

Leprosy – the source of infection and its mode of transmission

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Leprosy is a communicable disease caused by Mycobacterium leprae. Two principal factors involved in the transmission of the disease are the source of infection and the mode of entry. Although a lot is known about the source of M. leprae, the mode of transmission, till date, is shrouded in mystery. In this paper, I shall attempt to present to you a review of the relevant literature on the subject and add some of my own observations.

Source of infection

Until recently man was the only known source of infection. With the accumulating evidences showing feral armadillos harboring a disease caused by an acid-fast organism indistinguishable from M. leprae using all the now known tests for identification (1), it can no longer be said that man is the only source of infection. Recently, some cultivable and noncultivable acid-fast organisms from sphagnum and moss vegetation in coastal Norway and other parts of the European continent have been isolated (2). The results on studies to identify these organisms are awaited with great interest.

In a recent paper it has been said that the role of armadillos in the transmission of M. leprae to man is negligible (3). It is important to further investigate the armadillo as a natural reservoir of M. leprae.

Leprosy patients can be broadly divided into two groups - those who are bacilliferous to such an extent that organisms overflow from them into the environment and those who have a small number of bacilli limited to the intracellular locations and ordinarily have no means of exit from the body. The patients of the lepromatous and borderline lepromatous spectrum belong to the former and those who are classified as tuberculoid, borderline tuberculoid, indeterminate and purely neural come under the latter group. The patients of the lepromatous spectrum discharge M. leprae into the surrounding environment through nasal secretions, saliva, exudate from ulcers on the lepromatous skin, and normal secretions of the sweat, sebaceous and mammary glands.

The importance of nasal lesions and their role in the

dissemination of *M. leprae* has been reported as early as 1930 (4). According to Cochrane "a person with positive nasal secretion is relatively more infective than one in whom bacilli are found in the deeper parts of the corium of the skin" (5). The nose as a source of dissemination of *M. leprae* was rediscovered in the recent past and its importance reemphasized, perhaps, rightly so, by many workers. Pedley demonstrated the fact that a large number of acid-fast bacilli escape through the nasal secretions of lepromatous patients (6, 7). His reports were followed by that of Davey and Rees who showed severe nasal involvement in 53% of 295 patients in early lepromatous leprosy. They quantified the organisms in the nasal discharge and stated that 2.4×10^8 bacilli escape daily from the nose of lepromatous patients (8). The histopathological appearance of lepromatous lesions of the nose was well documented as early as 1966 by Job et al. (9) and recently by Barton et al. in 1973 (10).

Lepromatous granuloma was known to involve the mouth, pharynx and larynx as well (11). Lesions have been demonstrated in the lips, gums, teeth, tongue, oral mucosa, and hard and soft palate. Recently, discharge of a large number of bacilli in *saliya* has been identified and quantified. It is reported that 1.6×10^6 *M. leprae* can be isolated per mouth wash (12).

In a histopathological study of the skin lesions in leprosy acid-fast bacilli were demonstrated in sweat glands, sebaceous glands, hair follicles, epithelial cells and keratin (13). There is an earlier report of the presence of *M. leprae* in the epidermis (14). *M. leprae* is constantly discharged through unbroken skin of bacilliiferous lepromatous patients along with normal secretions of the glands and through keratin.

I believe that the mode of escape of the organisms from skin and nasal mucosa is similar and that the bacilli usually come out in small numbers if the epithelium is unbroken, along with the normal secretions of the subepithelial glands. When ulcerated, equally large numbers of *M. leprae* escape from the nose and skin. However, the lining epithelium of the mucous membrane of the nose is much thinner and more delicate and therefore given the same subepithelial nodular infiltration of lepromatous granuloma, the nasal mucous membrane ulcerates far more easily than the skin. Pedley has shown that human milk from lepromatous patients may also contain *M. leprae* and 4 ounces of milk may have up to 2 million bacilli (15).

A question often raised is whether non-lepromatous patients discharge bacilli into the surrounding environment or not. The lesions in this group of patients are usually in the skin and peripheral nerves and rarely in the mucous membrane. In almost all of them, the skin smears are negative for acid-fast bacilli using routine methods of examination, except during the reactive phase when ulceration of the skin lesion may occur. Nerve abscesses are known to produce sinuses, discharging caseous material containing bacilli. Histologically bacilli are seen in arrector pili muscles, Schwann cells, perineurial cells and very rarely macrophages. During the reactive phase, there is evidence of bacillary multiplication and

fairly large numbers of acid-fast bacilli are seen inside macrophages. It has been reported that in Nauru where 90% of the patients are maculo anesthetic 30% of the population have the disease (16). Brown, from his experience, states that most patients at sometime or other may be infectious (17). As one who studies the histomorphology of leprosy lesions, I see no reason to contribute to the view that nonlepromatous patients in general are infectious. However, I will admit that some of them may become infectious during the reactive phase when lesions show evidence of ulceration or sinus formation. The finding of so-called disproportionate prevalence of the disease in one endemic area where a large majority are of the tuberculoid spectrum, can be explained by other means. It should also be mentioned here that, to my knowledge, none has isolated enough organisms from nonlepromatous patients to infect the available animal models, even the most susceptible ones. Therefore, I would conclude that the role of nonlepromatous patients as a source of infection is comparatively very small indeed.

Are there carriers of *M. leprae*? If so, where do they carry the organisms? In a study of 7500 normal people in an endemic area by Chatterjee in 1976, 5000 skin biopsies were examined for *M. leprae* using the concentration technique (18). No histopathological examination was done. Acid-fast bacilli were isolated from 5.8% of the specimens studied. These organisms were noncultivable and their numbers were not large enough to grow in the mouse footpads. Similar findings were reported earlier by Figueredo and Desai in 1950 (19). It is not known whether these organisms are truly *M. leprae* and also in what part of the skin they remain. If these normal individuals carry viable *M. leprae* on their skin, they are possibly infectious and can be considered as carriers. In this connection it must be pointed out that there is a group of undiagnosed early asymptomatic lepromatous patients who carry a large number of bacilli in their skin and mucous membrane and are capable of disseminating *M. leprae*.

Finally, are patients under treatment infectious? The only method now available to test the viability of *M. leprae* is the mouse footpad culture. It has been shown that if the morphological index of a patient is 0, that is, if solid-staining bacilli are absent, the organisms fail to multiply in mouse footpads (20). It has also been shown that if a patient has had D.D.S. therapy for over 3 months, the organisms isolated from him are no more solid and are not cultivable in the footpads of mice (21). The conclusion drawn that non-solid-staining bacilli are nonviable and therefore noninfectious, is not accepted universally (22).

Retrospective studies show that infectivity of lepromatous patients on D.D.S. therapy is much reduced long before they become bacteriologically negative (23, 24). Lepromatous ulcers of the nose and skin heal quickly during antileprosy treatment as a result of lowered bacterial load and reduced edema of the lesions. Therefore, the overflow of the organisms into the environment from these patients is only through normal secretions which is much less. If

it is agreed that a significantly large number of organisms, if not all, in a treated patient is dead, the role of patients under treatment, in spreading the infection is negligible.

Mode of transmission

Pathogenic organisms enter the body generally along 3 routes, namely the skin, the gastrointestinal tract, and the respiratory passage. The establishment of the infection will depend on the virulence of the organism and the susceptibility of the individual. Virulence has 2 facets, namely the infectivity and the pathogenicity. Infectivity is the ability of the organism to get a foothold on the host and multiply there. Pathogenicity is its power to produce pathological changes and cause disease by altering the tissue components and interfering with their normal function. The susceptibility of the individual will depend on his constitution, environment, and immune mechanism. Each of these is a broad subject and I do not intend to dwell on any one of them. I will only review the findings that are relevant to the mode of transmission of *M. leprae*.

It was once thought that *M. leprae* which is not cultivable in laboratory media or tissue cultures, cannot survive for any length of time outside the human body and that intimate contact facilitates the organism discharged from the patient to be directly transmitted to the contact for the infection to take place. It is now known that *M. leprae* can remain alive in dried nasal secretions up to 7 days (8) and in moist soil at room temperature for 46 days (12). These findings are of great interest and bring a different dimension to the understanding of the mode of transmission. It is important to study further the survival of *M. leprae* in different environments.

M. leprae was thought to be only mildly infectious. The study of Godal et al. in 1976 has indicated that infectivity of *M. leprae* is very high. About 50% of the subjects with occupational or household exposure to *M. leprae* for more than 1 year gave a positive immune response to *M. leprae* using lymphoblast transformation test (25). However, it has been reported that only 5.8% of close contacts as between spouses develop the disease (26). Therefore, it is clear that although the infectivity of *M. leprae* is high, the pathogenicity is very low.

Transmission of leprosy can be both direct and indirect. In a study the attack rate is 4 times more in contacts than in noncontacts (24). In another study the attack rate among household contacts is 10 times higher than from the general population. This rate is doubled if there are multiple index patients in the same household (28). It is reasonable to accept that direct contact is perhaps far more effective in conveying the disease than indirect contact. Organisms may be carried live in clothes, objects used by the patient, food, water, dust, etc. The floor of the house or hospital or the ground where the infected material is shed, all

contain live bacilli. It must be conceded that indirect method of transport of bacilli is another important factor in the transmission of the disease.

Some workers have suggested that the blood sucking insects like fleas, bed bugs, lice, and mosquitoes can carry *M. leprae* (29, 30). Acid-fast bacilli isolated from mosquitoes have been identified as *M. leprae* using mouse footpad culture (31). Usually pathogens carried by vectors go through a cycle to become infectious as in plasmodium or they live and multiply in vectors, like rickettsia or viruses. Recently, Geater has reported the housefly as a vehicle for *M. leprae* (32). The housefly serves as a transport for many pathogens in the tropics. *M. leprae* can be conceived as one of its rare, and not quite so important passengers. The role of vectors in transferring *M. leprae* mechanically should be very small indeed.

What is the mode of entry of *M. leprae* into the body? Let me begin by saying the exact site and mode of entry is not yet defined. There are several hypotheses.

The age-old concept of making skin the favored site of entry has had its ups and downs. Several authors have identified *M. leprae* in the skin of contacts and it is also reported a higher percentage among those positive contacts develop leprosy (18, 19). Assuming that these organisms survive on their skin surface, they should have been transferred from the patients by direct contact, from fomites or by other mechanical means.

M. leprae is an inert organism, is nonmotile and is not known to produce any toxins. Therefore, it could not possibly penetrate the unbroken skin and the only way it gains access into the skin is through broken epithelium caused by minor injuries, insect bites or scabetic lesions. In a large majority of persons thus infected, the organisms could easily be taken up by macrophages and are destroyed by nonspecific and specific immune mechanisms. In a study it was found that *M. leprae* is ingested by macrophages within 20 minutes (33). In some individuals *M. leprae* may be engulfed by parenchymatous cells such as endothelial cells, arrectores pili muscles, or perineurial cells. Thus, much unlike other pathogens, *M. leprae* may get an unorthodox, unconventional entry into the body, and remain unrecognized or though unrecognized unharmed by the immune system. It is quite possible that this is the beginning of an indeterminate lesion, the primary lesion in leprosy.

It is known that the initial lesion is single and shows a regional variation influenced by socioeconomic factors and the secondary lesions are multiple and are in the peripheral parts of the body, being the preferential site of *M. leprae* (34). Further, there are patients who have a single nodular lepromatous lesion with no signs of the disease in any other parts of the body (35, 36). Certainly the skin entry of *M. leprae* is favored by many workers.

Recently a strong case is being put forward in favor of the infection through the respiratory tract (37). Rees has successfully infected T.900r mice by exposing their heads to an aerosol containing *M. leprae* (38). *M. leprae* is also isolated from the

lungs several months after the infection, although histopathological lesions in the lungs are not shown. It is quite possible lung tissue can serve as a transit point of *M. leprae* especially the alveolar macrophages. In a study by Chacko (39) of nasal biopsies of contacts, lesions suggestive of indeterminate leprosy have been demonstrated. However, it is felt that the epidemiological evidence is not suggestive of an airborne infection (34).

Pedley has pointed out that a breast fed infant of a lepromatous mother can ingest millions of bacilli in a day and has suggested that the gastrointestinal tract is a mode of entry of *M. leprae*. The transport of *M. leprae* by flies can easily carry them through contaminated food into the intestinal tract. As in tuberculosis, intestinal mucosa, without showing any pathological lesions can serve as an entry point of *M. leprae*. In an autopsy study, *M. leprae* was conspicuous by its absence in mesenteric glands (40). Certainly further studies are indicated to validate these hypotheses.

In this connection, I am reminded of the story of a few blind men who went to see an elephant. One felt the trunk and said "Elephant is like a snake," another felt its legs and exclaimed "Elephant is like a pillar, " yet another felt the tusk and thought "Elephant is like a spear," and so on. Unfortunately, none of them saw the elephant. This may summarize our present position with regard to the mode of transmission of *M. leprae*.

There is much more ground to be covered with regard to this subject, and I hope in the not too distant future we will be in a better position to define the mode of entry of *M. leprae* and thus be able to suggest measures to prevent its entry.

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