

THE "IMPROBABLE" HANSENIASIS VACCINATION

EDITORIAL

When Fernandez^{1,2} reported that Mitsuda-negative children were converted to Mitsuda-positivity after injections of BCG, the hansenological world almost evenly divided itself into two currents of opinion that fiercely combated with each other: the BCG "converters", very enthusiastic about the possibility of hanseniasis vaccination, and the skeptical "non-converters", who either could not duplicate Fernandez's observations or attributed eventual conversions to a kind of "maturation" or to the Mitsuda tests routinely performed before and after BCG, not to BCG itself.

A lone study³ diverged from both currents: BCG (as well as infection by *Myco. tuberculosis*) *does convert* the Mitsuda reactions from negativity to positivity, *but would not be useful* as a vaccine against hanseniasis. This seeming contradiction is based on an earlier theory^{4,5,6} in which about

20% of the human species is considered genetically incapable of becoming Mitsuda-positive after infection by *Myco. hansenii*, as postulated in the thirties, by *Myco. tuberculosis* or stimulation by BCG, as complemented 20 years later³. That hypothetical 20% group of "constitutional non-reactors" was named "Anergic Fringe", now renamed "Hansen-Anergic Fringe" (HAF), to stress the specificity of that anergy. The HAF, "a race within a race" as qualified by Kinnear Brown & Stone⁷ commenting on the theory, was supposedly the "human reservoir" of *Myco. hansenii*, responsible for the perpetuation of the endemic. As this minority "reservoir" was not affected by BCG — the 12.5 to 25% "exceptions" of the conversion in practically all studies that followed Fernandez's — its vaccinating possibility was put in doubt. On the other side, the majority who inherited a

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- (1) FERNANDEZ, J. M. M. Estudio comparativo de la reacción de Mitsuda con las reacciones tuberculinicas. **Rev. Argent. Dermatosis**, 23(3):425-453, 1939.
 - (2) FERNANDEZ, J. M. M. Sensitization to lepromin in presumably non-leprous individuals. *Int. J. Lepr.*, 11(1):15-22, 1943.
 - (3) ROTBERG, A. Fator "N" de resistência à lepra e relações com a reatividade leprominica e tuberculínica; valor duvidoso do B.C.G. na imunização antileprosa. (**N-Factor of resistance to leprosy and its relationship with reactivity to lepromin and tuberculin. Doubtful value of BCG In antileprous immunization**). *Rev. Bras. Leprol*, 25(2):85-106, 1957.
 - (4) ROTBERG, A. Some aspects of immunity in leprosy and their importance in epidemiology, pathogenesis and classification of forms of the disease. Based on 1529 lepromin tested cases. *Rev. Bras. Leprol.*, 5(n. esp.):45-97, 1937.
 - (5) ROTBERG, A. Modern trends in the study of the epidemiology of leprosy. In: PACIFIC SCIENCE CONGRESS, 6., Berkeley, 1939. **Proceedings**. Berkeley, 1939. v.5, p. 939-945.
 - (6) ROTBERG, A. The influence of allergic factors in the pathogenesis of leprosy. In: PACIFIC SCIENCE CONGRESS, 6., Berkeley, 1939. **Proceedings**. Berkeley, 1939. v.5, p. 977-982.
 - (7) BROWN, J. A. K. & STONE, M. M. Tuberculoid leprosy in identical twins. *Lepr. Rev.*, 29(1):53-55, 1958.

"natural factor of resistance" ("N-Factor") would become Mitsuda positive after the action of different stimuli, but this conversion is relatively unimportant from the epidemiological viewpoint.

These rather pessimistic conclusions of the "N-Factor/HAF" theory were unfortunately confirmed by extensive studies carried out by the W.H.O. in Burma^{8,9}, which led to the final statement of a W.H.O. Expert Committee 10 referring to the "improbability" of a specific hanseniasis vaccine in the near future. Although it should be repeated that an artificial anticipation of the Mitsuda reactivity by BCG in the "N-Factor" majority is desirable from the clinical point of view and certainly preferable to a late natural conversion by *Myco. tuberculosis* or *Myco. hansenii* 11 the discussion about BCG, which raged for over two decades, came almost abruptly to an end after the W.H.O.'s reports.

The possibility of obtaining considerable amounts of *Myco. hansenii* from experimentally infected armadillos triggered off a flare-up of vaccination studies. The hope behind this second phase is that which was not feasible with the live, but only cross-specific BCG, would now be feasible with the

killed, but specific *Myco. hansenii* in massive suspensions or concentrated extracts. In some studies the killed armadillo's bacilli are mixed with the live BCG. As the latter was already proved to be inoperative, it might be considered an inert part of the vaccination material — unless a synergistic effect of live BCG and killed *Myco. hansenii* is expected.

The preventive efficacy of those new armadillo vaccines deserves study, but not in the field again, at the moment. At the time of the BCG fiery discussions, the W.H.O.'s ample, long and expensive survey in Burma was possibly justified to settle a worldwide scientific conflict. It does not seem justifiable now, unless previous comparative studies between two small groups prove that the proposed new vaccines have a significant advantage over BCG as regards reducing the HAF and provoking strong (++) and (+++) Mitsuda reactions in the genetically conditioned non-reactors.

Although we would heartily welcome that scientific and prophylactic breakthrough, we prefer to remain skeptical for the time being and take sides with the W.H.O. Expert Committee who considered hanseniasis vaccination "improbable in the near future".

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- (8) BECHELLI, L. M.; GARBAJOSA, G.; UEMURA, K.; ENGLER, V.; MARTINEZ DOMINGUEZ, V.; PAREDES, L.; SUNDARESAN, T.; KOCH, G.; MATEJKA, M. B.C.G. vaccination of children against leprosy, preliminary findings of the WHO-controlled trial in Burma. **Bull. Wld. Hlth. Org.**, 42(2):235-281, 1970.
- (9) WORLD HEALTH ORGANIZATION. Expert Committee on Leprosy: fourth report. Geneva, n.º 459, 1970.
- (10) WORLD HEALTH ORGANIZATION. Expert Committee on Leprosy: fifth report, Geneva, n.º 607, 1977.
- (11) ROTBERG, A. Uma revisão panorâmica da leprologia moderna. (**A panoramic review of modern leprology**). In: **Medicina Tropical**. Lisboa, 1966. p. 83-96.