The "Hansen-anergic Fringe" and Renewed Doubts About Vaccination

TO THE EDITOR:

From extensive observations made during the years 1933–1938 in Sao Paulo, Brazil ([8, 9, 10, 11]), it was hypothesized that about 20% of the human species is genetically incapable of becoming Mitsuda positive after infection by Hansen's bacillus. This "Anergic Fringe," now renamed "Hansen-anergic Fringe" (HAF) in order to stress its specificity ([14]), was supposedly made up of the "predisposed" persons who, "accessory factors" concurring, would eventually develop the various clinico-pathological aspects of bacillary hanseniasis. On the other side, the majority who inherited a presumed "natural factor" ("N-factor") of resistance would react positively to the Mitsuda test after said infection and would either remain healthy ("subclinical infection") or, with the cooperation of those "accessory factors," would develop non-bacillary macular or tuberculoid disease. An intermediate range was supposed to be responsible for the "intermediate" (now called "borderline") aspects of the disease.

This pathogenetical theory diverged from the accepted notions of that time that predisposition depended on general debilita-

tion by malnutrition, alcoholism, various infections and infestations. It diverged also from Mitsuda's own viewpoint ([5]) that Mitsuda negativity was a consequence of advanced bacillary hanseniasis and contradicted the authors who believed that Mitsuda positivity or negativity depended, respectively, on a "general" hyper- or hypoergy of the skin to a variety of test substances.

The "N-factor/HAF" theory was rather skeptically received ([15]), but soon afterwards favorable editorials ([6, 7, 16]) and numerous articles began to admit its plausibility or validity. The hypothesis is now generally accepted, although most authors have coined a confusing and unnecessary variety of designations for the 46-year-old HAF ("constitutional anergy," "insufficient potential immunity," "monovalent anergy," "genetical incapability to develop resistance," "genetical defect," "inherent incapacity to react to Mitsuda" or "to recognize Hansen's bacilli," "primary cellular defect," etc.) and for the "N-factor" ("unconstitutional immunity," "potential immunity," "unknown constitutional factor," "genetical capability to develop resistance," "host-determined capability of recognizing Hansen's bacilli," "innate cell-mediated immunity," etc.).

Fernandez's observations ([3, 4]) that Mitsuda-negative children were converted to Mitsuda positivity by injections of BCG seemed to most authors to annul the existence of that HAF and to herald the beginning of successful vaccination. However, it was observed ([11]) that the HAF remained Mitsuda negative and could be identified in practically all the articles that followed Fernandez's by a 12.5%–25% fringe of "exceptions to the reversal." This fact has led to the admission of BCG and *Mycobacterium tuberculosis* as stimulants of Mitsuda positivity in the "N-factor" majority, but has also confirmed the existence of "non-reactors" and has cast doubts about its preventive usefulness. This rather pessimistic outlook was confirmed by the practically general failure of the World Health Organization's preventive studies with BCG ([1]), and by the statement of a WHO Committee ([2]) about the "improbability" of a specific vaccine in the near future.

New vaccines and techniques were recently introduced and are being extensively studied. It is obviously desirable that more optimistic conclusions should be reached. However, before extensive, costly, and time-consuming preventive studies in the field are programmed again, it would be advisable to demonstrate in advance that the various types of vaccines do eliminate or, at least, do significantly reduce, the HAF in comparative studies with BCG. This applies to animal experimentation.

Nevertheless, vaccination with BCG or with any other equivalent or more active material seems to be indicated for the general population of endemic areas, especially for contacts, since it artificially and precociously stimulates the "natural reactors," i.e., the "N-factor" majority. As previously stated ([11]), it would be better to induce the Mitsuda positivity of that majority and not wait for it to occur naturally after the occasional action of *M. tuberculosis* or, worse yet, of *M. hansenii* itself.

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