

 CME Article

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Leprosy – an overview of clinical features, diagnosis, and treatment

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Summary

Leprosy is a chronic infectious disease caused by *Mycobacterium (M.) leprae*. Worldwide, 210,758 new cases were diagnosed in 2015. The highest incidence is found in India, Brazil, and Indonesia. While the exact route of transmission remains unknown, nasal droplet infection is thought to be most likely.

The pathogen primarily affects the skin and peripheral nervous system. The disease course is determined by individual host immunity. Clinically, multibacillary lepromatous variants are distinguished from paucibacillary tuberculoid forms. Apart from the various characteristic skin lesions, the condition is marked by damage to the peripheral nervous system. Advanced disease is characterized by disfiguring mutilations. Current treatment options are based on WHO recommendations. Early treatment frequently results in complete remission without sequelae. While paucibacillary forms are treated with rifampicin and dapsone for at least six months, multibacillary leprosy is treated for at least twelve months, additionally requiring clofazimine. Leprosy reactions during therapy may considerably aggravate the disease course. Besides individual treatment, WHO-supported preventive measures and strategies play a key role in endemic areas.

Introduction

Since 2014, the German Dermatological Academy has annually offered several module-based Tropical Dermatology CME courses. Held in Germany and at dermatology departments in tropical countries, these courses are required for the certificate “Tropical and Travel Dermatology” to be acquired. In the basic and advanced courses in Germany, the participants are primarily familiarized with common tropical dermatoses encountered in travelers returning home as well as in migrants. One of the learning objectives is to show that early and correct interpretation of dermatological findings may frequently lead to the diagnosis of a tropical infectious disease. Given that it is unlikely to encounter a patient with leprosy in Germany, this complex disease entity has not been discussed in depth in the aforementioned course series. However, it has been shown – for instance, during a visit by course participants to Colombo (Sri Lanka) or the Regional Dermatology

Training Center (RDTC) in Moshi, Tanzania – that leprosy, as a chronic infectious disease, still plays an important role in basic dermatological patient care. Due to its clinical variability, it poses a challenge to every dermatologist working in these countries. This complex dermatological and neurological infectious disease continues to be an important risk factor for severe disability in endemic regions. Only early diagnosis of its characteristic skin lesions with initiation of adequate treatment will lead to complete remission. The objective of the present CME article is to highlight the various dermatological features as well as neurological signs and symptoms that may be recognized even by dermatologists. Moreover, readers are supposed to be familiarized with the terminology of the different clinical stages, as they will be expected to be familiar therewith when visiting dermatological treatment facilities in endemic regions.

History

Even known in ancient times, leprosy is considered one of the oldest human epidemic diseases.

In medieval times, leprosy was endemic all over Europe.

In 1873, the public health doctor Armauer Hansen (1841–1912) discovered *Mycobacterium leprae* in Bergen (Norway), thus confirming the infectiousness of leprosy.

Even known in ancient times, leprosy is considered one of the oldest human epidemic diseases. Dating back to the 5th century BC, descriptions of the characteristic disfiguring skin lesions are found in ancient Egypt and Persia. Europe-wide, the disease was considered infectious and incurable throughout and beyond the Middle Ages. Individuals thought to have leprosy or other chronic skin diseases were isolated as outcasts in leprosaria and leper colonies outside the city walls. In an 1864 article on the history of leprosy, Rudolf Virchow described how there were no fewer than 2,000 leprosaria in France alone in the 13th century [1]. In medieval times, leprosy was endemic all over Europe. During the renaissance, the disease vanished, at least from Central Europe, which was attributable to the strict isolation of those affected, thereby interrupting transmission. In some European regions, however, leprosy persisted into the 20th century. These regions included the Iberian Peninsula, Sicily, the Balkans, southern Romania, the Baltics, and Scandinavia. In Norway in particular, scientists investigated the disease referred to as “Spedalsked”, the Norwegian name for leprosy. Still relevant today, Boeck and Danielsen had authored pathological/anatomical descriptions some time before the public health doctor Armauer Hansen (1841–1912) eventually discovered *Mycobacterium leprae* in Bergen (Norway) in 1873, thus confirming the infectiousness of leprosy. On October 13, 1897, the first international leprosy conference was convened in Berlin by the Reich's Ministry of Health; the 155 participants were personally welcomed by the German emperor [2]. The first successful use of sulfonamides by Guy Henry Faget in Carville (Louisiana) in 1941 revolutionized the treatment of leprosy. In 1947, Robert G. Cochrane introduced dapsone into the treatment of leprosy. Until today, dapsone has been an integral component of any multidrug therapy, which were first introduced by the WHO in 1981 [3].

Epidemiology

In 2015, the number of newly diagnosed cases of leprosy was 210,758 worldwide.

Transmission of leprosy persists despite all efforts by the WHO.

A total of 176,176 patients from 138 countries, who were on treatment for leprosy on December 31, 2015, were reported to the WHO (registered prevalence). In 2015, the number of newly diagnosed cases of leprosy was 210,758 worldwide. That figure has thus remained largely constant over the past decade (for comparison, there were 265,661 cases in 2006). This shows that transmission of leprosy persists despite all efforts by the WHO and numerous national health programs. Although the ambitious goal – defined by the WHO in 1991 – of eliminating leprosy by the year 2000 has not been achieved, the success of the WHO-coordinated control measures has been groundbreaking in every way, especially following the

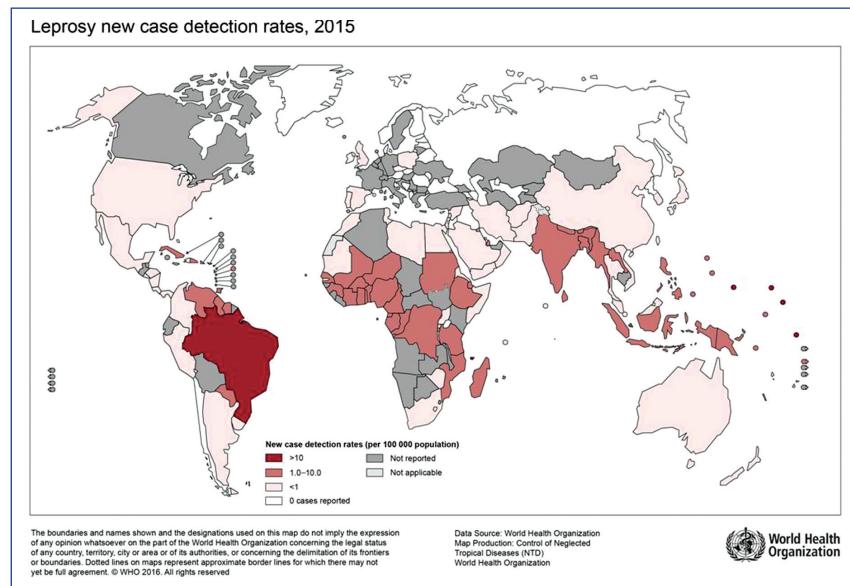


Figure 1 Newly diagnosed cases of leprosy worldwide (2015) (source: WHO).

introduction of multidrug therapy. As recently as 1982, more than 5.4 million people worldwide were still affected by leprosy.

Ninety-five percent of all newly registered leprosy cases are reported from 14 countries. In 2015, the highest incidence was seen in India, Brazil, and Indonesia.

Overall, 60.2 % of notified leprosy cases are multibacillary.

Currently, 95 % of all newly registered leprosy cases are reported from 14 countries. In 2015, the highest incidence was seen in India [127,326 cases (60 %)], Brazil [26,395 cases (13 %)], and Indonesia [17,202 cases (8 %)], followed by the Democratic Republic of Congo, Ethiopia, Madagascar, Mozambique, Nigeria, and Tanzania in Africa; Bangladesh, Myanmar, Nepal, and Sri Lanka in Southeast Asia; and the Philippines in the Western Pacific region [4] (Figure 1).

According to data reported to the WHO, 60.2 % of notified leprosy cases in 2015 were classified as multibacillary; 38.8 % of patients were women. It is considered particularly worrying when leprosy still occurs in children (8.9 %) and/or visible neurological deficits with mutilations (grade 2 disabilities) are found at the time of initial diagnosis. Albeit a small number ($n = 768$), the 2015 WHO report, for the first time, separately listed the occurrence of leprosy in patients with a migrant background [4].

In April 2016, the WHO defined three key objectives under the motto “2016–2020 accelerating towards a leprosy-free world”. These include the promotion of government measures to fight leprosy at the national level, the goal of early diagnosis to prevent grade 2 disabilities, and the inclusion of affected individuals in public life to prevent discrimination [5].

Pathogen/microbiology

Mycobacterium leprae is a non-motile, acid-fast rod.

Mycobacterium leprae cannot be cultured on any known medium.

Mycobacterium leprae is a non-motile, acid-fast rod, 4–7 µm long. Microscopically, *M. leprae* appears red on Ziehl-Neelsen stain as the dye carbolfuchsin cannot be washed out by hydrochloric or sulfuric acid. *Mycobacterium leprae* cannot be cultured on any known medium but only in animal cultures. Using animal cultures, the pathogen only grows in mouse paws and the nine-banded armadillo. Low temperatures facilitate the growth of *M. leprae*, which grows slowly and divides only about every twelve days. The *M. leprae* genome was decoded in 2001. It contains about 3.3 million base pairs; the number of functional genes is 1,600 and is thus much lower than in *M. tuberculosis* [6].

The exact route of transmission of *M. leprae* in humans has not yet been sufficiently elucidated.

Droplet infection via the nasal mucosa is assumed.

Prolonged contact with an infected individual with a high bacterial load is a predisposing factor for the transmission of *M. leprae*.

The clinical variability of leprosy is determined by the microorganism's tropism for the skin and peripheral nerve tissue and by the patient's genetically determined and individually variable susceptibility to *M. leprae*.

Manifest disease occurs in only about 5–10 % of infected individuals.

The initial stage of leprosy is characterized by one or more hypopigmented macules.

The diagnosis of indeterminate leprosy is difficult.

Transmission

The exact route of transmission of *M. leprae* in humans has not yet been sufficiently elucidated. To date, humans affected by leprosy are considered to be the only source of infection. The most important mode of transmission is droplet infection via the nasal mucosa, which is followed by the development of a localized primary lesion, similar to tuberculosis. However, transcutaneous transmission following direct skin contact with untreated, ulcerated, multibacillary lepromatous nodules is also thought to be a possible transmission pathway.

In endemic regions, asymptomatic latent infections can persist for years or even decades; however, they may also spontaneously resolve at any time. If they do lead to manifest disease, the average incubation period is roughly four years. A considerable percentage of the population in endemic regions is infected with the pathogen, with a large percentage showing spontaneous early resolution even in cases of manifest disease [7].

Several predisposing factors for transmission of *M. leprae* are thought to have been confirmed by now, including close and prolonged contact with an infected individual with a high bacterial load. In this context, patients with lepromatous leprosy are considered to be most contagious. Apart from exposure, the individual immunocompetence of an infected person determines whether clinical infection will develop following transmission.

Clinical variants

The clinical variability of leprosy is essentially determined by the microorganism's tropism for the skin and peripheral nerve tissue and by the patient's genetically determined and individually variable susceptibility to *M. leprae*.

Depending on the clinical variant, the clinical morphology in the skin varies considerably. There are marked differences both in the number of lesions as well as their distribution pattern. Occult subclinical infections are common in endemic regions. Manifest disease occurs in only about 5–10 % of infected individuals; the subsequent disease course is determined by the patient's genetically determined immune status in relation to the pathogen.

Indeterminate leprosy

Characterized by one or more hypopigmented macules, the initial stage of leprosy is rather unspectacular and offers no hint as the subsequent disease course.

The lesions are macular, hypochromic and sometimes poorly demarcated. Initially, there is neither erythema nor infiltration. These hypopigmented macules can occur anywhere on the body. Even in endemic regions, the predominantly young patients are frequently misdiagnosed as having tinea versicolor, pityriasis alba associated with atopic diathesis, vitiligo, or postinflammatory hypopigmentation associated with eczema. Indeterminate leprosy can last for up to five years. Towards the end of this disease stage, there may be initial signs of subtle neurological deficits such as decreased sweating and/or a loss of thermosensitivity, whereas pain sensitivity is still intact. The onset of these symptoms indicates the transition to a more advanced stage.

Diagnostic confirmation of clinically suspected indeterminate leprosy is difficult as – even if dermatopathology and bacteriology including molecular biology tests are available – the results of these tests do not allow for an unequivocal classification. A mild lymphohistiocytic infiltrate, which may be perivascular, peri-lesional or close to adnexal structures, is by itself not sufficient for a definitive



Figure 2 Indeterminate leprosy.
Manaus, Brazil, 2001.

At this early disease stage, leprosy is not contagious and permanent nerve damage is not to be expected following adequate treatment.

diagnosis to be made. Even using molecular biology methods, the detection of *Mycobacterium leprae* is extremely rare at this stage. Given that the occurrence of indeterminate leprosy is socially associated with stigmatization and ostracism, early definitive diagnosis, or reliable exclusion of a suspected diagnosis of leprosy, is particularly important and poses a dermatological challenge (Figure 2). At this early disease stage, leprosy is not contagious and permanent nerve damage is not to be expected following adequate treatment.

If this relatively asymptomatic early stage is not identified, the disease may progress into any other form of leprosy (determinate forms), depending on host immunity. The WHO classification distinguishes two opposing clinical variants: paucibacillary leprosy when the immune status is good and multibacillary leprosy in case of poor host immunity. Under field conditions with limited resources, this deliberately simplified classification has proven effective for clinical classification, diagnosis, and treatment.

In the scientific context, however, the Ridley-Jopling classification has been used since 1966; it is closely based on the histological picture. Apart from the two polar forms of tuberculoid (paucibacillary) and lepromatous (multibacillary) leprosy, it includes a broad intermediate stage (borderline type) (Table 1). Depending on the clinical and histological proximity to one of the two polar forms, this intermediate stage is further divided into three subgroups: borderline tuberculoid leprosy (BT), borderline borderline leprosy (BB) and borderline lepromatous leprosy (BL). The following clinical description is based on the Ridley-Jopling classification.

Table 1 Classification of leprosy according to Ridley-Jopling and the WHO [3].

Mild – defect of cell-mediated immunity – severe					
Ridley and Joplin	Tuberculoid leprosy (TT)	Borderline tuberculoid (BT)	Borderline borderline (BB)	Borderline lepromatous (BL)	Lepromatous leprosy (LL)
WHO	Paucibacillary leprosy (PB)		Multibacillary leprosy (MB)		

Good immunity: tuberculoid or paucibacillary leprosy (TT)

When host immunity is good, leprosy presents in its tuberculoid form, characterized by sharply demarcated erythematous plaques.

The skin lesions are paucibacillary.

Decrease in thermal, touch and pain sensitivity may already be present.

Lepromatous leprosy occurs in infected individuals with impaired T-cell immunity resulting in anergy. The clinical picture is characterized by multiple red-brown nodular infiltrates (lepromas).

Predilection sites are the face and auricles.

The symmetrical centrofacial distribution of the cushion-like lesions is referred to as "leonine facies".

When host immunity is good, leprosy presents in its tuberculoid form, characterized by solitary papules and plaques. These may coalesce into sharply demarcated erythematous plaques with raised borders and an annular appearance. At the center, the lesions are frequently atrophic and hypopigmented. Showing an asymmetrical distribution, tuberculoid leprosy lesions predominantly occur on the extremities. They are reminiscent of tinea corporis, which is a frequent misdiagnosis in this form of leprosy. Spontaneous resolution is possible. Given that the skin lesions are paucibacillary, tuberculoid leprosy is hardly contagious.

Even at this stage, a cursory neurological examination of affected skin sites may reveal a decrease in thermal, touch and pain sensitivity as well as anhidrosis, usually at the center of the lesion. These neurological deficits are asymmetrical.

Poor immunity: lepromatous or multibacillary leprosy (LL)

Lepromatous leprosy occurs in infected individuals with impaired T-cell immunity resulting in anergy. Clinically, this multibacillary form is characterized by multiple red-brown nodular infiltrates (lepromas) in the skin and mucous membranes (Figure 3). Predilection sites for these diffuse infiltrates are the face and auricles, especially the earlobes (Figure 4). The lesions occur symmetrically.

The symmetrical centrofacial distribution of the cushion-like lesions is referred to as "leonine facies"; loss of the eyelashes and eyebrows is also typical of lepromatous leprosy (Figure 5).

Involvement of the nasal mucosa leads to destruction of the septum and deformity of the nasal skeleton (saddle nose). Subsequently, this destructive

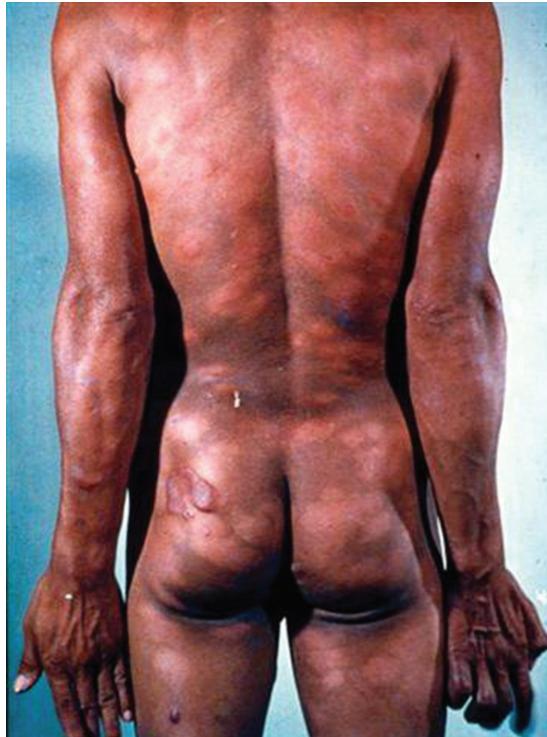


Figure 3 Lepromatous leprosy: multiple infiltrated lesions across the entire body (lepromas).



Figure 4 Lepromatous leprosy: characteristic infiltration of the auricle.

Ocular involvement, which may lead to blindness, is particularly feared.

inflammatory process may include the entire nasopharynx, clinically characterized by mucosal ulcerations of the palate and larynx.

One complication that is particularly feared with regard to the multibacillary forms of leprosy is ocular involvement, which leads to permanent loss of vision including complete blindness in up to 10 % of patients. Pathophysiological, the cause of blindness is multifactorial.

Lymphatic and hematogenous spread of *M. leprae* can lead to involvement of the kidneys (glomerulonephritis with nephrotic syndrome and subsequent

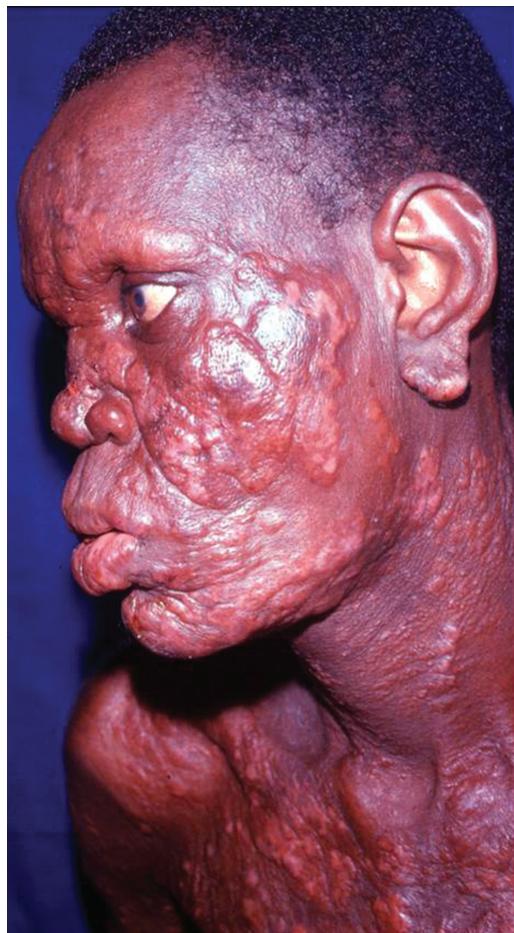


Figure 5 Lepromatous leprosy: cushion-like centrofacial infiltrates (leonine facies) (courtesy of: Dr. P. Traoré, Mali).

In lepromatous leprosy, the individual bacterial mass in the human body may amount to several kilograms.

amyloidosis), the liver (hepatitis and periportal fibrosis), and to acute orchitis. Osseous involvement presents with multibacillary bone marrow lepromas; joint involvement results in joint effusions.

The individual bacterial mass in the human body at this stage of advanced lepromatous leprosy is several kilograms.

Intermediate stage: borderline leprosy or dimorphic leprosy

In the majority of infected individuals, leprosy takes on an intermediate form, which may – to a variable degree – show clinical features of tuberculoid and lepromatous leprosy. Based on the Ridley and Jopling classification, borderline leprosy is clinically and histologically further divided into three subgroups depending on the patient's individual immune status.

Borderline tuberculoid form (BT)

Compared to tuberculoid leprosy, the skin lesions are more numerous and more extensive. The erythematous infiltrates with prominent borders are sharply demarcated and arranged in an asymmetrical fashion; at times, satellite lesions occur (Figure 6). There is sensory and motor nerve involvement. Histologically, this form too is characterized by granulomatous infiltrates, which may extend into the



Figure 6 Borderline tuberculoid leprosy (BT).

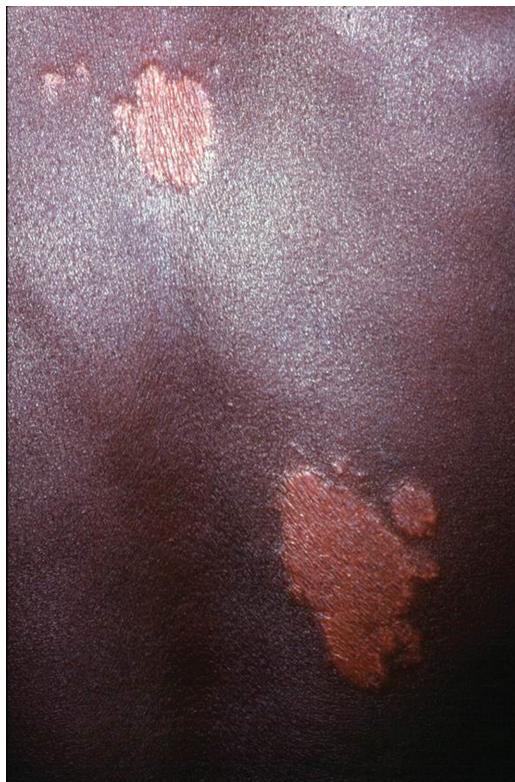


Figure 7 Borderline
borderline leprosy (BB).

subcutis. Compared to the tuberculoid form, nerve involvement seems to be less pronounced. Only very few mycobacteria can be detected (paucibacillary form).

In the majority of infected individuals, leprosy takes on an intermediate form, which may – to a variable degree – show clinical features of tuberculoid and lepromatous leprosy. This intermediate form is referred to as borderline leprosy.

Borderline borderline form (BB)

In this form, there is an overall increase in the number of lesions. They are distributed nearly symmetrically and may exhibit clinical features of both tuberculoid and lepromatous leprosy (Figure 7). Hair growth and sweating are hardly affected. Depending on the lesion, few or numerous bacteria may be detected. The histological picture is increasingly less characterized by granulomas. Peripheral nerves exhibit motor and sensory deficits.

Borderline lepromatous form (BL)

Multiple, poorly demarcated, hypopigmented papules, nodules, and infiltrated plaques are the hallmark of this form (Figure 8). Lesions are largely distributed symmetrically; unaltered skin can still be recognized as such. Hair growth and sweating are hardly affected. There is extensive peripheral nerve involvement. Histology is marked by the absence of granulomas with epithelioid and giant cells. Perineurally, there are histiocytic infiltrates. A vast number of mycobacteria arranged in clusters can be found.

Leprosy reactions

At no time must the assignment of a leprosy patient to any of the chronic forms – as specified by the Ridley-Jopling classification – be considered definitive. Up to



Figure 8 Borderline lepromatous leprosy (BL). The auricle is also affected. The patient was initially referred with the diagnosis of urticaria.

Up to 30 % of leprosy patients develop sometimes life-threatening acute exacerbations referred to as leprosy reactions. They are a manifestation of impaired immunological balance.

30 % of patients develop severe and sometimes life-threatening acute exacerbations, either spontaneously or during treatment; these flare-ups are referred to as leprosy reactions. They are generally a manifestation of a sudden impairment in the immunological balance – established over the preceding disease course – between the pathogen and the infected individual. These immune reactions can occur even after successful treatment. Three different types of leprosy reactions are distinguished [8].

Type 1 reaction

Urticular swelling of leprous skin lesions.
Affected nerves exhibit abscesses.

The condition may be associated with
high fever.

Leprosy reactions usually occur within
twelve months after treatment
initiation.

Pathophysiologically, this is a hypersensitivity reaction to *M. leprae* antigens clinically characterized by sudden onset of urticarial swelling of the leprous skin lesions. It may also be associated with acute and very painful neuritides with loss of sensory and motor function (Figures 9, 10). Affected nerves are markedly thickened and exhibit abscesses. The condition may be associated with high fever. It is the most common leprosy reaction and occurs in up to 30 % of patients with borderline tuberculoid (BT), borderline borderline (BB) and borderline lepromatous leprosy (BL), usually within twelve months after treatment initiation. Possible triggers include pregnancy, comorbidities, and therapies.

A type 1 reaction occurring on adequate therapy is usually a manifestation of immunological upgrading associated with a simultaneous increase in cell-mediated immunity, thus representing a transition to the tuberculoid type. Nevertheless, similar symptoms may also occur prior to treatment initiation, during pregnancy or during inadequate therapy. In the latter cases, however, histology shows degeneration toward the lepromatous pole. This kind of immune phenomenon in the context of a type 1 reaction is referred to as downgrading. When downgrading occurs, additional new lesions – similar to the lepromatous form – may develop. Histology reveals an increased number of macrophages along with a simultaneous uptick in bacteria.

Type 2 reaction (syn. erythema nodosum leprosum)

Clinically, this leprosy reaction is characterized by the occurrence of painful violaceous- erythematous cutaneous or subcutaneous nodules. Unlike classic erythema



Figure 9 Four months after treatment initiation, the patient depicted in Figure 8 developed a type 1 leprosy reaction. The figure shows the initial clinical findings.

The type 2 leprosy reaction presents with painful violaceous-erythematous cutaneous or subcutaneous nodules.

The skin lesions may ulcerate and become necrotic.

nodosum, they are found not only on the lower legs but across the entire body. The skin lesions may ulcerate and become necrotic. They occur predominantly on the extensor aspects of the extremities and on the face; the trunk may also be affected. Pathophysiologically, the reaction constitutes an immune complex vasculitis (Coombs and Gell type 3 reaction) with the histological correlate of



Figure 10 Prominent urticarial infiltration as a clinical sign of a type 1 leprosy reaction. Manaus, Brazil, 2001.

Pathophysiologically, the reaction constitutes an immune complex vasculitis (Coombs and Gell type 3 reaction) with the histological correlate of leukocytoclastic vasculitis.

The type 3 reaction is characterized by violaceous patches and bullous infiltrates. It occurs in untreated patients with lepromatous disease. Histologically, there is extensive vasculitis with endothelial proliferation.

Mycobacterium leprae exhibits tropism for the Schwann cells in nerve sheaths.

Granuloma formation causes intraneuronal pressure-induced atrophy and leads to progressive loss of neural function with necroses and abscesses. Peripheral sensory and motor nerves of the face and extremities are particularly affected.

Peripheral sensory and motor nerves of the face and extremities are particularly affected in tuberculoid leprosy.

The neurological motor and sensory deficits caused by mono- or polyneuropathy may lead to facial nerve paralysis and even blindness.

Progressive polyneuropathy of the extremities leads to severe neurological deficits with trophic ulcerations (mal perforans).

leukocytoclastic vasculitis, which may manifest itself not only in the skin but also as a systemic reaction with glomerulonephritis, lymphadenitis, iridocyclitis, and orchitis. Similar to erythema nodosum, the subcutis may also be involved in the form of septal and lobular panniculitis. Myalgia, arthralgia, and osseous pain are symptoms associated with a type 2 reaction. The occurrence of this type of leprosy reaction is observed in the borderline lepromatous and lepromatous variants following treatment initiation.

Type 3 reaction (syn. Lucio's phenomenon)

Recently designated as type 3 reaction, Lucio's phenomenon is distinct from the aforementioned leprosy reactions. Clinically, this frequently afebrile reaction is characterized by extensive violaceous patches and bullous infiltrates; it is observed in untreated patients with lepromatous disease.

Affected areas of the skin may ulcerate and become necrotic. In case of successful treatment, lesions heal with scarring. Histopathology shows extensive vasculitis with endothelial proliferation. At an advanced stage, this is clinically reflected by cutaneous infarctions, thromboses, and hemorrhages. *M. leprae* can be detected in endothelial cells.

Neurological involvement

Nerve involvement is found in all forms of leprosy and may also occur in the absence of skin lesions [9].

The rather moderate extent of skin lesions in tuberculoid leprosy must not hide the fact that this disease variant in particular may – as it progresses – lead to most severe motor and sensory nerve damage despite adequate immunity. From a pathophysiological point of view, these severe neurological deficits can be explained morphologically. *Mycobacterium leprae* exhibits tropism for the Schwann cells in nerve sheaths, which, in case of adequate immunity, leads to granuloma formation in these structures.

Clinically presenting with palpable nerve thickening, this granulomatous inflammatory process causes intraneuronal pressure-induced atrophy and leads to progressive loss of neural function with caseating necroses, as well as the formation of ulcerating abscesses in case of superficial nerve involvement. Histologically, there is also epi-, peri- and endoneurial fibrosis.

Peripheral sensory and motor nerves of the face and extremities are particularly affected in tuberculoid leprosy. The resultant impairment in sensitivity initially manifests as hyperesthesia and paresthesia; subsequently, as hypoesthesia or anesthesia. Similar to the skin lesions, nerve damage in tuberculoid leprosy is usually asymmetrical (Table 2).

The neurological motor and sensory deficits caused by mono- or polyneuropathy may lead to facial nerve paralysis and even blindness.

In analogy to diabetic neuropathy, progressive polyneuropathy of the extremities leads to severe neurological deficits in the form of trophic ulcerations (mal perforans) along with palmar and plantar hyperkeratosis. Secondary infections and osteomyelitis are common complications.

In addition, osseous resorption occurs in the phalanges, clinically leading to painless flexion of the fingers and toes as bone loss progresses; this may potentially result in severe mutilation with gradual autoamputation.

While motor and sensory deficits can progress rapidly, sometimes their onset may also be gradual and initially without any neuropathic pain (silent neuritis).

Table 2 Nerves that are particularly affected and clinically palpable in advanced stages.

- Ulnar nerve in the ulnar groove
- Median nerve prior to entering the carpal tunnel
- Common peroneal nerve at the level of the fibular head
- Posterior tibial nerve behind the medial malleolus
- Superficial branch of the radial nerve; nerve compression syndrome (Wartenberg's syndrome) with sensory deficits (dorsoradial aspect of the hand)
- Sural nerve behind the lateral malleolus
- Great auricular nerve at the posterior margin of the sternocleidomastoid muscle
- Facial nerve, frontal branches and cervical branches

In lepromatous leprosy (LL) with poor immunity, the perineurial inflammatory process is initially less pronounced than in the tuberculoid forms in which many mycobacteria can be detected in the Schwann cells. The clinical course is characterized by distal symmetrical peripheral polyneuropathy. In borderline leprosy, one or more of the aforementioned nerves may be affected. These multiple mononeuropathies lead to severe motor deficits associated with deformities in the areas they supply (Figure 11, 12).

Neurological examination by the dermatologist

In endemic regions, dermatologists should be familiar with the visible and palpable neurological symptoms of leprosy. Even on skin inspection, pseudoabscesses along nerves and visible nerve thickening may be noted, for example, along the course of the retroauricular nerve and superficial peroneal nerve. Thickened nerves can be detected by palpation along the course of the supraorbital, retroauricular, ulnar, median, superficial radial, common peroneal, superficial peroneal, posterior tibial, and sural nerves. Simple functional tests show weakness (paresis) or loss (paralysis) of muscle strength, for instance, impaired dorsiflexion of the great toe.

With respect to testing sensory nerve function in the field, there is no need for sophisticated neurological equipment, either.



Figure 11 Claw hand due to damage of the ulnar nerve. Kabul, Afghanistan, 2002.



Figure 12 Plantar ulceration; patient depicted in Figure 4. Banda Aceh, Sumatra, Indonesia, tsunami humanitarian aid mission, Joint German Military Forces field hospital, 2005.

A test tube can be used to obtain information about impaired thermosensitivity.

Even a test tube can be used to obtain information about impaired thermosensitivity: a test tube containing water is first cautiously heated with a lighter and then held to individual skin lesions and the surrounding skin. Another test tube contains water at room temperature and is also alternately held to lesional and perilesional skin. With his/her eyes closed, the patient is then asked if he/she detects a difference between hot and cold (Figure 13).

Decreased touch sensitivity can be detected by applying a cotton ball; touching with the corner of a sheet of paper may also provide information about this kind of sensory impairment.

The neurological examination conducted by a specialist includes EMG, nerve ultrasound, and magnetic resonance imaging. Nerve biopsies are preferably taken



Figure 13 Loss of thermosensitivity: test tube with warm water.

from thickened superficial and thus readily accessible nerves such as the sural nerve, the superficial peroneal nerve, the ulnar nerve, and the saphenous nerve.

Ocular involvement

Pathophysiologically, the high rates of blindness in lepromatous forms are due to multiple factors.

Ocular muscle paralysis leads to lagophthalmos.

The resulting blank facial expression is referred to as antonine facies.

In multibacillary forms of leprosy, *Mycobacterium leprae* penetrates the anterior and posterior segments of the eye.

In previously untreated multibacillary forms of leprosy, bacteria can be detected by light microscopy by obtaining tissue fluid through scarification.

The tissue fluid is applied to a slide and stained using the Ziehl-Neelsen method.

In paucibacillary forms, bacterial detection is rarely – if ever – successful.

Skin lesions on the earlobes are a particularly suitable source of tissue fluid for bacterial detection.

Pathophysiologically, the high rates of blindness in lepromatous forms are due to multiple factors, one of them being damage to the facial nerve, especially its occipitotemporal and zygomatic branches.

Clinically, the resultant ocular muscle paralysis causes lagophthalmos, subsequently facilitating secondary corneal infections due to incomplete lid closure (Bell's palsy) (Figure 14). The resulting blank facial expression is referred to as antonine facies. Sensory loss of the ophthalmic branch (V1) of the trigeminal nerve, too, results in corneal anesthesia, thus facilitating bacterial corneal ulceration. Apart from the motor and sensory nerve damage in multibacillary forms of leprosy, *M. leprae* also penetrates the anterior and posterior segments of the eye. Clinical signs include nodular infiltrates in the cornea (punctate keratitis), the conjunctivae, and iris. *Mycobacterium leprae* also infects the ciliary body where it multiplies. The pronounced disturbance in touch sensitivity frequently associated with severe visual impairment is particularly ominous for affected patients and leads to injuries.

Diagnosis

Apart from the correct classification of clinical signs in multibacillary forms of leprosy, previously untreated cases usually allow for bacteria to be detected by light microscopy. Lymph fluid is obtained from suspect skin lesions and the nasal mucosa by scarification and expression. The tissue fluid thus acquired is applied to a slide and stained using the Ziehl-Neelsen method (Figure 15).

In paucibacillary forms, bacterial detection is rarely – if ever – successful. The diagnosis is therefore primarily based on clinical and possibly histopathological findings.

Besides suspect skin lesions, the earlobes are a particularly suitable source of tissue fluid for bacterial detection in the field, even if they do not yet appear to be infiltrated at first glance.



Figure 14 Lagophthalmos (Bell's palsy). Manaus, Brazil, 2001.

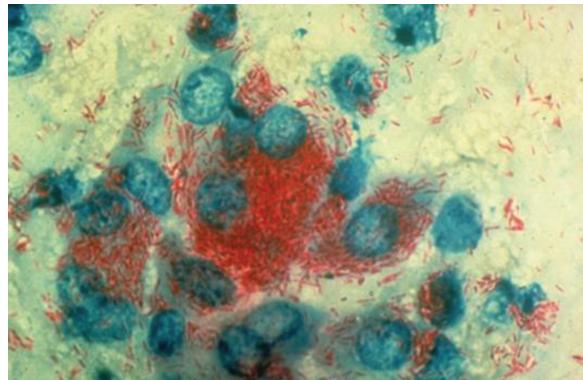


Figure 15 Lepromatous leprosy with high bacterial load: vast number of *M. leprae* in a skin smear – Ziehl-Neelsen stain (© Deutsche Lepra- und Tuberkulosehilfe e. V. [DAHW]) [3].

The bacterial index (BI) provides information about the severity of infection.

The bacterial intensity, which provides information about the severity of infection and the therapeutic success, is measured using the bacterial index (BI). The bacterial count per visual field(s) is determined after assessing 100 visual fields. A smear is only classified as negative after 100 visual fields have been examined (Table 3).

In addition to the bacterial index, the morphological index (MI) is calculated as well. The latter gives information about the ratio of morphologically intact, regularly stained and therefore vital bacteria to the total bacterial count. Dead or degenerated bacteria stain irregularly and appear fragmented. Determination of the morphological index allows for conclusions to be drawn regarding the therapeutic response.

PCR

PCR studies are most sensitive in detecting *M. leprae* in multibacillary forms.

PCR studies are most sensitive in detecting *M. leprae* in multibacillary forms. However, they do not improve the diagnostic possibilities in paucibacillary forms; here, the sensitivity is 34–80 %. Beyond routine diagnostic tests, sequencing of resistance genes allows for the identification of strains resistant to rifampicin and dapsone based on characteristic gene mutations.

Table 3 Bacterial index: scale for assessing the number of leprosy bacteria in skin smears.

Bacterial count per visual field(s)	Bacterial index (BI)
1–10/100	1 +
1–10/10	2 +
1–10/1	3 +
10–100/1	4 +
100–1000/1	5 +
> 1000/1	6 +

Serology

The detection of antibodies against phenolic glycolipid is a test with good sensitivity in multibacillary forms. It is not suitable for diagnostic confirmation of paucibacillary forms of leprosy.

Assignment of a patient to any of the various forms of leprosy is never solely based on histological changes but always requires clinicopathological correlation. Preferably, skin biopsies are to be taken from the margins of the lesions.

Compared to Ziehl-Neelsen staining, the Fite-Faraco method is more sensitive with respect to staining *M. leprae*.

A serological test method with good sensitivity in multibacillary forms (approximately 70 %) involves the measurement of antibodies against a phenolic glycolipid (PGL-1; 35 kDa) in the bacterial cell wall. In these cases, however, microscopic detection is usually also successful. There is an increase in antibody levels along the spectrum from tuberculoid to lepromatous leprosy. Given their moderate sensitivity, serological tests are not suitable for diagnostic confirmation of paucibacillary forms of leprosy.

Histopathology

Depending on clinical presentation, the histopathological spectrum of leprosy is extremely diverse. Assignment of a patient to any of the various forms of leprosy is never solely based on histological changes but always requires clinicopathological correlation.

Preferably, skin biopsies are to be taken from the margins of the lesions and should also include subcutaneous tissue. Compared to Ziehl-Neelsen staining, the Fite-Faraco method is more sensitive with respect to staining *M. leprae*.

Indeterminate leprosy

There are sparse perivascular and perineural infiltrates without granuloma formation. Intraneuronal lymphocytes are frequently seen. In early disease stages, few mycobacteria may be found perineurally, in the arrector pili muscles, or directly beneath the epidermis.

Tuberculoid leprosy (TT)

Tuberculoid leprosy is characterized by dermal tuberculoid granulomas with epithelioid cells, some located directly beneath the epidermis, others around deep vessels and nerves (Figure 16).

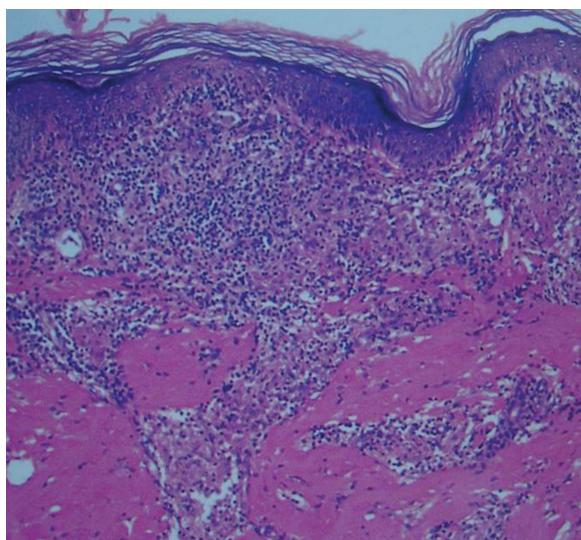


Figure 16 Tuberculoid leprosy. Well-defined sarcoidal granuloma.

Tuberculoid leprosy is characterized by a predominant TH1 immune response.

There are multinucleated giant cells (Langerhans type). Superficial subepidermal granulomas may ulcerate. Peripheral nerves are often markedly thickened, showing intraneuronal lymphocytic infiltrates. Granulomas with central necrosis are detected. Tuberculoid leprosy is characterized by a predominant TH1 immune response, mediated by CD4 lymphocytes, interleukin (IL) 2, and interferon gamma. Bacteria are rarely seen (Fite-Faraco stain).

Borderline tuberculoid leprosy (BT)

Nerve destruction is less pronounced compared to the tuberculoid form. The subepidermal grenz zone usually remains free of granulomas. Lymphocytes and Langerhans cells are less numerous than in tuberculoid leprosy. There are perineural lymphocytic infiltrates without pronounced granuloma formation. The sweat glands and arrector pili muscles may be surrounded by granulomas. Few mycobacteria, primarily found in Schwann cells.

Borderline borderline leprosy (BB)

An intermediate stage immunologically, this form also shows a dichotomous histological picture: on the one hand, there are granulomas with epithelioid macrophages, which are less well defined compared to the tuberculoid forms; on the other hand, there are macrophages with abundant granular cytoplasm. Langerhans cells are absent. Numerous mycobacteria may be present.

Borderline lepromatous leprosy (BL)

Borderline lepromatous leprosy (BL) is marked by macrophages with abundant granular, occasionally foamy cytoplasm (Virchow cells).

Histologically, this variant is marked by macrophages with abundant granular, occasionally foamy cytoplasm (Virchow cells), which are characteristic of lepromatous forms. There is a normal subepidermal grenz zone. The infiltrate contains a few – frequently perineural – lymphocytes. Numerous mycobacteria are present.

Lepromatous leprosy (LL)

There is a vast number of mycobacteria arranged in clusters.

This type is characterized by bluish-gray foamy macrophages (Virchow cells) that form diffuse or nodular infiltrates. Lymphocytes are sparse. There is a grenz zone between epidermis and dermis. Nerves may show lamination of the perineurium, giving them an onion-skin appearance. Immunohistochemistry shows predominant CD8-positive infiltrates with a TH2 response as well as IL-4 and IL-10. There is a vast number of mycobacteria arranged in clusters [10].

Lepromin test

Following intradermal injection of heat-killed mycobacteria (*M. leprae*), a violaceous-erythematous papule may occur.

This form of reaction suggests the presence of a cell-mediated immune response to *M. leprae* and is usually very pronounced in tuberculoid forms.

The lepromin test is not primarily used to establish the diagnosis of leprosy. Rather, it provides an indication as to the individual immune response to be expected from the patient. Following intradermal injection of 0.1 ml of a standardized suspension of heat-killed mycobacteria (*M. leprae*), a delayed hypersensitivity reaction develops over 3–4 weeks in the form of a violaceous-erythematous papule (Mitsuda reaction). This form of reaction suggests the presence of a cell-mediated immune response to *M. leprae* and is usually very pronounced in tuberculoid forms. However, it may be entirely absent in borderline and lepromatous leprosy.

Treatment of leprosy is standardized worldwide and is based on WHO recommendations issued in 1982. Dapsone, rifampicin, and clofazimine are the three drugs of first choice. Monotherapy is obsolete due to resistance development.

Dapsone has a bacteriostatic effect on *M. leprae*.

Pregnancy is not a contraindication.

Rifampicin has bactericidal effects.

Rifampicin causes a red-orange discoloration of body fluids such as saliva, urine, and tears.

Caution: rifampicin is teratogenic and reduces the efficacy of oral contraceptives.

Clofazimine has predominantly antiinflammatory effects.

More than 75 % of patients treated with clofazimine develop pronounced red-brown hyperpigmentation of the leprosy lesions after only a few weeks.

Treatment

Treatment of leprosy is standardized worldwide and is based on WHO recommendations issued in 1982. Similar to tuberculosis, the treatment of leprosy involves multi-drug therapy (MDT). The three drugs of first choice are: dapsone, rifampicin, and clofazimine. Monotherapy using only one of these drugs is obsolete due to resistance development [9].

Dapsone

Synthesized in Germany in 1908, dapsone (4,4'-diaminodiphenylsulfone) was first used as monotherapy in the treatment of leprosy in 1941. By inhibiting bacterial folic acid synthesis, it has a bacteriostatic effect on *M. leprae*.

Side effects include dose-dependent hemolysis and methemoglobin formation, the severity of which is more pronounced in case of glucose-6-phosphate dehydrogenase deficiency. Other side effects are gastrointestinal symptoms, headache, and fatigue. Rare side effects include phototoxic reactions, urticaria, fixed drug eruption, erythema multiforme, DRESS syndrome, agranulocytosis, and hepatitis. There is no known teratogenicity and pregnancy is not a contraindication.

The daily dose is 100 mg in all forms of leprosy.

Rifampicin

Rifampicin was initially synthesized in Italy from gram-positive soil bacteria (*Amycolatopsis rifamycinica*) of the *Actinomycetales* order and has been industrially manufactured since 1965. By inhibiting bacterial RNA polymerase, it has a bactericidal effect on mycobacteria. Within just a few days of treatment, there are hardly any bacteria detectable in both cutaneous and mucosal lesions, even in the lepromatous forms of leprosy. The resistance rate is currently 5 %, which prohibits monotherapy. Severe side effects, which are observed in case of alcohol abuse in particular, include hepatotoxicity with elevated liver function tests and intrahepatic cholestasis. Other side effects relate to the gastrointestinal tract (nausea, vomiting, diarrhea). Skin manifestations in the form of erythematous macules on the face and scalp may occur 2–3 hours after intake. Rifampicin causes a red-orange discoloration of body fluids such as saliva, urine, and tears.

Rifampicin is teratogenic and also reduces the efficacy of oral contraceptives due to enzyme induction. In the treatment of leprosy, the dose for adults is 600 mg once a month. The drug should be taken with meals.

Clofazimine

Synthesized in Dublin in 1954, clofazimine is a red dye that was first used in the treatment of leprosy in Nigeria in 1959. It has predominantly antiinflammatory and only minor bactericidal effect; it is the drug of first choice in the treatment of multibacillary leprosy.

Clofazimine is also suitable for treating type 2 leprosy reactions. More than 75 % of patients treated with clofazimine develop pronounced red-brown hyperpigmentation of the leprosy lesions after only a few weeks, which is particularly prominent in Caucasians. These skin changes resolve very slowly over months and years, and only after treatment has been discontinued; they are a frequent cause of premature cessation of treatment in young women, resulting in relapse and the occurrence of leprosy reactions. Apart from the conjunctivae, body fluids also

Table 4 WHO recommendation for the treatment of paucibacillary leprosy (fewer than five lesions, no bacteria detected).

Adults	Once a month (taken under supervision): rifampicin 600 mg and dapsone 100 mg Daily: dapsone 100 mg
Children	Once a month (taken under supervision): rifampicin 450 mg and dapsone 50 mg Daily: dapsone 50 mg
Treatment duration	Six months or intake of six supervised monthly doses within 9 months

become discolored. Other side effects include xerosis and frequently gastrointestinal symptoms; the latter have been attributed to the accumulation of clofazimine crystals in the intestinal mucosa.

Treatment regimens

Two treatment regimens have been established by the WHO.

Worldwide, the drugs are uniformly marketed in blister packs.

Two treatment regimens have been established by the WHO, corresponding to the clinical classification into a paucibacillary and a multibacillary form (Tables 4, 5). They differ with respect to the combination of drugs as well as treatment duration. Both regimens are administered on an outpatient basis. Each month, the drugs, which are uniformly marketed in blister packs worldwide, are personally issued to patients at the various treatment centers (Figure 17). In endemic regions, the actual taking of the drugs is supervised and documented as well. Thus, the course of treatment is accompanied by trained personnel with the aim of ensuring adequate compliance and promptly identifying any leprosy reactions that may occur.

Note: In case of co-infection with tuberculosis and leprosy, treatment with rifampicin is based on the recommendations for tuberculosis treatment.

Alternatives

Apart from these two standard therapies, ofloxacin, minocycline, and clarithromycin may be used as alternatives in case of intolerance to one or more of the three standard drugs [9].

Table 5 WHO recommendation for the treatment of multibacillary leprosy (more than five lesions, bacteria detected).

Adults	Once a month (taken under supervision): rifampicin 600 mg, clofazimine 300 mg, dapsone 100 mg. Daily: clofazimine 50 mg and dapsone 100 mg
Children	Once a month (taken under supervision): rifampicin 450 mg, clofazimine 150 mg, dapsone 50 mg Every other day: clofazimine 50 mg Daily: dapsone 50 mg
Treatment duration	Twelve months or intake of twelve supervised monthly doses within 18 months

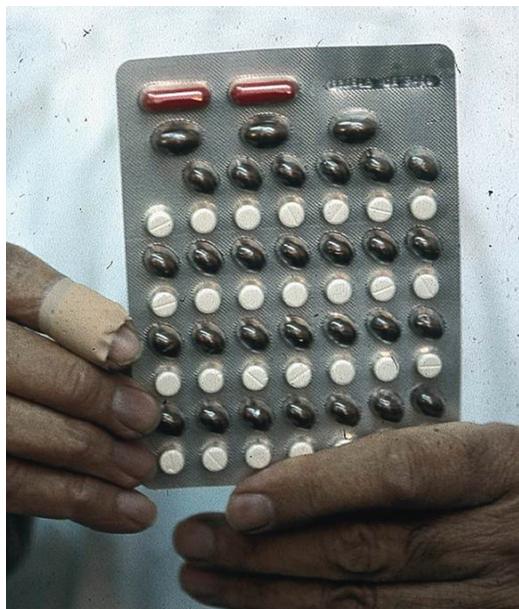


Figure 17 WHO standard treatment regimen for leprosy: blister pack for multibacillary treatment, including rifampicin, dapsone, and clofazimine.

After four weeks of ofloxacin treatment (400 mg QD), more than 99 % of *M. leprae* can be classified as nonvital based on their staining behavior. Minocycline – at a daily dose of 100 mg – is the only bactericidal tetracycline with respect to *M. leprae*; however, its bactericidal potency is less than that of rifampicin. As regards clarithromycin, a macrolide antibiotic, four weeks of treatment (500 mg QD) results in 99 % of *M. leprae* being killed. None of these alternative therapeutic agents is ever used as monotherapy but given in the following combinations.

In case of intolerance to dapsone

Paucibacillary form: rifampicin 600 mg and clofazimine 50 mg once a month (taken under supervision); clofazimine 50 mg QD. Treatment is concluded after a total of six monthly doses within nine months.

Multibacillary form: rifampicin 450 mg, clofazimine 300 mg, and ofloxacin 400 mg or minocycline 100 mg once a month (taken under supervision); clofazimine 50 mg and ofloxacin 400 mg or minocycline 100 mg QD. Treatment is concluded after a total of twelve monthly doses within 18 months.

In case of intolerance to rifampicin

Paucibacillary form: dapsone 100 mg and ofloxacin 400 mg or minocycline 100 mg once a month (taken under supervision); dapsone 100 mg and ofloxacin 400 mg or minocycline 100 mg QD. Treatment is concluded after a total of six monthly doses within nine months.

Multibacillary form: dapsone 100 mg and ofloxacin 400 mg or minocycline 100 mg, plus clofazimine 300 mg once a month (taken under supervision); dapsone 100 mg, ofloxacin 400 mg or minocycline 100 mg, and clofazimine 50 mg QD. Treatment is concluded after a total of 24 monthly doses within 36 months.

In case of intolerance to rifampicin and dapsone

Paucibacillary form: clofazimine 50 mg and ofloxacin 400 mg or minocycline 100 mg once a month (taken under supervision), clofazimine and ofloxacin 400 mg or minocycline 100 mg QD. Treatment is concluded after a total of six monthly doses within nine months.

Multibacillary form: clofazimine 300 mg, ofloxacin 400 mg, and minocycline 100 mg once a month (taken under supervision for the first six months), plus clofazimine 50 mg, ofloxacin 400 mg, and minocycline 100 mg QD. Subsequently, for another 18 months: clofazimine 300 mg and ofloxacin 400 mg or minocycline 100 mg once a month (taken under supervision); clofazimine 50 mg and ofloxacin 400 mg or minocycline 100 mg QD. Treatment is concluded after a total of 24 monthly doses within 36 months.

In case of intolerance to clofazimine

Ofloxacin, minocycline, and clarithromycin may be used as alternatives in case of intolerance to one or more of the three standard drugs.

This only affects patients with multibacillary leprosy: rifampicin 600 mg, dapsone 100 mg, and ofloxacin 400 mg or minocycline 100 mg once a month (taken under supervision); dapsone 100 mg and ofloxacin 400 mg or minocycline 100 mg QD.

ROM treatment regimen

In indeterminate or tuberculoid leprosy with only one cutaneous lesion and no nerve involvement, the ROM treatment regimen is used, which recommends single treatment with rifampicin 600 mg, ofloxacin 400 mg, and minocycline 100 mg. Children over the age of five receive 50 % of the aforementioned doses.

Treatment of leprosy reactions

Type 1 reaction

Type 1 reaction: systemic treatment with corticosteroids.

The treatment of type 1 reactions involves systemic corticosteroids, starting at a dose of 40–60 mg prednisolone QD for 14 days, followed by a gradual taper (5 mg every 14 days), depending on the regression of symptoms.

Type 2 reaction (syn. erythema nodosum leprosum)

Type 2 reaction (syn. erythema nodosum leprosum): depending on the severity of the reaction, thalidomide is the treatment of first choice. In addition, the use of systemic corticosteroids may also be necessary.

Depending on the severity of the reaction, thalidomide (100–400 mg QD) is the treatment of first choice. In addition, the use of systemic corticosteroids (prednisolone 40 mg QD for five days, then gradual taper) may also be necessary. Severe cases require months-long treatment with thalidomide, followed by a gradual dose reduction (100 mg) at 20- to 30-day intervals. Given its well-known teratogenic effects, it is imperative that women of child-bearing age use contraceptive measures under the supervision of their gynecologist.

Type 3 reaction (syn. Lucio's phenomenon)

Systemic corticosteroids are the treatment of choice.

Note: with regard to all leprosy reactions, antibacterial treatment is not interrupted and must be continued.



Figure 18 Status post adequate drug treatment; the mutilations persist. Manaus, Brazil, 2001.

Further treatment measures for patients who have already developed nerve damage: active and passive physical therapy of paretic or contracted extremities and intensive skin care in acral regions. Avoidance of minor injuries. If acral mutilations have already occurred, provision of orthopedic footwear is essential.

A number of reconstructive surgical measures have been developed to mitigate long-term sequelae, both functionally and aesthetically.

Preventive measures start during the initial consultation.

Further measures

Apart from adequate drug treatment, patients who have already developed nerve damage require further measures (prevention of disabilities; PoD). These include active and passive physical therapy of paretic or contracted extremities as well as intensive skin care in acral regions. In addition, preventive measures should be adopted to avoid minor injuries at home and at the workplace (Figure 18). For this purpose, patients are specifically educated and should be supplied, whenever possible, with cooking utensils with special insulated handles and work gloves, for example. The priority is to enable patients to return to a normal social life without stigmatization and permanent medical care.

Acral mutilations require the provision of orthopedic footwear. A number of reconstructive surgical measures have been developed to mitigate long-term sequelae, both functionally and aesthetically. Common surgical procedures include plastic reconstruction of the nose, restoration of lid closure by tarsorrhaphy, and correction of claw hand deformity by tendon transfer of the flexor digitorum superficialis or extensor carpi radialis longus or brevis muscles. Tendon transfer of the tibialis posterior muscle is performed to correct foot drop.

The complexity of the aforementioned procedures illustrates the considerable demands posed to surgeons and patients. Such surgeries can only be performed at selected centers, for example in Brazil or Thailand.

In addition to medical care, socioeconomic rehabilitation measures specifically seek to return those affected back into social life. Given their frequently young age, such measures involve occupational training programs and financial start-up help for vocational training.

Prevention

Preventive measures – as outlined and postulated by the WHO and national (disease) control programs – start during the initial consultation by asking the patient whether other family members or close friends also have skin lesions.



Figure 19 Campaign for the early detection of “hanseniasis” launched by the Brazilian ministry of health, aimed at a young target group.

An increased disease incidence in individual neighborhoods or certain regions requires informing the population about the disease.

The fact that in Brazil the stigmatizing term “leprosy” is never used when speaking to patients facilitates a frank discussion about the contagiousness and the resultant dangers of the disease for those close to them. Nevertheless, patients do receive in-depth information about the disease known throughout the country as “*hanseniasis*”. With their assistance, it is ensured that family members and close friends present to a dermatological outpatient clinic as soon as possible. Personnel specifically trained in leprosy prevention record patients’ exact place of residence. If there is an increased disease incidence in individual neighborhoods or certain regions, they – in coordination with local health authorities – initiate measures to inform the population about the disease. This may be achieved with posters, distribution of information material, as well as special classes in schools and public institutions, on local television, and on the Internet. (Figure 19a, b).

Dermatological mass screening in mobile screening units allows for early detection – as intended by the WHO – even in remote regions undersupplied with dermatologists (Figure 20).

Apart from their participation in examining “the epidemiology of outbreaks”, dermatologists in Brazil are also successfully involved in prevention by acting as multipliers and tutors for general physicians and other medical personnel. Continued training of general practitioners at dermatological institutions is meant to familiarize physicians, especially those practicing in rural areas, with the dermatological and neurological features of leprosy and their potential differential diagnoses. For example, in Brazil, this successful contribution by dermatologists to basic medical training has resulted in the phenomenon that, despite an overall drop in prevalence, the number of newly detected leprosy cases has remained statistically stable in recent years. Apart from continued transmission, this may also be attributed to successful early detection.

The education of political decision makers by dermatologists at the community level generates awareness of the disease. Tangible and dermatologically feasible, these preventive measures represent an important building block in the higher and

Continued training of general practitioners at dermatological institutions is meant to familiarize physicians, especially those practicing in rural areas, with the dermatological and neurological features of leprosy and their potential differential diagnoses.



Figure 20 Mobile diagnostic unit for the early detection of “hanseniasis”, Brazilian ministry of health.

often politically determined objectives of the WHO and national health authorities in fighting this disease.

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Fragen zur Zertifizierung durch die DDG

1. Welche Antwort ist falsch?

Mycobacterium leprae ...

- a) ist ein säurefestes Stäbchenbakterium.
- b) kann mit der Färbung nach Ziehl-Neelsen angefärbt werden.
- c) wächst analog zu *M. tuberculosis* langsam auf Löwenstein-Jensen-Agar.
- d) wurde durch den norwegischen Arzt Armauer Hansen erstmals beschrieben.
- e) lässt sich in Mäusepfoten und im Gürteltier anzüchten.

2. Welche Antwort ist richtig?

- a) Die Lepra zeigt weltweit die höchste Inzidenz in Mauretanien.
- b) Länder mit jährlich hohen neuen Fallzahlen sind Indien, Brasilien und Indonesien.
- c) Frauen sind häufiger als Männer von Lepra betroffen.
- d) Seit 1982 wird eine jährlich steigende Anzahl von Neuerkrankungen weltweit beobachtet.
- e) Lepra wird in Deutschland oft als Zufallsbefund in den reisemedizinischen Sprechstunden der Tropeninstitute diagnostiziert.

3. Welche Antwort ist falsch? Die Übertragung der Lepra ...

- a) ist bis heute nicht hinreichend geklärt.
- b) beruht wahrscheinlich auf einer Tröpfcheninfektion.
- c) beruht auf der extrem hohen Kontagiosität des Erregers.
- d) findet oft im Kindesalter statt.
- e) wird durch schlechte sozioökonomische Bedingungen begünstigt.

4. Welche Antwort ist falsch? Die indeterminierte Lepra ...

- a) ist diagnostisch einfach zuzuordnen.
- b) zeigt sich oft mit einer einzigen Hypopigmentierung.
- c) kann bis zu fünf Jahre dauern.

- d) ist histologisch noch nicht eindeutig einer tuberkuloiden oder lepromatösen Verlaufsform zuzuordnen.
- e) wird häufig als Pityriasis versicolor, Pityriasis alba oder Vitiligo fehldiagnostiziert.

5. Welche Aussage ist falsch? Bei der tuberkuloiden Lepra ...

- a) können nur sehr selten Mykobakterien mit Spezialfärbungen (Fite-Faraco) oder mit Hilfe molekularbiologischer Untersuchungsmethoden (PCR-Diagnostik) nachgewiesen werden. Meist gelingt dieser Nachweis nicht.
- b) kann bereits eine schwere Schädigung eines peripheren Nervens eingetreten sein.
- c) wird das histologische Bild durch tuberkuloide Granulome geprägt.
- d) tritt häufig klinisch eine Facies leonina mit zentrofazialen polsterförmigen Infiltraten auf.
- e) kann die Berührungs-, Schmerz- und Thermosensibilität beeinträchtigen sein.

6. Welche Aussage ist falsch? Bei der lepromatösen Lepra ...

- a) treten symmetrische verteilt diffuse Infiltrate am gesamten Integument auf.
- b) sind häufig die Ohrläppchen betroffen.
- c) kann ein Schleimhautbefall endonasal zu einer vollständigen Destruktion des Nasenseptums führen.
- d) spielt ein plötzlich einsetzender Hörverlust unter dem Verlust der Sinneswahrnehmungen eine führende Rolle.
- e) können auch innere Organe wie Niere und Leber geschädigt werden.

7. Welche Antwort ist richtig? Die Leprareaktionen ...

- a) treten immer zu Therapiebeginn auf.
- b) sind nach wenigen Tagen selbstlimitierend und erfordern daher keine weitere Therapie.
- c) können sich klinisch mit einem plötzlichen ödematösen, urtiariellen Anschwellen der leprösen Hautläsionen manifestieren und mit akuten, sehr schmerzhaften Neuritiden mit sensiblen und motorischen Funktionsverlust einhergehen.
- d) werden immer mit Thalidomid behandelt.
- e) treten ausschließlich bei schlechter Immunlage auf.

8. Welche Aussage ist falsch? Die Diagnose einer Lepra ...

- a) kann durch den Nachweis von Mykobakterien bei den lepromatösen Verlaufsformen in *skin smears* und histopathologisch gesichert werden.
- b) beruht bei den paucibazillären Formen auf dem klinischen Erscheinungsbild und dem histopathologischen Nachweis von Granulomen.
- c) kann sicher serologisch durch den Nachweis von Antikörpern gegenüber phenolischem Glycolipid bei allen Lepraformen gestellt werden.
- d) und die Zuordnung zu einer bestimmten Verlaufsform beruht stets auf der Zusammenschau dermatologischer und neurologischer Symptome.
- e) ist bei den bakterienarmen Verlaufsformen schwieriger zu stellen.

9. Welche Aussage ist falsch? Die Therapie der Lepra ...

- a) ist abhängig von der Verlaufsform.
- b) ist aufgrund möglicher Resistenzentwicklung immer eine sogenannte Multidrug-Therapie.
- c) beruht bei den multibazillären Verlaufsformen auf Clofazimin,

- Rifampicin und Dapson für mindestens zwölf Monate.
- d) ist weltweit durch die WHO einheitlich standardisiert und wird in Blistern ausgegeben.
 - e) muss aufgrund der anhaltenden Kontagiosität des Erregers über mindestens sechs Monate durchgeführt werden.
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10. Welche Aussage ist falsch?

- a) Bei jungen Frauen stellt die Compliance bei der Medikamenteneinnahme aufgrund der Clofazimin-bedingten

- Hyperpigmentierungen oft ein schweres Problem dar.
- b) Dermatologische Reihenuntersuchungen in mobilen Untersuchungseinrichtungen ermöglichen die von der WHO angestrebte Früherkennung.
 - c) Bei frühzeitigem Therapiebeginn heilt die Lepra in der Regel folgenlos aus.
 - d) Jede Lepraform zeigt Hautveränderungen, ein isolierter Nervenbefall kommt nicht vor.
 - e) Bei bis zu 30 % der Lepra-Patienten treten – spontan oder unter Therapie – heftige, zum Teil lebensbedrohlich verlaufende Leprareaktionen auf.

Liebe Leserinnen und Leser,
der Einsendeschluss an die DDA für diese Ausgabe ist der 30. September 2017. Die richtige Lösung zum Thema „Die chronische venöse Insuffizienz – Eine Zusammenfassung der Pathophysiologie, Diagnostik und Therapie“ in Heft 5 (Mai 2017): (1c, 2e, 3b, 4d, 5c, 6d, 7c, 8e, 9a, 10c).

Bitte verwenden Sie für Ihre Einsendung das aktuelle Formblatt auf der folgenden Seite oder aber geben Sie Ihre Lösung online unter <http://jddg.akademie-dda.de> ein
