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A PROPOS THE BCG TEST[1]

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Tuberculosis specialists should have much interest in keeping abreast with the published works on allergy in leprosy (7). The BCG test, an allergic reaction to bacillary bodies, is comparable to the Mitsuda lepromin test, which has been widely used in leprosy since 1933 (3, 5, 8).

With regard to the study of allergy to the bacillus bodies in tuberculosis, I think that the antigen should be prepared from bacilli killed by heat. The inoculation of living BCG into the organism must be considered as a true vaccination, capable of producing a state of allergy. So long as the test is made with a very small dose of dead bacilli, and if it is not repeated at too short intervals, it has virtually no allergizing action. It may, at most, produce an extremely weak and transient allergy.[2]

Furthermore, the antigen should, in my opinion, consist of a saline suspension of heat-killed virulent Koch bacilli, and not BCG, which is a Koch bacillus made avirulent by laboratory artifices. I have, in fact, shown that the intensity of the reaction to acid-alcohol resistant bacillary bodies depends on the degree of virulence of the bacilli used in the preparation of the antigen (1, 2).

Finally, the introduction of the antigen into the organism should be by intradermal injection. This is the only precise method, and in addition it permits easy reading of the reaction. Tests made by skin scarification or by multipuncture are not to be recommended. The quantity of bacilli inoculated into the organism by such methods is certainly very variable from one person to another, and the intensity of the reaction will therefore not serve to evaluate the degree of allergy of the persons so tested.

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[1] Reprinted in translation with permission, from *Revue de la Tuberculose* 21 (1957) 530-533. The references have been completed and set up according to JOURNAL practice.—EDITOR.

[2] In leprosy, the allergizing effect of repeated lepromin tests has not been studied fully. In experimenting with man, it has never been taken into account that the change of the reaction to lepromin may be a manifestation in the course of a latent leprosy infection, or a result of infection by the Koch bacillus. Personally, since 1939 I have tested all my patients with lepromin once a year, and I have never seen the slightest indication that would permit one to suppose that these widely-spaced tests had had an allergizing effect. In experiments on animals, it is not impossible that the possible sensitization produced may be due to repeated injections of the human tissues contained in the lepromin.

From 1940 to 1944 I studied the action of the antigen composed of heat-killed virulent Koch bacilli, and found that it would provoke, in persons infected with the Koch bacillus, a reaction that was similar, clinically and histopathologically, to the Mitsuda reaction in leprosy (1-4).

A positive reaction practically always begins 24 to 48 hours after the injection of the antigen, with a more or less pronounced localized acute inflammatory process, with congestion and edema. This early reaction is comparable to the early reaction of Fernandez in leprosy, and probably has the same significance. During the following days there is formed a small chronic infiltration of nodular aspect, violaceous-red in color, which increases in size and attains a maximum in one or two weeks. This nodular infiltration is the positive reaction, properly speaking. In very strong reactions the center of the nodule ulcerates and there is a seropurulent surface. Involution of the infiltration occurs gradually, but in the ulcerated reactions it may take several months for the regression to be completed. No visible reaction can be seen in persons free from tuberculosis, or if any appears it is only slight reddening for a few days.

This nodular reaction is therefore analogous to the late Mitsuda reaction in leprosy, the only difference being that the height of the nodular reaction induced by the heat-killed Koch-bacillus antigen is reached at the end of one to two weeks, whereas the height of the late lepromin reaction generally occurs in the third or fourth week.

Should it be desired only to ascertain whether the result is positive or negative, the reading could be made after one week. But if, on the other hand, one wishes to know the degree of intensity of the reaction, which is important, the reading should be made between one and two weeks after the injection of the antigen. In this case one should adopt the criteria established for the reading of the lepromin test (6).

In my opinion, the allergy to the bacillary bodies should therefore be studied, in relation to tuberculosis, by means of intradermal injections of a suspension of virulent Koch bacilli, killed by heat and phenolized 0.5 per cent[3]. The quantity of bacilli to be injected, suspended in 0.1 cc. of saline solution, should be 0.1 mgm. for individuals nonreactive to tuberculin, and 0.001 mgm. to 0.01 mgm. for tuberculin sensitives. The injection of a quantity of bacillus bodies equal to or more than 0.1 mgm. results in ulcerated reactions in persons positive to tuberculin.

This test should be performed routinely in persons who do not react to tuberculin, or in those who react only to very high doses of tuberculin.

Regarding false positive reactions to tuberculin, I did not observe any in testing over 2,000 persons with crude tuberculin in progressive doses up to 1 cgm. It is easy to demonstrate that the clearly positive reactions in

[3] The BCG vaccine is a suspension of avirulent Koch bacilli in aqueous solutions of different chemicals which vary from one laboratory to another. The addition of 0.5% phenol notably delays the lysis of the bacillus bodies, making it possible to store the antigen for years.

individuals sensitive only to 1 cgm. of crude tuberculin cannot be considered as false reactions, since these subjects also react positively to the intradermal injection of heat-killed Koch bacilli.

Persons who have been vaccinated with BCG and who are insensitive to tuberculin but who nevertheless react to the antigen prepared with heat-killed virulent Koch bacilli, I regard as relatively immune, because this reaction is a Koch phenomenon, and because subjects who are artifically desensitized to tuberculin react to this antigen. The tuberculin allergy and the allergy to bacillus bodies are two different phenomena, the former being a sensitization to toxins and the latter constituting an index of the state of resistance of the organism to superinfections.[4]

It is possible, furthermore, that the use of very weak doses of this antigen may elicit, in individuals infected with the Koch bacillus, a reaction quite similar to that of Mitsuda in leprosy, the intensity of the allergic reaction indicating the degree of resistance of the infected person to superinfection.

Finally, one should not forget that, in countries where leprosy is endemic, subjects free from tuberculosis but infected by the Hansen bacillus and sensitive to lepromin will generally react to the antigen prepared from the Koch bacillus.

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[4] In leprosy an analogous significance can be attributed to the late Mitsuda reaction. Individuals who are allergic to lepromin may resist superinfections, whereas those who remains anergic in spite of being infected with leprosy bacilli are susceptible to superinfections.