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Perspective

Leprosy: The Dental Perspective!!

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Abstract

Leprosy is a chronic granulomatous disease caused by the bacillus Mycobacterium leprae. It primarily affects the skin and peripheral nerves and is still endemic in various regions of the world. Clinical presentation depends on the patient's immune status at the time of infection and during the course of the disease. Leprosy is associated with disability and marginalization.

Diagnosis is clinical and is made when the patient has at least 1 of the following cardinal signs specified by the World Health Organization: hypopigmented or erythematous macules with sensory loss; thickened peripheral nerves; or positive acid-fast skin smear or skin biopsy with loss of adnexa at affected sites.

Leprosy is treated with a multidrug combination of rifampicin, clofazimine, and dapsone. Two main regimens are used depending on whether the patient has paucibacillary or multibacillary disease.

Keywords: Leprosy; Paucibacillary; Multibacillary; Multidrug Therapy; Hansen Disease; Mycobacteria Leprae; Disability; Smear Test

What is Leprosy?

Leprosy or Hansen disease is a chronic granulomatous bacterial infection that primarily affects the skin and peripheral nerves. The disease is caused by an obligate intracellular bacillus, *Mycobacterium leprae*, which was identified in the 19th century by the Norwegian physician Gerhard Henrik Armauer Hansen [1]. The clinical presentation and histopathologic changes depend on the immune status of the patient at the time of infection and over the natural course of the disease. Diagnosis is currently based on 3 cardinal signs specified by the World Health Organization (WHO): hypopigmented or erythematous macules with sensory loss, thickened peripheral nerves, and a positive acid-alcohol fast smear or skin biopsy [2]. Modern multidrug therapy and new antibiotics of proven efficacy have made it possible to meet the WHO's targeted reduction in the incidence of *M. leprae* infection to a single case per 10 000 inhabitants in countries where the disease is endemic. A new pathogen, *Mycobacterium lepromatosis*, has recently been found to cause endemic disease in Mexico and the Caribbean [3]. These developments call for new medical perspectives on how to cope with a problem that is still far from resolved.

Epidemiology

Leprosy is a chronic infection of the skin and nerves with Mycobacte¬rium leprae, which, although rarely fatal, is a significant cause of dis¬ability. Over the past 20 years there have been dramatic changes in the prevalence of leprosy since the introduction of multidrug therapy (MDT) [4,5]. There is a pool of 2–3 million patients with permanent nerve impairment as a consequence of leprosy [6].

Leprosy is widely distributed in tropical and warm temperate countries and >1 billion people live in regions where there is active trans¬mission of *M. leprae*. The prevalence rate of new cases has fallen to <1/10 000 in almost all endemic countries, although there are pockets of high prevalence within individual countries. Currently eight coun¬tries account for 88% of new leprosy patients worldwide:

- India (59% of all new cases detected); and
- Brazil, Indonesia, Democratic Republic of Congo, Nigeria, Nepal, Bangladesh and Tanzania, in descending order [7].

Because of the long incubation period of leprosy an individual from an endemic country may develop leprosy years after migration else¬where. Delay in diagnosis is usually longer in non-endemic than endemic regions, and therefore leprosy should be considered as a diagnostic possibility in any person who is from an endemic country and has chronic lesions of the skin or impaired function of peripheral nerves.

Microbiology

M. leprae is an acid-alcohol-fast, gram-positive obligate intracellular bacillus that shows tropism for cells of the reticuloendothelial system and peripheral nervous system (notably Schwann cells); this mycobacterium is the only one with these characteristics. The taxonomic order is Actinomycetales, the family Mycobacteriaceae. *M. leprae* organisms are slightly curved, measure from 1 to 8 mm in length and 0.3 _m in diameter; like other mycobacteria, they replicate by binary fission [8].

Classification with Clinical Features

Indeterminate Leprosy

This is the earliest form and occurs as a single, slightly hypopigmented ill-defined macule in children, who are often contacts of leprosy patients [9,10]. The majority of these lesions are self-limiting and resolve without therapy. A minority (<25%) develop into defined lesions within the clinical spectrum.

Tuberculoid Leprosy

These lesions occur as one to three large asymmetric macules or plaques with sharply defined borders and hypopigmented anesthetic centers [9,10]. Although leprosy lesions are usually hypopig¬mented, in light skins the macules may appear erythematous or dys¬chromic. Involvement of sweat glands and hair follicles results in dryness and loss of hair. Enlarged cutaneous nerves may be palpable at the edge of the lesion, but nerve trunk involvement is minimal.

Borderline-Tuberculoid Leprosy

This is the commonest form of leprosy. The skin lesions resemble those in TT leprosy, but are more frequent and variable in appearance and their borders are less well demarcated. The outline may be irregular with adjacent 'satellite' lesions suggesting local spread. Occasionally, large patches of BT leprosy may involve a whole limb. Asymmetric enlargement of several peripheral nerves is usual and patients may present with muscle weakness or trauma secondary to sensory impairment. Progressive nerve damage is common.

Mid-borderline Leprosy

This is the most immunologically unstable form with the propensity to shift rapidly towards BT leprosy during a reversal reaction or to downgrade towards BL leprosy. The skin lesions are numerous and vary in size, shape and distribution. They may be hypopigmented or erythematous. The characteristic 'target' lesion has a broad, erythema¬tous border with a vague outer edge and 'punched-out' pale center with sensory impairment.

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Borderline-Lepromatous Leprosy

In BL leprosy there are numerous small erythematous macules, which initially may be limited in distribution but become progressively more symmetric [9,10]. Papules, nodules and succulent plaques may develop and, in contrast to tuberculoid leprosy, the lesions have normal sensa¬tion. The intervening skin is normal. Widespread nerve involvement is typical, especially if the patient has downgraded from BT leprosy.

Lepromatous Leprosy

This is a systemic disease with a generalized bacteremia leading to widespread involvement of the skin and other organs [11,12]. The first manifestation may be a diffuse infiltration of the dermis causing a smooth shiny appearance of the skin. More typically, there are numerous symmetrically distributed macules, papules or nodules, and sensation may be retained in lepromatous lesions. Progressive thickening of the skin results in coarsening of the facial features and nodular thickening of the ear lobes. With time the eyebrows and eyelashes become thinned.

Bacillary infiltration is responsible for gradual tissue damage in the involved organs. The nasal mucosa is infiltrated at an early stage, resulting in discharge and obstruction. Erosion of the cartilage and nasomaxillary bones results in perforation of the nasal septum, collapse of the nose and saddle-nose deformity. Laryngeal involvement produces hoarseness and stridor. Direct bacillary involvement of the eye causes keratitis and iritis.

Infiltration of the dermal nerves results in a peripheral sensory loss similar to that of a 'glove and stocking' neuropathy [13], which leaves the skin susceptible to ulceration and secondary infection. Reactional epi-sodes cause edema of the feet, shins and hands. Dactylitis develops in the hands and feet and, together with trauma and osteomyelitis, results in phalangeal erosion.

Both testicular infiltration and orchitis contribute to testicular atrophy and secondary gynecomastia. Glomerulonephritis may occur and is usually associated with ENL. Secondary amyloidosis is a consequence of recurrent ENL reactions.

Oral manifestations related to Hansen Disease

The oral lesions in leprosy develop insidiously, are generally asymptomatic and are secondary to nasal changes [14]. The most frequently affected site is the hard palate [15-17]. The greater prevalence in men could be explained by the fact that women seek doctor's advice earlier, perhaps for esthetical reasons [18].

M. leprae favors temperatures a little below the body temperature for its multiplication [19], Based on this fact, a pathophysiologic mechanism is postulated for oral involvement: a nasal lesion with obstruction of the air flow leads to oral breathing (mouth breathing), which is very common in lepromatous leprosy. This causes a decrease in the intra-oral temperature, mainly in sites near the air intake, the anterior areas, facilitating the harboring of the bacillus [20].

The sequence of pathological alterations would follow the same pattern described by Pinkerton in 1932 in the nasal and oral mucous membranes: congestion, infiltration, and formation of nodules, possible ulceration, atrophies and fibrosis [21]. Important medical and odontologic complications may follow the involvement of the oral and nasal mucous membrane and the bones of the face in leprosy [22].

In the advanced stages, there may be deformities and functional alterations, such as fibrosis and retraction of the soft palate or perforation of the hard palate, with serious disturbances in phonation, and nasal regurgitation of food. Scheepers and Lemmer postulate that erythema nodosum leprosum (or reaction type II) is an important cause for destruction, perforation and deformation of the palate and uvula, alerting one to the need for more effective treatment of that condition [22].

Some authors have emphasized the epidemiological importance of oral lesions as an infection source, since viable bacilli have been detected in these lesions by histopathological exam through smears and by rinsing of the oral cavity. For others, the prevalence is of granulous bacilli.

Morphologically the lesions vary from enanthemas to ulcers, perforations and scars, passing through papules, nodules (lepromas) and superficial erosions. They can involve the following areas:

- **Palate:** Although most authors have found more serious changes in the mid-forward portions, some have found the soft palate to be more commonly affected area [23]. The most varied types of lesions are observed: infiltration, ulceration, perforation, and reddish or yellow-reddish nodules, sessile or pedunculated, varying from 2 to 10 mm, some confluent, and prone to ulceration.
- **Tongue:** It is affected in 17% to 25% of the cases [24], mainly the dorsal surface, especially the anterior two-thirds. Changes from superficial erosions with loss of the papillae and longitudinal fissures have been described to nodular infiltration, that could lead to a "paving stone appearance". Scarring can also occur. Unlike other subcutaneous muscles, in which a great number of bacilli are observed, the muscles of the tongue do not exhibit significant numbers. Mukjerhee and Bucci., *et al*. suggest that the lesions of the base of the tongue could originate from highly infectious nasal secretions, which pass from the nasal to the oral cavity.
- **Uvula:** In extreme cases there is intense fibrosis with partial loss or even complete destruction of the uvula.
- **Lips:** There may be macrocheilia (caused by infiltration) or microstomia (caused by ulceration and subsequent repair with fibrosis of perioral or lip lepromas).
- **Gums**: They are usually affected in the area behind the upper central incisors, often by contiguity, of lesions of the hard palate. Chronic gingivitis, periodontitis and periodontoclasia may occur [25].

How is the disease diagnosed?

A diagnosis of leprosy is usually straightforward if it is suspected as a cause of any skin or peripheral nerve lesion in a person from an endemic country. The cardinal signs of leprosy [26] are:

- Skin patch with sensory loss;
- Nerve enlargement; and
- Acid-Fast bacilli (AFB) in the skin.

The presence of one or more of these features establishes the diagnosis, which should be confirmed with a full-thickness skin biopsy.

The WHO's Cardinal Signs for the diagnosis, classification and treatment of leprosy are given in table 1.

Cardinal Signs[a]	Classification for treatment[a]
Hypopigmented or slightly erythematous macules with evident sensory loss Thickened peripheral nerves	Paucibacillary (1 to 5 skin lesions)
Positive acid-alcohol-fast smear or skin biopsy	Multibacillary (6 or more skin lesions)

Table 1: Any single cardinal sign is diagnostic and indicates the clinical classification for guiding treatment according to the World Health Organization (WHO).

Source: Britton., *et al*. [2]

Currently, diagnosis can be based on the phenolic glycolipid 1 (PGL-1) antibody titer and on polymerase chain reaction (PCR). PGL-1 antibody detection is useful in multibacillary cases but is of little use in paucibacillary patients [27]. PCR detection of the bacillus is highly specific and sensitive, but the cost of this technique and the required infrastructure stand in the way of routine use.

How to treat this disease?

The elimination of leprosy as a world health problem is feasible, as this infectious disease is one of the few that meet certain strict requirements for eradication.

Among the requirements leprosy meets are its spread by a single means of transmission (from untreated infected individuals) and the possibility of diagnosis by means of simple, practical tools. Furthermore, effective therapy is available and once prevalence falls below a certain level in a population, the likelihood of resurgence is very remote. Finally, unlike the situation with tuberculosis, leprosy infection does not seem to be unfavourably influenced by human immunodeficiency virus infection. By 2003 leprosy had been eliminated from 117 countries, but the disease continues to present a public health problem in 17 countries [28]. In 1981 the WHO introduced multidrug therapy with rifampicin, clofazimine, and dapsone (diaminodiphenyl sulfone) for first-line treatment [29]. All patients should receive this drug combination monthly under supervision (Table 2).

Minocycline, ofloxacin, and clarithromycin are among the drugs used as second-line treatments. The strengths of multidrug therapy are the prevention of resistance to dapsone, the rapid decline of infectivity of infected individuals, and the low rate of recurrence and reactions [30]. Nonetheless, this treatment period is long and presents logistical problems; adherence is difficult to achieve.

Presentation	Monthly, Supervised	Daily	Duration
Paucibacillary	Rifampicin 600 mg	Dapsone 100 mg	6 mo
Multibacillary	Rifampicin 600 mg	Clofazimine 50 mg	12 mo
	Clofazimine 300 mg	Dapsone 100 mg	
Single-lesion paucibacillary	Rifampicin 600 mg		Single dose
	Ofloxacin 400 mg		
	Minocycline 100 mg		

Table 2

Source: World Health Organization

Prevention

The chief means of preventing leprosy is interruption of transmission by treating those with infectious leprosy early. Multidrug therapy (MDT) was introduced because of the increasing spread of primary and secondary dapsone resistance worldwide. Its advantages are its proven efficacy and improved compliance, which is related to the limited duration of therapy and its monthly observed component Furthermore, early treatment before the onset of nerve damage reduces the long-term disability associated with leprosy [30]. The effectiveness of MDT prompted a World Health Orga¬nization coordinated campaign to implement MDT in all endemic countries, with the aim of reducing the prevalence rate of leprosy to less than 1/10 000.1,2 This has been successful at a national level, but some regions of endemic countries have yet to attain this goal. Impor¬tantly, the case detection rate has been slower to fall and has persisted around 250 000 cases per annum, indicating that leprosy control must be sustained through case detection and treatment of leprosy within integrated health programs. The recent WHO Expert Committee recommended a move from emphasizing a statistical leprosy elimination target based on case detection rates to the goal of reducing nerve func¬tion impairment and disability in leprosy patients [2].

Meta-analysis has confirmed the significant protective effect of immunization with Bacille Calmette–Guérin (BCG) against leprosy in both clinical trials and case-control studies [20]. In a major trial in Malawi, BCG induced 50% protective efficacy against

clinical leprosy, both tuberculoid and lepromatous forms. Re-immunization enhanced the protective effect by a further 50% [21]. Extensive BCG immunization of children in endemic countries has probably made a significant contri¬bution to the decline of leprosy. The addition of heat-killed M. leprae to BCG did not increase the observed protective efficacy of BCG in two trials. Other experimental vaccines protect against experimental leprosy infection [22,23].

Chemoprophylaxis may also be useful in the control of leprosy, particularly in low endemic regions. A large, randomized control trial in Bangladesh showed that a single dose of rifampin given to the close contacts of newly diagnosed leprosy patients resulted in a significant reduction of 57% (95% CI 33–72) in the incidence of leprosy in the contacts at 4 years [24]. Leprosy is commonly associated with poverty and overcrowding, and improved socioeconomic conditions have also contributed to the decline of leprosy in Europe and some Asian countries.

Conclusion

Hansen disease remains a concern today. All physicians must have a basic understanding of this disease in order to diagnose it and prevent disability and/or contagion. Knowledge of immunopathologic mechanisms reveals the complexity of certain diseases and provides the basis for understanding and treating them. Our current level of knowledge makes it possible to eliminate leprosy, a goal that calls for the concerted efforts of medical, social, political, and scientific resources to prevent the spread of an infection that should no longer exist.

World Leprosy Day is observed internationally every year on the last Sunday of January to increase the public awareness of the Leprosy or Hansen's Disease. This day was chosen in commemoration of the death of Gandhi, the leader of India who understood the importance of leprosy. This year it will be celebrated on 30th January 2019 i.e. Wednesday.

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