiltrate contains lymphocytes + plasma cells	Bacilli vary directly with the severity
Tuberculosis orificialis	Normal or atrophic	Granuloma around a median central superficial ulcer with caseous necrosis in deep dermis	Tuberculoid type	Infrequent
Papulonecrotic tuberculid		Area of necrosis into dermis	Granulomatous infiltrate with leukocytoclastic vasculitis, perivascular oedema, or follicular necrosis with suppuration	Negative
Scrofuloderma	Atrophic or hypertrophic or ulceration	Massive central necrosis with abscess and suppuration	Periphery showing traces of granuloma	Can be found
Metastatic abscess or gumma	Normal	Central ulceration with abundant caseous necrosis	Rim of giant cell and macrophages surrounding necrosis	Frequent

16.3.8 Tuberculids

Tuberculids are believed to be a cutaneous immunological reaction to the presence of occult TB in a patient with moderate to high immunity. They indicate active tuberculosis and/or episodic bacteraemia with a hyperergic expressions of active TB [81]. Types include papulonecrotic form, erythema induratum of Bazin, and lichen scrofulosorum.

16.3.8.1 Papulonecrotic Tuberculid

It is characterized by painless erythematous to violaceous papulonodular lesions around the face, ears, extensors of trunk, extremities, and buttocks. The lesions resolve spontaneously leaving varioliform scars [73]. AFB is usually negative [82]. In histology dermis shows granulomatous infiltrate with leukocytoclastic vasculitis, perivascular oedema, or follicular necrosis with suppuration [82].

16.3.8.2 Lichen Scrofulosorum

Lichen scrofulosorum is also known as "tuberculosis cutis lichenoides". It is a rare tuberculid characterized by numerous minute lichenoid papules in children and adolescents with tuberculosis. The lesions are usually asymptomatic, closely grouped, yellow-red to brown-red follicular or perifollicular papules of size 1–5 mm present preferably over trunk, abdomen, and proximal parts of the limbs. Strongly positive tuberculin reaction is found in the affected patients [83]. Usually the lesion has a smooth surface; however, spiny projections with fine scales may be found occasionally. Histopathology shows non-caseating, epithelioid cell granulomas in upper dermis and around dermal appendages. AFB is not found. The lesions respond rapidly within 4–6 weeks of starting anti-tubercular treatment with complete clearance in 12 weeks, irrespective of the systemic tubercular focus [77, 84].

16.3.8.3 Erythema Induratum of Bazin

Erythema Induratum of Bazin (EIB) is a granulomatous lobular panniculitis associated with tuberculosis. Young and middle aged are affected with lower limb being the site of predilection [85, 86]. Cold temperature, associated circulatory disorders of lower limbs, and obesity are associated risk factors. It starts as purplish to red subcutaneous nodules on posterior legs and thighs and subsequently ulcerates to discharge caseous materials. The ulcers are usually shallow with violaceous border with necrotic slough at the base. The ulcers heal with depressed scars with or without treatment. Histology shows predominantly lobular panniculitis with fat necrosis, mixed inflammatory infiltrate of lymphocytes, plasma cells, and histiocytes forming granulomas. In two-third cases, non-caseating granulomatous inflammation is found.

16.3.9 Treatment of Cutaneous Tuberculosis

The cutaneous TB usually responds to anti-tubercular drugs. The ATT have been classified into first line and second line (Tables 16.8, 16.9, and 16.10)

First-line anti-tubercular drugs	Second-line anti-tubercular drugs
Isoniazid	Streptomycin
Rifampicin	Amikacin
Rifapentine	Capreomycin
Ethambutol	Ethionamide
Pyrazinamide	Cycloserine
	p-amino salicylic acid
	Levofloxacin
	Moxifloxacin

Table 16.8 Dosing schedule of first-line anti-tubercular drug [80]

Medication	Adult dose	Children dose
Isoniazid (H)	5 mg/kg daily, max 300 mg 15 mg/kg TIW, max 900 mg	10–15 mg/kg daily 20–30 mg/kg intermittently
Rifampicin (R)	10 mg/kg daily, max 300 mg mg/kg TIW, max 300 mg	10–20 mg/kg daily or BIW
Pyrazinamide (Z)	20–25 mg/kg daily, max 2 g 30–40 mg/kg daily, max 3 g	15–30 mg/kg daily 40–50 mg/kg BIW
Ethambutol (E)	15–20 mg/kg daily, max 1600 mg 25–35 mg/kg TIW, max 2400 mg	15–20 mg/kg daily 50 mg/kg BIW

Table 16.9 Regimen of anti-tubercular drug

Regimen	Drugs	Duration (months)
Intensive phase	RHZE	2
Maintenance phase	RH	6

Table 16.10 Regimen of anti-tubercular dosing in special situations [80]

Special situation	Dosing
Elder patient	Same dose adjusted with weight
Renal insufficiency	Dose decreased if creatinine clearance >30 ml/mine
Hepatic insufficiency	Should avoid hepatotoxic drugs like isoniazid, rifampicin, and pyrazinamide
Pregnancy	Ethambutol and streptomycin are contraindicated due to teratogenic effect

16.4 Atypical Mycobacteria

16.4.1 Classification of Atypical Mycobacterium Species [87]

Rapid growing	Slow growing
Mycobacterium abscessus	*Mycobacterium avium intracellular complex*
Mycobacterium chelonae	*Mycobacterium haemophilum*
Mycobacterium fortuitum	*Mycobacterium kansasii*
	Mycobacterium marinum
	Mycobacterium scrofulaceum
	Mycobacterium ulcerans
	Mycobacterium xenopi
	Mycobacterium malmoense

16.4.2 *Cutaneous Manifestation of Atypical Mycobacterial Infection* (Table 16.11)

M. marinum: It causes swimming pool granuloma or fish tank granuloma at the site of inoculation mostly the trauma prone areas like extremities with finger being the commonest area [88, 89]. Cutaneous lesions include erythematous papules or pustules, nodules, verrucous plaques, or multiple granuloma with or without ulceration. In immunocompromised patients, there is disseminated lesions involving tendons,

Table 16.11 Treatment of atypical mycobacterial infection [95]

Species	Treatment
M. marinum	*Antibiotic therapy* 1. Tetracyclines monotherapy—Minocycline or doxycycline 100 mg BD till complete resolution 2. Clarithromycin 500 mg twice a day, rifampicin 600 mg daily, and ethambutol 25 mg/kg daily till complete resolution 3. Co-trimoxazole monotherapy 4. Streptomycin 5. Ethionamide *Other modalities* 1. Surgery, cryotherapy, electrode therapy, and irradiation 2. Co-trimoxazole effective
M. kansasii	1. Daily isoniazid (300–600 mg/day), rifampicin (600 mg/day), and ethambutol (15 mg/kg/day) for 18–24 months 2. Surgical debridement of the lesions combined with oral ethambutol, cycloserine, and rifampicin
M. abscessus	Clarithromycin 1000 mg/day for 12 months along with surgical debridement of localized disease
M. ulcerans	1. Rifampicin combined with amikacin (15 mg/kg IM twice daily) or streptomycin (15 mg/kg IM daily) with or without surgical therapy for 4 to 8 weeks 2. Clofazimine and cotrimoxazole
M. chelonae	1. Minocycline monotherapy 2. Surgical debridement combined with IV cefoxitin for 1 month and oral ciprofloxacin for 6 weeks
Mycobacterium Avium-Intracellulare	1. Three-times-weekly regimen [clarithromycin (1000 mg) or azithromycin (500 mg), rifampin (600 mg), and ethambutol (25 mg/kg)] 2. Daily regimen of clarithromycin (500–1000 mg) or azithromycin (250 mg), rifampicin (600 mg) or rifabutin (150–300 mg), and ethambutol (15 mg/kg) with consideration of three-times-weekly amikacin or streptomycin 3. Monotherapy with minocycline 100 mg twice a day Treatment should be given for 1 year
Mycobacterium Scrofulaceum	1. Quinolones, tetracyclines, and anti-tubercular drugs, such as isoniazid, rifampicin, and ethambutol 2. Clarithromycin monotherapy

bones, joints, and bursae. Histopathology shows nonspecific inflammation in most of the cases with granulomatous infiltrate in some. Healing occurs with scarring.

M. kansasii: Cutaneous lesions include papules and pustules which subsequently turn into verrucous or granulomatous plaques or nodules which can ulcerate. A sporotrichoid distribution and cellulitis like presentation may be seen [90]. Histopathology shows granulomatous inflammation with mixed inflammatory infiltrate, and acid-fast bacilli in histiocytes.

M. abscessus: Cutaneous lesions include erythematous papules, pustules, and ulcerated nodules mostly involving lower extremities, upper extremities, and trunk [91]. Histopathology shows nodular or granulomatous pattern [92].

M. ulcerans: More common in young patients with female preponderance. The lesion starts as a painless subcutaneous swelling commonly on legs and forearms that rapidly enlarges to form firm nodules which subsequently ulcerate [93, 94]. The ulcer is painless, shallow, necrotic and named as buruli ulcer. Granulomatous inflammation with predominant subcutaneous fat necrosis is usually found in histology.

M. chelonae: Multiple erythematous papules and nodules with draining fistulas appear in a non-contiguous and nonlinear pattern involving distal extremity. Histopathology shows suppurative granuloma without caseation [95].

M. fortuitum: The lesions appear at the surgical site or at the site of trauma in immunocompromised patients. Lesions can vary from painful nodules, abscesses, ulcers, draining sinus tracts, or cellulitis. Suspicion should arise when patients present with nonhealing furuncles on the lower extremity with history of recent procedure [96]. Histopathology of acute lesions shows suppurative granulomas without caseation and mixed infiltrate [95].

Mycobacterium Avium-Intracellulare: Cutaneous lesions appear as painful or painless subcutaneous nodules in the cervical, submandibular, submaxillary, or preauricular region [95]. The nodules are usually unilateral and may ulcerate discharging serosanguineous material. Granulomatous inflammation with presence of macrophages containing large numbers of acid-fast bacilli is found in histopathology [95].

Mycobacterium Scrofulaceum: Cutaneous lesions present as lymphadenitis with fistulas in submandibular or submaxillary region. Other variants include erythematous papules and ulcerated nodules [95]. Skin lesions also present as erythematous papules that slowly progress to ulcerated nodules. Histopathology shows central necrosis and abscess formation surrounded by tuberculoid granuloma with neutrophils, epithelioid histiocytes, and lymphocytes [95].

16.5 Mycetoma

Mycetoma is a chronic, granulomatous infection of the subcutaneous tissue, which gradually affects the deep structures and bone. Mycetoma can be due to bacteria (actinomycetoma) or fungi (eumycetoma) [97]. Male to female ratios are in the

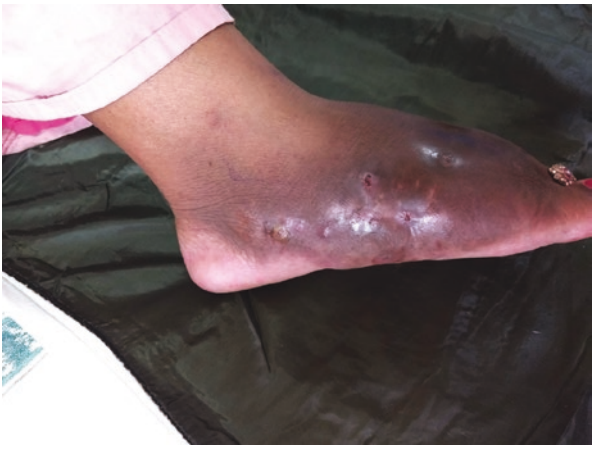

Fig. 16.9 Mycetoma in a female presenting with firm to hard pigmented swelling with multiple sinus

range of 1·6–6·6:1 both in children and adults [97]. The triad includes painless subcutaneous nodules, multiple sinus formation, and discharge of grains. The disease starts as a small subcutaneous nodule (at site of entry of the organism) which gradually spreads to other areas of the skin and deep structures along with sinus formation (Fig. 16.9). There is woody induration of skin and subsequently the solid mass causes deeper structure involvement resulting in deformity and loss of function [97].

Diagnosis of mycetoma is mostly clinical in endemic areas. However, ultrasound and fine needle aspiration can confirm the diagnosis easily. Grains are seen as sharp hyper-reflective echoes in USG. Cavities are seen in eumycetoma with or without acoustic enhancement, whereas in actinomycetoma, the grains are not distinct because of small size and absence of cement and found at the bottom of the cavities [98]. Examination of the grains under microscope can help in differentiating actinomycetoma and eumycetoma. Fine filaments which can take Gram stain are seen in actinomycetoma, whereas filaments of eumycetoma take periodic acid–Schiff stain. Grains can be inoculated in culture media to identify the specific organisms [97]. Histopathologic examination of mycetoma shows a marked inflammatory response, scarring, suppuration, ulceration, and epithelial hyperplasia. The inflammatory response surrounds the ball of organisms "grains". The morphology of grains often helps in differentiating eumycetoma and actinomycetoma.

Treatment of mycetoma depends upon causative organism. Small size mycetoma can be easily treated and has good prognosis. Actinomycetoma usually responds to prolonged medical treatment and eumycetoma requires prolonged antifungals along with surgical management. Currently, the first-line treatment for actinomycetoma includes 48 mg/kg/day of co-trimoxazole (trimethoprim and sulfamethoxazole in a ratio of 1:5) in cycles for 5 weeks and amikacin 15 mg/kg/day in a divided dose every 12 h for 3 weeks. The 2-week interval of amikacin in the 5-week cycle is used for renal and audiometric monitoring. Amongst the antifungals itraconazole gives relatively good results with lesion size reduction making the surgery less mutilating [99]. Terbinafine has limited efficacy in eumycetoma [100]. Other antifungals tried in eumycetoma with promising results include voriconazole, posaconazole, isavuconazole, and fosravuconazole [101, 102].

16.6 Leishmaniasis

Leishmaniasis is caused by *Leishmania donovani*. The animals (canines and rodents-zoonotic cycle) and humans act as reservoir of the organism. The disease is usually transmitted by sand fly (Lutzomyia and phlebotomus). A total of 12 million people are estimated to be infected worldwide and 2 million new cases are reported annually [103]. Leishmaniasis can be of cutaneous type and visceral type [104, 105] (Tables 16.12, 16.13, and 16.14).

Table 16.12 Clinical manifestations of Leishmaniasis [104, 105]

Disease type	Species	Clinical features
Visceral leishmaniasis	*Leishmania donovani*	Fever, weight loss, hepatosplenomegaly, lymphadenopathy, pancytopenia, bleeding hypergammaglobulinemia, skin pigmentation Death due to severe secondary infection
Post-kalazar dermal leishmaniasis	*Leishmania donovani*	Skin lesions around mouth and other parts of body Hypopigmented macules, nodular lesions
Cutaneous leishmaniasis	Most common type *Leishmania donovani*	Most common type Ulcerated or crusted papule
Leishmaniasis recidivans	*Leishmania tropica*	Tuberculoid lesions develop around scars of healed cutaneous ulcers
Diffuse cutaneous leishmaniasis	*L. mexicana* complex	Dissemination of skin lesions occurs over face and extremities, high parasite numbers due to poor cell-mediated immune response
Mucocutaneous leishmaniasis	*L. mexicana* complex	Mainly in south America. (espundia) Involve nose, oral cavity, and pharynx resulting in difficulty with eating, secondary infection

Table 16.13 Treatment modalities [106–110]

Local treatment	Systemic treatment
1. Local heat (37–43 degree) for 12 h in a day 2. Curettage 3. Cryosurgery—freezing with CO_2 snow 4. Intralesional—5% mepacrine and 5-aminolevulinic acid with photodynamic therapy, pentavalent antimony 1–2 ml 5. Topical imiquimod, 15% paromomycin in 12% methyl benzethonium chloride ointment	1. Sodium stibogluconate/meglumine antimonate (20 mg/kg body weight, max 850 mg) intravenously or intramuscularly till the lesion regresses clinically, usually takes 15–30 days 2. Pentamidine isethionate (4 mg/kg) once weekly until clinical regression (preferred for *L. aethiopica*) 3. Miltefosine—2.5 mg/kg/day bin two or three divided doses for 1–2 months 4. Lipoid amphotericin B—Preferred in resistant and destructive MCL (mucocutaneous leishmaniasis) 0.15–0.2 mg/kg/BW by drip infusion, if tolerated 50 mg over 6–8 h in 2–4 doses in a week for 6–17 weeks 5. Maesabalide III (isolated from Maesa balansae) 6. ketoconazole—400–800 mg/day for 4–8 weeks 7. Others—rifampicin, metronidazole, levamisole, dapsone, and chloroquine

Table 16.14 Cutaneous manifestations [111, 112]

Clinical feature	Causative agent	Initial lesion	Evolution
Schistosomal dermatitis	*S. haematobium*	Papular itchy eruption	Papules with central haemorrhage or vesiculation followed by crusting Heals by 1–3 weeks
Urticarial reaction (Katayama disease/ urticarial fever)	*S. japonicum* *S. mansoni*	Redish wheals Associated with fever, arthralgia, abdominal pain, hepatosplenomegaly	Cutaneous lesions include urticaria, purpura and transient oedema of face, limbs, genitalia
Paragenital fistulous tract	*S. haematobium* *S. japonicum* *S. mansoni*	Papular lesion	Progress to nodular, warty, vegetating or polypoidal mass Granulomatous mass with sinuses and fistulous tract Secondary lymphoedema, elephantiasis
Ectopic cutaneous schistosomiasis		Pruritic papules in paraumbilical area	Coalesce to oval plaques with scaly surface Older lesions ulcerate May have dermatomal distribution

16.7 Schistosomiasis

Schistosomiasis is caused by *S. haematobium* and *S. mansoni*. In childhood and adolescence, it presents with fever, haematuria, weakness, anaemia, weight loss, lower genital tract disease, poor growth, obstructive uropathy, liver cirrhosis, and delayed puberty. In adult females, *S. haematobium* causes liver cirrhosis, obstructive uropathy and *S. mansoni* leads to portal hypertension and gastro-intestinal obstruction.

Treatment of schistosomiasis

1. Praziquantel (drug of choice for all species)—40 mg/kg single dose in two divided doses 4–6 h apart
2. Oxamniquine (*S. mansoni*)—15 mg/kg single dose
3. Metrifonate (only against *S. haematobium*)—10 mg/kg three doses at 2 weekly intervals

16.8 Dracunculiasis/Guinea Worm

Dracunculiasis is caused by the agent "*Dracunculus medinensis" and transmitted by* crustaceans called copepods or water fleas which harbour inactive larvae. Ingested copepods are killed by digestive juice in stomach, the larvae are released and move to small intestine. They penetrate the intestinal wall and migrate to connective tissues of the thorax, where male and female larvae are released and mate

60–90 days after infection. Females mature and migrate to surface of body, where they form burrows in subcutaneous tissues. With maturity a blister is formed which eventually ruptures exposing worm. Systemic features include severe pruritus, pain, nausea, vomiting, diarrhoea, and dizziness. Worms emerge in the lower extremities, but also can appear in upper extremities, trunk, buttocks, and genitalia. No treatment or vaccine is available. The worm may be gently removed by rolling it over a stick with care of ulcer [113].

16.9 Onchocerciasis

Onchocerciasis is caused by *Onchocerca volvulus.* Skin lesions include hypo- or hyperpigmentation, skin atrophy, excoriation alone or in combination. Pruritus is caused by dead filaria left under skin after invasion of live parasite which produces scratching and acute popular skin eruption. Systemic symptoms include generalized body ache, joint pain, and poor vision. During pregnancy, there is rapid exacerbation of skin lesions and deterioration of papular and pustular lesions. Ivermectin once yearly for 10–15 years is given as treatment [114].

16.10 Lymphatic Filariasis

Lymphatic filariasis is caused by microfilaria of *Wuchereria bancrofti*, *Brugia malayi and Brugia timori* (Asia) [lymphatic dweller], *Onchocerca volvulus* [subcutaneous dweller]. Transmission occurs by *Culexquinque fasciatus*. Majority of patients have asymptomatic microfilaremia. Symptoms include fever, lymphadenitis in the form of inguinal swelling, and lymphoedema of legs. However, it can involve arms, breasts, and genitalia [115, 116]. Allergic response to organism can lead to vesiculobullous and urticarial lesions amongst the patients. Long-standing filariasis can be complicated with secondary infection, filarial abscess, chronic obstructive filariasis, and elephantiasis nostrosa. Treatment of filariasis includes diethylcarbamazine (DEC) for 12 days. Other drugs like ivermectin 12 mg, metrifonate 10–15 mg/kg every 14 days for 5–16 courses, levamisole (2.5 mg/kg/week), mebendazole (500 mg tid for 3 weeks), and doxycycline 200 mg/day for 4–6 weeks have been found to be useful. For lymphoedema limb elevation, exercises, skin and wound care, compression therapy, and surgery are being done [117–119].

References

1. Pandey KR. From health for all to universal health coverage: Alma Ata is still relevant. Glob Health. 2018;14(1):62. https://doi.org/10.1186/s12992-018-0381-6.
2. Amazigo U. Onchocerciasis and women's reproductive health: indigenous and biomedical concepts. Trop Dr. 1993;23(4):149–51.

3. http://www.who.int/neglected_diseases/en/. Accessed 18 January 2021.
4. Hotez PJ, Kamath A. Neglected tropical diseases in sub-Saharan Africa: Review of their prevalence, distribution, and disease burden. PLoS Negl Trop Dis. 2009;3:e412.
5. Molyneux DH. The 'neglected tropical diseases': now a brand identity, responsibilities, context and promise. Parasit Vectors. 2012;5:23.
6. https://www.cdc.gov/globalhealth/ntd/diseases/index.html. Accessed 15 January 2021.
7. Yotsu RR. Integrated management of skin NTDs-lessons learned from existing practice and field research. Trop Med Infect Dis. 2018;3(4):120.
8. Engelman D, Fuller L, Solomon A, McCarthy J, Hay R, Lammie P, Steer A. Opportunities for integrated control of neglected tropical diseases that affect the skin. Trends Parasitol. 2016;32:843–54.
9. Mitja O, Marks M, Bertran L, Kollie K, Argaw D, Fahal AH, Fitzpatrick C, Fuller LC, Garcia IB, Hay R, et al. Integrated control and management of neglected tropical skin diseases. PLoS Negl Trop Dis. 2017;11:e0005136.
10. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/number-of-new-leprosy-cases. Accessed 24 January 2021.
11. Galhotra A, Panigrahi SK, Pal A. Leprosy–a raging persistent enigma. J Family Med Prim Care. 2019;8:1863–6.
12. https://www.jfmpc.com/text.asp?2019/8/6/1863/261391. Accessed 15 January 2021.
13. Rao PN, Suneetha S. Current situation of leprosy in India and its future implications. Indian Dermatol Online J. 2018;9(2):83–9.
14. Shepard CC. The nasal excretion of Mycobacterium leprae in leprosy. Int J Lepr. 1962;30:10–8.
15. Martins AC, Miranda A, Oliveira ML, Bührer-Sékula S, Martinez A. Estudo da mucosa nasal de contatos de hanseníase, com positividade para o antígenoglicolipídiofenólico 1. Braz J Otorhinolaryngol. 2010;76:579–87.
16. Job CK. Nasal mucosa and abraded skin are the two routes of entry of Mycobacterium leprae. Star. 1990;49:1.
17. Ghorpade A. Inoculation (tattoo) leprosy: a report of 31 cases. J Eur Acad Dermatol Venereol. 2002;16:494–9.
18. Santos AR, Balassiano V, Oliveira ML, Pereira MA, Santos PB, Degrave WM, et al. Detection of Mycobacterium leprae DNA by polymerase chain reaction in the blood of individuals, eight years after completion of anti-leprosy therapy. Mem Inst Oswaldo Cruz. 2001;96:1129–33.
19. Melsom R, Harboe M, Duncan ME, Bergsvik H. IgA and IgM antibodies against Mycobacterium leprae in cord sera and in patients with leprosy: an indicator of intrauterine infection in leprosy. Scand J Immunol. 1981;14:343–52.
20. Pedley JC. The presence of M. leprae in human milk. Lepr Rev. 1967;38:239–42.
21. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A fivegroup system. Int J Lepr Other Mycobact Dis. 1966;34:255–73.
22. Cardama JE. Early lesions (indeterminate forms). In: Latapi F, Saul A, Rodriguez O, Malacara M, Browne SG, editors. Leprosy. Amsterdam: Excerpta Medica; 1980. p. 68–74.
23. Sarkar R, Pradhan S. Leprosy and women. Int J Women Dermatol. 2016;2(4):117–21.
24. Lastória JC, Abreu MA. Leprosy: review of the epidemiological, clinical, and etiopathogenic aspects - part 1. An Bras Dermatol. 2014;89(2):205–18.
25. Dongre VV, Ganapati R, Chulawala RG. A study of mono-neuritic lesions in a leprosy clinic. Lepr India. 1976;48(2):132–7.
26. Pradhan S, Padhi T, Sirka CS, Nayak BP, Dash M. Clinico-epidemiological profile of pure neuritic Hansen's disease in western Odisha: a hospital based retrospective cross sectional study. Indian J Lepr. 2018;90:253–9.
27. Annigeri SR, Metgud SC, Patel JR. Lepromatous leprosy of histoid type: a case report. Indian J Med Microbiol. 2007;25:70–1.
28. Latapi F, Zamora AC. The spotted leprosy of Lucio: an introduction to its clinical and histopathological study. Int J Lepr Other Mycobact Dis. 1948;16:421–9.

29. Nery JAC, Sales AM, Illarramendi X, Duppre NC, Jardim MR, Machado AM. Contribuiçãoaodiagnóstico e manejo dos estadosreacionais: Uma abordagemprática. An Bras Dermatol. 2006;81(4):367–75.
30. Kahawita IP, Walker SL, Lockwood DNJ. Leprosy type 1 reactions and erythema nodosum leprosum. An Bras Dermatol. 2008;83:75–82.
31. Kumar B, Dogra S, Kaur I. Epidemiological characteristics of leprosy reactions: 15 years experience from North India. Int J Lepr Other Mycobact Dis. 2004;72:125–33.
32. Lockwood DN, Sinha HH. Pregnancy and leprosy: a comprehensive literature review. Int J Lepr Other Mycobact Dis. 1999;67:6–12.
33. Nanda S, Bansal S, Grover C, Garg V, Reddy BS. Lazarine leprosy-revisited? Indian J Lepr. 2004;76:351–4.
34. Costa IMC, Kawano LB, Pereira CP, Nogueira LSC. Lucio's phenomenon: a case report and review of the literature. Int J Dermatol. 2005;44(7):566–71.
35. Prem Anand P, Oommen N, Sunil S, Deepa MS, Potturu M. Pretty leprosy: another face of Hansen's disease! A review. Egypt J Chest Dis Tuberc. 2014;63(4):1087–90.
36. Chandrashekar L, Kumari R, Thappa D, et al. Is it Lucio phenomenon or necrotic erythema nodosum leprosum? Indian J Dermatol. 2013;58(2):160.
37. Sehgal VN. Lucio's phenomenon/erythema necroticans. Int J Dermatol. 2005;44(7):602–5.
38. Duncan ME, Melsom R, Pearson JM, Ridley DS. The association of pregnancy and leprosy. I. New cases, relapse of cured patients and deterioration in patients on treatment during pregnancy and lactation- results of a prospective study of 154 pregnancies in 147 Ethiopian women. Lepr Rev. 1981;52(3):245–62.
39. Duncan ME, Pearson JM, Ridley DS, Melson R, Bjune G. Pregnancy and leprosy: the consequences of alteration of cell mediated and humoral immunity during pregnancy and lactation. Int J Lepr Other Mycobact Dis. 1982;50(4):425–35.
40. Jejeebhoy SJ, Sebastian MP. Actions that protect: promoting sexual and reproductive health and choice among young people in India. New Delhi: Population Council; 2003.
41. Sharma SC, Kumar B, Dhall K, Kaur S, Malhotra S, Aikat M. Leprosy and female reproductive organs. Int J Lepr Other Mycobact Dis. 1981;49(2):177–9.
42. Fleger J, Biric B, Prica S. Importance of leprosy in gynaecology and midwifery. Trop Dis Bull. 1963;60:446–7.
43. King JA, Marks A. Pregnancy and leprosy; a review of 52 pregnancies in 26 patients with leprosy. Am J Obstet Gynecol. 1958;76(2):438–42.
44. Bogush TG. The question of the menstrual function in women with lepromatous leprosy before pubescence. Sci Works Lepr Res Inst. 1976;9:116–8.
45. Khanna N, Singh M, Rasool S, Ammini A, Bhatla N, Garg V. Menstrual irregularities, fertility status, and ovarian function in female patients with leprosy in India. Int J Dermatol. 2014;53(9):1114–8.
46. Chacko CJ. Microbiology. In: Thangaraj RH, editor. A manual of leprosy. 4th ed. New Delhi: The Leprosy Mission; 1985. p. 43–60.
47. Ridley DS. Skin biopsy in leprosy. 2nd ed. Basle: Documenta-Giegy; 1985.
48. Murthy SV, Rao SM, Thejaswini A, Mannan K. De novo histoid leprosy. J Lab Phys. 2011;3(2):110–2.
49. Lockwood DN, Lucas SB, Desikan KV, Ebenezer G, Suneetha S, Nicholls P. The histological diagnosis of leprosy type 1 reactions: identification of key variables and an analysis of the process of histological diagnosis. J Clin Pathol. 2008;61:595–600.
50. Tripathy T, Panda M, Kar BR, et al. Facial lazarine leprosy in post-elimination era: a case report. Indian J Lepr. 2018;90:313–8.
51. Adhe V, Dongre A, Khopkar U. A retrospective analysis of histopathology of 64 cases of lepra reactions. Indian J Dermatol. 2012;57:114–7.
52. Vargas-Ocampo F. Diffuse leprosy of Lucio and Latapí: a histologic study. Lepr Rev. 2007;78(3):248–60.

53. Izumi S, Fujiwara T, Ikeda M, Nishimura Y, Sugiyama K, Kawatsu K. Novel gelatin particle agglutination test for serodiagnosis of leprosy in the field. J Clin Microbiol. 1990;28:525–9.
54. Buhrer-Sekula S, Smits HL, Gussenhoven GC, et al. Simple and fast lateral flow test for classification of leprosy patients and identification of contacts with high risk of developing leprosy. J Clin Microbiol. 2003;41:1991–5.
55. Sinha S, McEntergart A, Girdhar BK, Bhatia AS, Sengupta U. Appraisal of two Mycobacterium leprae-specific serological assays for monitoring chemotherapy in lepromatous (LL/BL) patients. Int J Lepr Other Mycobact Dis. 1989;57:24–32.
56. Chaturvedi V, Sinha S, Girdhar BK, Sengupta U. On the value of sequential serology with a Mycobacterium leprae-specific antibody competition ELISA in monitoring leprosy chemotherapy. Int J Lepr Other Mycobact Dis. 1991;59:32–40.
57. Duthie MS, Ireton GC, Kanaujia GV, Goto W, Liang H, Bhatia A, et al. Selection of antigens and development of prototype tests for point-of-care leprosy diagnosis. Clin Vaccine Immunol. 2008;15:1590–7.
58. Spencer JS, Duthie MS, Geluk A, Balagon M, Kim HJ, Wheat WH, et al. Identification of serological biomarkers of infection, disease progression and treatment efficacy for leprosy. Mem Inst Oswaldo Cruz. 2012;107:79–89.
59. Sengupta U. Recent laboratory advances in diagnostics and monitoring response to treatment in leprosy. Indian Dermatol Online J. 2019;10:106–14.
60. Venturini J, Soares CT, Belone Ade F, Barreto JA, Ura S, Lauris JR, et al. In vitro and skin lesion cytokine profile in Brazilian patients with borderline tuberculoid and borderline lepromatous leprosy. Lepr Rev. 2011;82:25–35.
61. Bang PD, Suzuki K, Phuong LT, Chu TM, Ishii N, Khang TH. Evaluation of polymerase chain-reaction based detection of Mycobacterium leprae for the diagnosis of leprosy. J Dermatol. 2009;36:269–76.
62. Marquees W, Barreira AA. Normal median nerve near potential. Braz J Med Biol Res. 1997;30:1431–5.
63. Samant G, Shetty VP, Upelkar MW, Antia NH. Clinical and electrophysiological evaluation of nerve function impairment, following cessation of multidrug therapy in leprosy. Lepr Rev. 1999;70:10–20.
64. Jain S, Visser LH, Praveen TL, Rao PN, Surekha T, Ramesh E, et al. High-resolution sonography: a new technique to detect nerve damage in leprosy. PLoS Negl Trop Dis. 2009;3:498.
65. Peters ES, Eshiet AL. Male–female (sex) differences in leprosy patients in south eastern Nigeria: females present late for diagnosis and treatment and have higher rates of deformity. Lepr Rev. 2002;73(3):262–7.
66. https://www.who.int/bulletin/volumes/89/7/10-085662/en/. Accessed 31 January 2021.
67. Salih MH, Landers T. The concept analysis of stigma towards chronic illness patient. Hos Pal Med Int J. 2019;3(4):132–6.
68. Ahmedani BK. Mental health stigma: society, individuals, and the profession. J Soc Work Values Ethics. 2011;8(2):41–416.
69. Le Grand A. Women and Leprosy: A Review. Lepr Rev. 1997;68:203–11.
70. World Health Organization. Lobal tuberculosis report 2017: Leave no one behind - Unite to end TB. 2017.
71. Pandhi D, Reddy BS, Chowdhary S, Khurana N. Cutaneous tuberculosis in Indian children: the importance of screening for involvement of internal organs. J Eur Acad Dermatol Venereol. 2004;18:546–51.
72. van Zyl L, du Plessis J, Viljoen J. Cutaneous tuberculosis overview and current treatment regimens. Tuberculosis. 2018;95:629–38.
73. Azulay RD, Azulay DR, Azulay DR. Dermatologia. 5th ed. Rio de Janeiro: Guanabara Koogan; 2011.
74. Bravo FG, Gotuzzo E. Cutaneous tuberculosis. Clin Dermatol. 2007;25:173–80.
75. Lai-Cheong JE, Perez A, Tang V, Martinez A, Hill V, Menagé HP. Cutaneous manifestations of tuberculosis. Clin Exp Dermatol. 2007;32:461–6.

76. Abebe F, Bjune G. The protective role of antibody responses during Mycobacterium tuberculosis infection. Clin Exp Immunol. 2009;157:235–43.
77. MacGregor RR. Cutaneous tuberculosis. Clin Dermatol. 1995;13:245–55.
78. Hu Y, Coates A. Non-multiplying bacteria are profoundly tolerant to antibiotics. Handb Exp Pharmacol. 2012;211:99–119.
79. Ramos-E-Silva M, Castro MCR. Cutaneous tuberculosis. In: Bolognia JL, Jorizzo JL, Rapini RP, editors. Dermatology. 2th ed. New York: Mosby Elsevier; 2008. p. 1114–9.
80. Santos JB, Figueiredo AR, Ferraz CE, Oliveira MH, Silva PG, Medeiros VL. Cutaneous tuberculosis: diagnosis, histopathology and treatment - part II. An Bras Dermatol. 2014;89(4):545–55.
81. Concha M, Fch F, Rabagliati R, et al. Cutaneous tuberculosis: two case reports and review. Rev Infectol. 2011;28(3):262–8.
82. Vashisht P, Sahoo B, Khurana N, Reddy BS. Cutaneous tuberculosis in children and adolescents: a clinicohistological study. J Eur Acad Dermatol Venereol. 2007;21:40–7.
83. Singhal P, Patel PH, Marfatia YS. Lichen scrofulosorum: a diagnosis overlooked. Indian Dermatol Online J. 2012;3(3):190–2.
84. Frankel A, Penrose C, Emer J. Cutaneous tuberculosis: a practical case report and review for the dermatologist. J Clin Aesthet Dermatol. 2009;2:19–27.
85. Tyring A, Stephen K, Lupi A, Omar A, Hengge A, Ulrich R. Tropical dermatology. 2nd ed. Edinburgh: Elsevier; 2017.
86. Sharon V, Goodarzi H, Chambers CJ, Fung MA, Armstrong AW. Erythema induratum of Bazin. Dermatol Online J. 2010;16:1.
87. Rahama O, Thaker H. Atypical mycobacteria: an important differential for the general physician. Clin Med. 2013;13(5):504–6.
88. Kullavanijaya P. Atypical mycobacterial cutaneous infection. Clin Dermatol. 1999;17:153–8.
89. Van Seymortier P, Verellen K, De Jonge I. Mycobacterium marinum causing tenosynovitis. "Fish tank finger". Acta Orthop Belg. 2004;70(3):279–82.
90. Hsu PY, Yang YH, Hsiao CH, et al. Mycobacterium kansasii infection presenting as cellulitis in a patient with systemic lupus erythematosus. J Formos Med Assoc. 2002;101(8):581–4.
91. Tang P, Walsh S, Murray C, et al. Outbreak of acupuncture-associated cutaneous Mycobacterium abscessus infections. J Cutan Med Surg. 2006;10(4):166–9.
92. Prinz BM, Michaelis S, Kettelhack N, et al. Subcutaneous infection with Mycobacterium abscessus in a renal transplant recipient. Dermatology. 2004;208(3):259–61.
93. Gart GS, Forstall GJ, Tomecki KJ. Mycobacterial skin disease: approaches to therapy. Semin Dermatol. 1993;12:352–6.
94. Wagner D, Young LS. Nontuberculous mycobacterial infections: a clinical review. Infection. 2004;32:257–70.
95. Bhambri S, Bhambri A, Del Rosso JQ. Atypical mycobacterial cutaneous infections. Dermatol Clin. 2009;27(1):63–73.
96. Redbord KP, Shearer DA, Gloster H, et al. Atypical Mycobacterium furunculosis occurring after pedicures. J Am Acad Dermatol. 2006;54:520–4.
97. Zijlstra EE, van de Sande WWJ, Welsh O, Mahgoub ES, Goodfellow M, Fahal AH. Mycetoma: a unique neglected tropical disease. Lancet Infect Dis. 2016;16(1):100–12.
98. Fahal AH, Sheik HE, Homeida MM, Arabi YE, Mahgoub ES. Ultrasonographic imaging of mycetoma. Br J Surg. 1997;84:1120–2.
99. Fahal AH, Rahman IA, El-Hassan AM, Rahman ME, Zijlstra EE. The safety and efficacy of itraconazole for the treatment of patients with eumycetoma due to Madurellamycetomatis. Trans R Soc Trop Med Hyg. 2011;105:127–32.
100. N'diaye B, Dieng MT, Perez A, Stockmeyer M, Bakshi R. Clinical efficacy and safety of oral terbinafi ne in fungal mycetoma. Int J Dermatol. 2006;45:154–7.
101. Kloezen W, Meis JF, Curfs-Breuker I, Fahal AH, van de Sande WW. In vitro antifungal activity of isavuconazole against Madurellamycetomatis. Antimicrob Agents Chemother. 2012;56:6054–6.

102. Ahmed SA, Kloezen W, Duncanson F, et al. Madurellamycetomatis is highly susceptible to ravuconazole. PLoS Negl Trop Dis. 2014;8:e2942.
103. Okwor I, Mou Z, Liu D, Uzonna J. Protective immunity and vaccination against cutaneous leishmaniasis. Front Immunol. 2012;3:128.
104. Mohamed K, Narayani K, Arvidan K. Indigenous cutaneous leishmaniasis. Indian J Dermatol Venereol Leprol. 1990;56:228–9.
105. Kalla G, Singhi MK. Cutaneous leishmaniasis in Jodhpur District. Indian J Dermatol Venereol Leprol. 1996;62:149–51.
106. Currie MA. Treatment of cutaneous leishmaniasis by curettage. Br Med J. 1983;287:1053–6.
107. Leibovici V, Arman H. Cryotherapy in acute cutaneous leishmaniasis. Int J Dermatol. 1986;25:473–5.
108. Ramesh V, Katara GK, Verma S, Salotra P. Miltefosine as an effective choice in the treatment of post-kala-azar dermal leishmaniasis. Br J Dermatol. 2011;165:411–4.
109. Dogra J, Lal BB, Mishra SN. Dapsone in the treatment of cutaneous leishmaniasis. Int J Dermatol. 1986;25:398–400.
110. Kjetland EF, Leutscher PD, Ndhlovu PD. Trends Parasitol. 2012;28:58–65.
111. Milligan A, Burns DA. Ectopic cutaneous schistosomiasis and schistosomal ocular inflammatory disease. Br J Dermatol. 1988;114:793–8.
112. Mahmoud AAF. Praziquantel for the treatment of helminthic infections. In: Stollerman GH, editor. Advances in internal medicine. Chicago: Year Book Medical Publishers; 1987. p. 419–34.
113. https://www.cdc.gov/parasites/guineaworm/disease.html. Accessed 13 February 2021.
114. https://www.cdc.gov/parasites/onchocerciasis/index.html. Accessed 13 February 2021.
115. Dondero TJ, Bhattacharya NC, Black HR. Clinical manifestations of Bancroftian filariasis in suburbs of Calcutta (India). Am J Trop Med Hyg. 1976;25:64–73.
116. Saran R, Sanyal RK. Diurnal variation in eosinophil count and vacuolation of eosinophils in tropical eosinophilia. Indian J Chest Dis. 1971;15:209–13.
117. Moulia JP. Combination ivermectin plus diethylcarbamazine a new effective tool for control of lymphatic filariasis. Trop Med Parasitol. 1995;46:9–12.
118. Goodwin LG. Recent advances in research on filariasis: chemotherapy. Trans R Soc Trop Med Hyg. 1984;78:1–8.
119. https://www.cdc.gov/parasites/lymphaticfilariasis/treatment.html. Accessed 13 February 2021.