

Ana Carla Pereira*

LEPROSY: GENETIC OR NON-GENETIC? NO MORE A QUESTION.

The history of leprosy was always permeated by the discussion about the contribution of genetics for its occurrence. Even in the Middle Ages, when the divine nature of the disease was widely considered, the idea of heredity was raised. The association of a microorganism to disease, by Gerhard Henrik Hansen Armauer in 1873, sparked great debate between hereditarians and those who believed exclusively in the infectious disease theory. This can be observed from registered discussions between the young Hansen and his superiors, Carl Wilhelm Boeck and Daniel Cornelius Danielssen, enthusiasts of the theory of heritable nature of leprosy, as copied below.

"...your opinions about leprosy are completely wrong. You believe that the disease is hereditary but not infectious. The truth is that it is infectious but not hereditary".¹

"I want to say that, if I formerly may have doubted the theory about the heredity of the disease, I have now no longer any doubts about it."²

The bacillus discovery grounded the discussion about the causality of disease in the First International Conference on Leprosy, in Berlin, 1897, ending by putting it as a purely infectious and isolation as recommended treatment.

The infectious nature of leprosy became undeniable, however, observations continued to show that the presence of the bacillus, although necessary, was not sufficient to trigger the disease. The multifactorial nature has served as a backdrop to the first obstacle encountered by Hansen in experiments *in anima nobile*, from its attempts to fulfill Koch's postulates, i.e. the existence of natural resistance.

In the twentieth century, twin studies and epidemiological studies, indicating the ethnic and familial

Pereira AC, Hanseníase: genética ou não genética? Não mais uma questão. *Hansen Int.* 2010; 35(2), p. 9-16.

aggregation of the disease, gave the keynote for a new discussion about the disease causality. The clinical form stability presented by patients, observed by Opromolla as an indicative of the genetics role in the disease course, and the persistence of the disease in some countries, despite of elimination strategies taken by WHO since 1991, also reinforces the idea of genetics factors as a determinant of leprosy outcome. Thus, the multifactorial nature of leprosy was evident, so that any simplistic view to the cause of this infectious disease should be reviewed. In this context, in the 1960s, Bernardo

Beiguelman's studies in Brazil, contributed greatly to the establishment of the idea of multifactorial disease. The progress of studies in genetic epidemiology

best explained the complex nature of the disease, making it a model for investigations about genetics in infectious diseases, due to factors such as, clinical presentation classified into clusters defined by the immunology of the host.

In recent decades, the rapid development of molecular tools and the consequent unraveling of the human genome have stimulated research on genes and markers involved in the predisposition for diseases. However, data are still weak and there is much to be done. Some

* Pharmaceutical Sciences, Ph.D, Scientific Research at Lauro de Souza Lima Institute.

genes, such as the HLA complex and interleukin-10 are well established as participants in the hazards, while others do not have data replicated for different populations.

It is important to underline also the contribution of genetics to the discovery of the host-pathogen interaction process and better understanding of the pathophysiology of diseases. As an example, from a recent “genome wide association” study, conducted to the Chinese population, a relevant parallel could be established between leprosy and Crohn’s disease due to the identity of susceptibility markers, which underlies some analogy between the pathogenic mechanisms involved in these diseases³.

On current science, the discussion had lost the nuance observed in contagionists and anticontagionists debates. In these days, when the character of complex disease is unquestionable, the studies aim to unfold predictive risk markers to improve the management of the diseased or to point prophylaxis strategies for contacts under high risk.

Finally, after one century of discussions, proved the feasibility of inheritance for leprosy susceptibility, genetic epidemiology becomes an area of great interest for leprology, with promises of large improvement in this area of knowledge.

REFERENCES

- 1 Marmor MF (2002) The ophthalmic trials of G. H. A. Hansen. *Surv Ophthalmol* 47:275–287.
- 2 Pandya S (1998) Anti-contagionism in leprosy, 1844–1897. *Int J Lepr Other Mycobact Dis* 66:374–384.
- 3 Zhang FR, Huang W, Chen SM *et al.* (2009) Genomewide association study of leprosy. *N. Engl. J. Med.* 361(27): 2609-2618.