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On the Frontlines Against Leprosy: Navigating Challenges and Advancements - A Comprehensive Review

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INTRODUCTION

Leprosy is a chronic infectious disease caused by Mycobacterium leprae[1]. M. leprae is an acid fast bacillus with high infectivity. Leprosy also known as hansen's disease that primarily affects the skin and the peripheral nerves[2].Leprosy occurs in different clinico –pathological forms which depends on the status of host immune system[3][4]. Oral and Nasal lesions are common in lepromatous form which are probably source of spread of bacilli and transmission of disease[5][6][7][8]. Peripheral nerve damage occurs across the spectrum. Nerve damage may occur before, during, or after treatment. Some people have no nerve damage , while others develop anaesthesia of the hands and feet, which puts them at risk of developing neuropathic injury. Weakness and paralysis of the small muscles of the hands, feet, and eyes put people at risk of developing deformity and contractures. Loss of the fingers and toes is caused by repeated injury in a weak, anaesthetic limb. These visible deformities cause stigmatisation. Classification is based on clinical appearance and bacterial index of lesions. The WHO field leprosy classification is based on the number of skin lesions: paucibacillary leprosy (1–5 skin lesions) and multibacillary leprosy (more than 5 skin lesion)[9] . The mycobacterium has a preference for peripheral tissue to survive better at a temperature close to 30ºC rather than 37ºC. Hence it affects the skin, peripheral nerves, the mucosa of the upper airways and other tissues such as bone and some viscera [10,11,12].

PREVALENCE

INDIA

India has the largest number of cured and newly diagnosed leprosy patients in the world. The eyes of many of these patients are particularly vulnerable to injury. There have been several reports on fungal infections involving the cornea of leprosy patients[13,14,15,16,17].During the 54th World Health Assembly held in 2001, WHO declared that the historic target of global leprosy elimination was attained [18]. Globally over the last two decades, the registered leprosy prevalence has fallen by almost 90% and new case detection has fallen by about 50%. In terms of new case detection, the global decline is contributed entirely by India[19].

World

Worldwide , abot 250,000 new cases of leprosy are reported each year and about two million people have leprosy related disabilities.Three major endemic countries (India,Brazil ,Indonesia) accounts for 77% of all new cases[20,21]. Cohort studies show a peak of disease presentation between 10 and 20 years of age[22].In 1985, 122 countries in the world had leprosy prevalence of over 1 case per 10,000 population.By 2006, this number came down to six countries [23].These countries are: Brazil, Democratic Republic of Congo, Madagascar, Mozambique, Nepal and United Republic of Tanzania . Even countries like United States of America continue to report new cases[24].

RISK FACTORS

M leprae is discharged from the nasal mucosa of people with untreated lepromatous leprosy and spreads to infect skin and nerves[25].Risk factors for infection include household contact with a person with leprosy. There is no good evidence of an association with HIV infection, nutrition [26,27,28]. Complications of leprosy include nerve damage, immunological reactions and bacillary infiltration. Many people have peripheral nerve damage at the time of diagnosis, ranging from 15% in Bangladesh to 55% in Ethiopia [29].

SYMPTOMS

Signs and symptoms of leprosy usually appear three to five years after becoming infected with Mycobacterium leprae - the bacteria responsible for the disease. Leprosy usually affects the skin and peripheral nerves. Numbness and loss of temperature sensation (cannot sense very hot or cold temperatures) are some of the first symptoms that patients experience. As the disease progresses, the sensations of touch, then pain, and eventually deep pressure are decreased or lost. Signs that occur, such as relatively painless ulcers, skin lesions of hypopigmented macules (flat, pale areas of skin), and eye damage (dryness, reduced blinking) are experienced before the large ulcerations and loss of digits develop [30] .

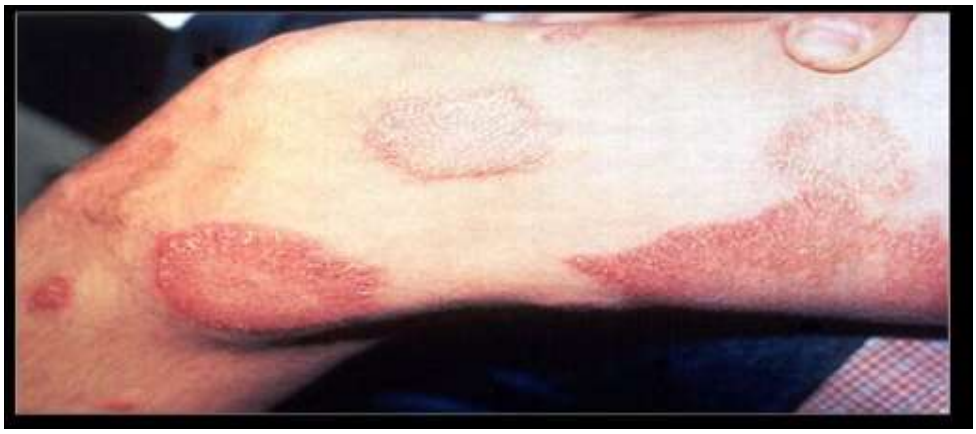

FIGURE1.

Long-term developing sequence of events begins and continues on the cooler areas of the body (for example, hands, feet, face, and knees) [medicine net,com]. Oral manifestations usually appear in lepromatous leprosy and occur in 20-60% of cases. They may take the form of multiple nodules (lepromas) that progress to necrosis and ulceration. The lesions are usually located on the hard and soft palate, in the uvula, on the underside of the tongue, and on the lips and gums. There may also be destruction of the anterior maxilla and loss of teeth [31,32,33,34]

CLASSIFICATION

Ridley and Jopling were the first to suggest a subdivision of leprosy on an immunological basis into five types; tuberculoid (TT), borderline tuberculoid (BT), midborderline (BB), borderline lepromatous (BL) & lepromatous (LL) [35] . Later they further developed this idea and correlated clinical and bacteriological findings in each group with respective immunological and histological findings [36]. This thorough classic classification has been replaced by a simpler and briefer one that considers two polar (TT, LL) and several borderline forms[37,38,39].

The Ridley-Jopling system is composed of five forms or classifications, listed below according to increasing severity of symptoms :-.

Borderline tuberculoid leprosy: lesions like tuberculoid leprosy but smaller and more numerous with less nerve enlargement; this form may persist, revert to tuberculoid leprosy, or advance to other forms.

Mid-borderline leprosy: many reddish plaques that are asymmetrically distributed, moderately anesthetic, with regional adenopathy (swollen lymph nodes); the form may persist, regress to another form, or progress .

Borderline lepromatous leprosy: many skin lesions with macules (flat lesions) papules (raised bumps), plaques, and nodules, sometimes with or without anesthesia; the form may persist, regress or progress to lepromatous leprosy .

Lepromatous leprosy: Early lesions are pale macules (flat areas) that are diffuse and symmetric; later many M. leprae organisms can be found in them. Alopecia (hair loss) occurs; often patients have no eyebrows or eyelashes. As the disease progresses, nerve involvement leads to anesthetic areas and limb weakness[40].

PATHOPHYSIOLOGY

The mechanism of transmission of leprosy is prolonged close contact and transmission by nasal droplet[41]. In addition to humans, leprosy has been observed in nine-banded armadillo, and three species of primates [42]. The bacterium can also be grown in the laboratory by injection into the footpads of mice[43]. There is evidence that not all people who are infected with M. leprae develop leprosy, and genetic factors have long been thought to play a role. It is estimated that due to genetic factors, only 5% of the population is susceptible to leprosy[44]. This is mostly because the body is naturally immune to the bacteria, and those persons who do become infected are experiencing a severe allergic reaction to the disease. However, the role of genetic factors is not entirely clear in determining this clinical expression and transmission[45].

The invading M. leprae has three main targets: periphera neural tissues (Schwann cells), small vessels (endothelial cells and pericytes), and the monocyte–macrophage system. The bacilli may survive and replicate within the Schwan cells and secondarily penetrate the perineural tissues[46][47]. In summary, entry through the respiratory route appears the most prevelent route, although other routes, particularly broken skin, cannot be ignored. The CDC states about the transmission of the disease that: "Although the mode of transmission of Hansen's disease remains uncertain, most investigators think that M. leprae is usually spread from person to person in respiratory droplets[48].

DIAGNOSIS

The diagnosis of leprosy is based on the 3 cardinal signs of the disease .

Which are:-

1. Skin patch with loss of sensation

2. Enlarged peripheral nerve

3. Positive slit-skin smear

The 1st cardinal sign: skin patch with loss of sensation

Sensory loss in macules or plaques is diagnostic of leprosy. Macules and plaques in leprosy may show several other typical abnormalities. The color can be hypo-pigmented , hyper-pigmented , erythematous or copper-colored . The texture of the surface may be dry and rough for loss of sweat in some forms of the disease, or shiny and smooth in others. There may be loss of hair growth. The lesions may become acutely infiltrated, swollen and erythematous. Some leprologists consider “characteristic” skin lesions an additional cardinal sign.

The 2nd cardinal sign of leprosy: enlarged peripheral nerve

An enlarged peripheral nerve represents the 2nd cardinal sign of leprosy . Enlarged peripheral nerves are very rarely found except in leprosy. In a leprosy endemic area, the finding of enlarged peripheral nerves is an important element to establish the diagnosis.

The 3rd cardinal sign of leprosy: positive slit-skin smear

Leprosy is the only disease in which there can be a massive invasion of the dermis or nasal mucosa with acid-fast bacilli (AFB). In some forms of the disease bacilli are demonstrated in slit-skin smears or in nasal mucus or scrapings. One gram of skin tissue in lepromatous leprosy may contain as many as 7000 million leprosy bacilli (Yawalkar S J2002).

There are leprosy cases where none of the cardinal signs is present. In the indeterminate (I) form of leprosy the 3 cardinal signs are negative. In this form of the disease , diagnosis is based on the development of the lesions over time and on histopathology. In pure neural leprosy all the 3 signs may be absent [49].

TREATMENT

The first-line drugs against leprosy are rifampicin, clofazimine, and dapsone. All patients should receive a multidrug combination with monthly supervision. Current controversies focus on the length of treatment , the mode of treatment, and relapse rates. Dapsone was the first effective antimicrobial agent against M leprae [50]. Clofazimine has a useful anti-inflammatory effect in erythema nodosum leprosum (ENL) and can be used as 300 mg daily for several months [51]. Moderately inflammed skin lesions should be treated with corticosteroids. Standard courses of prednisolone have been used, starting at 40–60 mg daily, decreasing by 5 mg every 2–4 weeks after evidence of improvement[52][53]. BCG was the first vaccine to be considered against leprosy [54][55]. The BCG vaccine is basically known to protect against infection with Mycobacterium tuberculosis, which has a number of antigens in common with Mycobacterium leprae. BCG vaccination might therefore also protect against M. leprae infection [56]. Leprosy is part of the World Health Organization’s (WHO) Expanded Program of Immunization and is known to decrease the risk of leprosy[57]. The protectiveness against leprosy of new generation of vaccines has yet to be determined, while it is well known that BCG protects against Leprosy [58].

BREAKTHROUGH

India has developed the world’s first laprosy vaccine. Mycobacterium indicus pranii (MIP) vaccine has been developed by National Institute of Immunology(NII). Drug controller General of India (DCGI) and the US Food and Drug Administration (FDA) have approved the vaccine.

CONCLUSION

Leprosy is caused by a bacteria called Mycobacterium leprae or Hansen's bacillus. Leprosy is named after a Norwegian physician Gerhard H. Armauer Hansen. It is unclear how leprosy goes from body to body, some think it is from inhaling the bacteria. Symptoms of leprosy seem to occur 3-5 years after infection. First, there are white or rosy patches of skin, called skin lesions. Nerves can be seriously damaged and hands and feet could become weak if the disease is not treated. There are two types of leprosy, tuberculoid and lepromatous. To treat leprosy, a mixture of three drugs, Dapsone , Rifampicin,

and Clofazimine, will kill most of the bacteria. Today, leprosy affects five to six million people throughout the world. It's found mostly in the tropics, like Africa, central and South America, India, and southeast Asia.

REFERENCES

1.noorden sk,lopez bravo l,sundaresan tk,Estimated number of leprosy cases in the world .BULL WHO 1992;70:7-10.

2.Tan SY, Graham C. Armuer Hansen(1841-1912): discoverer of the cause of leprosy. Singapore Med J 2008:49(7):520-21.

3.Panday AN,Tailor HJ.clinicohistopathological correlation of leprosy.Ind J Dermatol Venerol Leprol 2008;74:174-76

4.Sengupta U.Leprosy:Immunology.In:Valia RG and Valia AR(eds).IADVL Textbook and Atlas of Dermatology,2nd edn.Mumbai. Bhalani Publishing House.2001.pp.1573.

5.Brasil J, Opromolla DV, Freitas JA, Rossi JE. Histological and bacteriological study of lepromatous lesions of oral mucosa. Estamatol Cult 1973;7:113-9.

6.Reichart P. Facial and Oral manifestations in leprosy. An evaluation of seventy cases. Oral Surg Oral Med Oral Pathol 1976;41:385-9.

7.Mukherjee A, Girdhar BK, Desikan KV. The histopathology of tongue lesions in leprosy. Lepr Rev 1979;50:37-43.

8.Scheepers A, Lemmer J, Lownie JF. Oral manifestations of leprosy Lepr Rev 1993;64:37-43.

9. WHO Expert Committee on Leprosy.World Health Organ Tech Rep Ser 1988 ;768:1–51.

10. Aufderheide AC, Rodríguez-Martín C, eds. The Cambridge Encyclopedia of Human Paleopathology. Cambridge: Cambridge University Press; 1998. p. 141-54.

11. Laskaris G. Lepra. En: Atlas de enfermedades orales. Barcelona: Masson; 2005. p. 196-8.

12. Scheepers A. Correlation of oral surface temperatures and the lesions of leprosy. Int J Lepr Other Mycobact Dis 1998;66:214-7.

13. ANANDI, V., SURYAWANSHI, N. B., KOSHI, G., PADHYE, A. A. and AJELLO, L. Corneal ulcer caused by Bipolaris hawaiiensis. J. Med. Vet. Mycol. 26 (1988) 301.306.

14. DANIEL, E., MATHEWS, M. and CHACKO, S. Al-ternaria keratomycosis in a lepromatous leprosy patient. Int. J. Lepr. 65 (1997) 492.497.

15. HEMASHETTAR, B. M., VEERAPPA, T. S., VERMA, P. V., HANCHINAMANI, S., PATIL, C. S. and THAMMAYYA, A. Mycotic keratitis caused by Bipolaris spicifera.

Indian J. Pathol. Microbiol. 35 (1992) 274.277.

16. MATHEWS, M. S. and MAHARAJAN, S. V. Exsero-hilum rostratum causing keratitis in India. Med. Mycol. 37 (1998) 131.132.

17. TENDOLKAR, U. M., VARAIYA, A., AHUJA A. S.,MOTWANE, S. A., AND GOGATE, A. S. Corneal ulcer caused by Nocadia asteroides in a patient with leprosy. J. Clin. Microbiol. 37 (1999) 2392.

18. World Health Organization. Leprosy: Global Target attained- remaining endemic countries pose greatest challenge. Press release, 16th May, 2002 WHA /2, World Health Organization, 2002.

19. World Health Organization. Global leprosy situation, 2006. Wkly Epidemiol Rec 2006;81(32):309-16.

20. 9.Global leprosy situation,2009.Wkiy Epidemiol Rec 2009;84:333-340.

21.WHO Expertcommittee on leprosy.Seventh report . WHO Technical Report Series No 874,1998.

22. Fine PE. Leprosy: the epidemiology of a slow bacterium. Epidemiol Rev 1982.

23. World Health Organization. Global leprosy situation, 2006. Wkly Epidemiol Rec 2006;81(32):309-16.

24. World Health Organization. Addendum to global leprosy situation, 2006. Wkly Epidemiol Rec. 2006;81(37):353.

25. Desikan KV,Sreevatsa. Extended studies on the viability of Mycobacterium leprae outside the human body.Lepr Rev 1995;66:287-295.

26. Lienhardt C, Kamate B ,Jamet P,et al. Effect of HIV infection on leprosy: a three year survey in Bamako, Mali.int j Lepr Other Mycobact Dis 1996;64:383-391.

27. Lawn SD, Lockwood DNJ.Leprosy after starting antiretroviral treatment.BMJ 2007;334;217-218.

28. Ustianowski AP, Lawn SD,Lockwood DNJ. Interactions between HIV infection and leprosy: a paradox . Lancet Infect Dis 2006;6:350-360.

29. Oo KN,Yin NN,Han TT, et al.Serological response to chemoprophylaxis in extended contacts in leprosy: a randomized controlled trial . Nihon Hansenbyo Gakkai Zasshi: Japan J Leprosy 2008;77:3-10.

30. keherenf | November 29, 2007 .

31. Aufderheide AC, Rodríguez-Martín C, eds. The Cambridge Encyclopedia of Human Paleopathology. Cambridge: Cambridge University Press; 1998. p. 141-54.

32. Laskaris G. Lepra. En: Atlas de enfermedades orales. Barcelona: Masson; 2005. p. 196-8.

33. Fucci da Costa AP, Da Costa Nery JA, Wan-del-Rey de Oliveira ML, Cuzzi T, Ramos-e-Silva M. Oral lesions in leprosy. Indian J Dermatol Venereol Leprol 2003;69:381-5

34. Núñez-Martí JM, Bagán JV, Scully C, Peñarrocha M. Leprosy: dental and periodontal status of the anterior maxilla in 76 patients. Oral Diseases 2004;10:19-21.

35. Ridley DS, Jopling WH. A classification for research purposes. Lepr Rev 1962; 33: 119.

36. Ridley DS, Jopling WH. Classification of leprosy according to immunity: a five group system. Int J Lep 1996; 34: 255-77.

37. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five group system. Int J Lepr 1966; 34: 255–273.

38. Ridley DS. Histological classification and the immunological spectrum of leprosy. Bull WHO 1974; 51: 451–465.

39. Abulafia J. Historia natural de la lepra (hanseniasis). Resistencia e inmunidad. Arch Argent Dermat 1982; 32: 281–318.

40. Sehgal VN, Jain MK, Srivastava G. Evolution of the classification of leprosy. Int J Dermatol 1989; 28: 161–167.

41. "Leprosy". WHO. 2009-08-01. http://www.who.int/mediacentre/factsheets/fs101/en/. Retrieved 2010-01-31.

42. Rojas-Espinosa O, Løvik M (2001). "Mycobacterium leprae and Mycobacterium lepraemurium infections in domestic and wild animals". Rev. - Off. Int. Epizoot. 20 (1): 219–51. PMID 11288514.

43. Hastings RC, Gillis TP, Krahenbuhl JL, Franzblau SG (1988-07-01). "Leprosy". Clin. Microbiol. Rev. 1 (3): 330–48. PMC 358054. PMID 3058299. http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=358054.

44. "AR Dept of Health debunks leprosy fears". 2008-02-08. http://www.kfsm.com/Global/story.asp?S=7845322. Retrieved 2008-04-08 .

45. Kaur H, Van Brakel W (2002). "Dehabilitation of leprosy-affected people- a study on leprosy-affected beggars". Leprosy review 73 (4): 346–55. PMID 12549842.

46. Turkel SB, van Hale HM, Rea TH. Ultrastructure of dermal microvasculature in leprosy. Int J Lepr Other micromorphology of Mycobacterium leprae. Mycobact Dis 1983; 50: 164–171.

47. Mukherjee A, Misra RS, Meyers WM.An electron microscopic study of lymphatics in dermal lesions human leprosy. Int J Lepr Other Mycobact Dis 57: 506–510.

48. CDC Disease Info hansens_t Hansen's Disease (Leprosy).

49. Diagnosis of Leprosy Salvatore Noto and Pieter A M Schreuder Leprosy Mailing List, April 2010.

50. Britton WJ. Leprosy. In: Cohen J, Powerly WG, eds. Infectious diseases, 2nd edn. London: Mosby, 2004: 1507–13.

51.Rambukkana A, Yamada H, Zanazzi G, et al. Role of alpha-dystroglycan as a Schwann cell receptor for Mycobacterium leprae.Science 1998; 282: 2076–79.

52. Britton WJ. The management of leprosy reversal reactions. Lepr Rev 1998; 69: 225–34.33

53. Kiran KU, Hogeweg M, Suneetha S. Treatment of recent facial nerve damage with lagophthalmos, using a semistandardized steroid regimen. Lepr Rev 1991; 62: 150–54.

54. Fernandez JM. The early reaction induced by lepromin. Int J Lepr 1940;70:561—6.

55. Shepard CC. Vaccination against experimental infection with M. leprae. Am J Epidemiol 1965;81:150—63.

56. . Bagshawe A, Scott GC, Russell DA, Wingley SC, Merianos A, Berry G. BCG vaccination in leprosy: final results of the trial in Karimui, Papua New Guinea, 1963-79. Bull WHO 1989;67: 389—99.

57. Barreto ML, Pereira S, Ferreira AA. BCG vaccine: efficacy and indications for vaccination and revaccination. J Pediatr (Rio J) 2006;82(3):s45–54.

58. Setia MS, Steinmaus C, Ho CS, Rutherford GW. The role of BCG in prevention of leprosy: a meta-analysis. Lancet Infect Dis 2006;6(3):162–70.