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Editorial

World Leprosy Day 2018: How forward respecting the past?

The World Leprosy Day is a day set aside to raise awareness for people affected by leprosy. The French humanitarian Raoul Follereau selected the date for World Leprosy Day in 1953. He wished to pay homage to the life of Mahatma Gandhi and his death on 30th January, 1948. It is being observed on the last Sunday of January every year since 1954. The theme for this year is 'Zero Disabilities in Girls and Boys'.

How can leprosy be prevented? The epidemiology of leprosy is not yet fully understood. To treat it, yes. However, during treatment, the damage to the nerves may get worse, and the patient may become more physically challenged than before. To cure it? After antibacterial treatment is stopped, the immunological disease will remain for years to come, and nerve damage may cause new problems throughout life.

The fact that leprosy can be prevented, treated and cured may not become true if leprosy is not diagnosed early and treated immediately before the *Mycobacterium leprae* antigenic determinants and new determinants induced by *M. leprae* have done irreversible damage. Is it possible to diagnose the patients early? None of the presently used tests is able to do this. These tests can only indicate that a person has been in contact with *M. leprae*, but not whether he or she will develop the disease. There is no test to predict who will develop disease after they have been exposed. Infection can be demonstrated with polymerase chain reaction (PCR) and other methods, but often contamination by *M. leprae* as well. However, not whether the patient has disease or was only exposed.

Only an estimated 20 per cent of humans are capable to develop leprosy (unpublished observation), 80 per cent are not, not even if severely immune-depressed (HIV and drug induced). Of the 20 per cent who are capable to develop the disease, only 5-10 per cent will show active leprosy (unpublished observation), and do that along an immunological spectrum as described by Ridley and Jopling and independently by Leiker in the same year, 1966. In the other 90-95 per cent, it is the adaptive immunity that prevents the disease from developing.

The first immunological test available was the lepromin test, an intracutaneous test developed by Mitsuda in 1919[1]. In 1941-1942, Dharmendra made a slight change in manufacturing and it was standardized in 1979 by Sengupta[2]. This test has been replaced in laboratories by tests that measure the cell-mediated immunity (CMI) against *M. leprae* antigenic determinants. However, these tests showed only to be useful during the follow up and not in the diagnosis[3].

Just after the Second World War, the first articles on leprosy serology came from Argentina[4] and later from Japan[5,6]. The first major useful serological test came from the laboratory of Patrick Brennan in the early 1980s[7]. This test [anti-phenolic glycolipid I (PGL-I)] made an important contribution to the study of epidemiology, but could not diagnose leprosy. Duthie *et al*[8] developed a lateral flow test readable by mobile phone that used a fusion protein of two *M. leprae*-specific proteins [leprosy IDRI diagnostic-1 (LID-1)] and PGL-1. The LID test could also not diagnose leprosy as disease and was only marginally better than the anti-PGL-1 test.

When it was realized that immunological tests were of little value, PCR was advocated and different PCR tests were used[9]. Though some of these tests may indicate that the bacilli are alive in the sample these do not diagnose leprosy as a disease. There are a large number of people who carry *M. leprae* DNA or RNA without developing the disease.

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In 1975 Antia *et al*[10] showed that even clinically uninvolved nerves could show some pathology. Antia hypothesized that contacts might also show some nerve involvement (personal communication). Last year, during the Brazilian congress Santos and colleagues[11] from the group of Goulart (Uberlândia, MG, Brazil) reported demyelination in contacts of leprosy patients, both in PGL-1 positive as well as in PGL-1 negative. They treated these contacts, but it would be interesting to see if all these 'patients' developed leprosy.

It is known that PGL-1 can damage the nerve, but also looking for lipoarabinomannan (LAM) in the PGL-1 negative may be of interest. According to the group of Baas and Das[12,13], LAM damages the Schwann cell by complement activation. LAM is an antigen which remains for a long time after the host has been 'infected' and *M. leprae* is dead. But again: does detectable nerve involvement mean that the disease will develop?

How does *M. leprae* survive in the body and cause disease? As per one hypothesis it enters a host cell and once inside manipulates the cell to create the environment in which it can survive and multiply. This mechanism has been described for viral as well for bacterial infections[14]. Whether it has to transform to a stem cell as Hess and Rambukkana[15] have proposed may be going too far. To identify this reprogramming of a host cell may be a way to diagnose leprosy as a disease.

In 2016, 8.9 per cent of the new cases were children and 6.7 per cent presented with visible deformities[16]. How can children be saved from this disease? The only way may be to 'go back to the past', to teach again the clinical skills to diagnose leprosy and to go out into the 'field', to search and diagnose the children with leprosy and to treat them under careful follow up, most importantly to treat any reactive phenomena as soon as possible. This is an enormous undertaking which requires the input and involvement of everyone, from the government to the clinicians and the individuals living in the leprosy endemic areas. It is, however, most important to diminish the stigma associated with leprosy.

One must realizes that leprosy is one of the oldest recorded diseases in the world, and it targets the nervous system, especially the nerves in the cooler and mobile parts of the body - the hands, feet and face. Since the infected person does not die, the consequences of the damage will stay with the patient all his life. It will contribute to his or her disability, will diminish the quality of life and will increase the fear in his or her surroundings. We need to diminish this fear and turn it into cooperation because only then we will be able to achieve zero disability in girls and boys.

***Conflicts of Interest*:** None.

Bernard Naafs[1-4]

[1]Foundation Global Dermatology, Munnekeburen, The Netherlands, [2]Regional Dermatology Training Centre, Moshi, Tanzania, [3]Instituto Lauro de Souza Lima, Bauru, SP, Brazil & [4]Department of Dermatology, Ayder Referral Hospital, University of Mekelle, Mekelle, Tigrae, Ethiopia
benaafs@dds.nl

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