Cutaneous Testing in the Elderly Patient with Tuberculosis*

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A hypothesis is presented that the fully developed cutaneous reaction to tuberculin, as exemplified by diagnostic cutaneous testing in culture-positive patients with tuberculosis, is an “all-or-nothing” phenomenon. In the elderly, this characteristic is maintained, with the value of the test being limited only by an increase in anergy.

A cutaneous test with tuberculin is now generally requisite to the diagnosis and classification of tuberculosis,1,2 however, the utilization of the test in older individuals remains controversial because a variety of results have been reported3-5 which suggest that a gradual waning in sensitivity occurs. This waning is manifested as both smaller responses (hyperpy) and an increased number of complete nonreactors (anergy). Similar deficiencies have been recorded with a variety of other antigens producing cutaneous delayed hypersensitivity responses.6

This retrospective study of recent experience with the test in bacteriologically proven cases of tuberculosis does not confirm any age-related loss in the sizes of measured reactions. There is, rather, only an increase in the number of totally nonreactive patients, and the behavior of the test over the span of life would appear to be “all or none,” rather than gradually waning.

MATERIALS AND METHODS

The Division of Tuberculosis Control in British Columbia maintains a registry of all reported cases, which is reinforced by operation of a central mycobacteriology laboratory and diagnostic and treatment services, including supply of material for cutaneous testing with tuberculin and antituberculin medications. Thus, in the years from 1970 to 1974 (inclusive), I was able to obtain the case notes on 776 patients who had been tested with tuberculin at the time of diagnosis and in whom there was confirmation of the disease by cultural isolation of Mycobacterium tuberculosis.

Mantoux testing was the sole method employed, and only the results of cutaneous tests done within three weeks of the date of diagnosis were accepted. The large number available was possible because of a policy of repeating all tests more than two years old on initial referral. Five tuberculin units of purified protein derivative of tuberculin (PPD) (Connaught Laboratories) was used, this product being stabilized with polysorbate 80 (Tweem 80) and conforming in strength to International Standard Tuberculin PPD (product information circular). Reading was as the transverse diameter of induration after 48 hours, and all tests with recorded numerical values including those from 1 to 4 mm were used. The term, “anergic” (0 mm), is used in this report in the literal sense of complete failure of the immune mechanism to respond, as was originally intended by Von Pirquet.7 A frequency histogram comparing anergic and reactive patients by decade was constructed (Fig 1), and the means and standard deviations of the latter were then derived (Fig 2).

RESULTS

Sixty-seven (9 percent) of the patients were anergic at the time of diagnosis. Their distribution by decade indicated a slowly progressive increase to 18 percent in those 80 years of age and over (Fig 1); however, when only those showing some response were considered, there was no loss in the measured diameters of reactions, even in the very aged (Fig 2). Cutaneous sensitivity is apparently either well maintained or else fails completely.

The sixty-seven anergic patients were further evaluated and found to include 46 whose disease was advanced or miliary in extent. There were also 18 alcoholics, six with prior gastrectomy, six diabetic patients, four patients with cancer, and one receiving long-term adrenal corticoid therapy.

Four were reverters from previous reactivity (two with miliary tuberculosis, one with peritonitis, and one with far advanced disease), and although not all patients were retested, 24 of the 67 subsequently had conversion of their cutaneous reaction to tuberculin after a period of treatment. Eighteen were dead by 1978.

DISCUSSION

The results of cutaneous testing with tuberculin in these patients were clear-cut. They were either reactive or they were not, with only the latter (anergy) being increased in the aged. The consistency in measurements otherwise seen over the span of life was almost certainly contributed to by the method of using 5 tuberculin units of stabilized PPD and by restriction of the study to culturally proven cases.

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Five tuberculin units has been shown to be, in effect, a supramaximal stimulus, and it was given here to patients harboring *M. tuberculosis*, which would have provided all of the antigen necessary to "boost" their cutaneous hypersensitivity as much as possible.

The so-called booster effect from external testing is much more common in older patients and often presents a problem in evaluation of results. If it is understood as being a recall of waning sensitivity by the introduction of additional antigen, these data suggest that it cannot be expected to occur in someone already maximally primed from within. An increasing degree of response, then, would be better taken to indicate that no active disease is present, rather than being considered an apparent conversion.

The phenomenon of anergy is also separate from the declining reactivity of a "burnt-out" infection. In this study, anergy is confirmed as being a part of the aging process, but whether it is due to the presence of suppressor lymphocytes (as was recently suggested in the case of pleural effusions) or to other factors more related to immunosenescence remains to be established. The gradual increment with age suggests the latter.

The cutaneous test with tuberculin is the prototype of delayed hypersensitivity responses, and the hypothesis that it is an "all-or-none" phenomenon when the dosage of antigen is optimal and the host response is sufficiently primed should be confirmed by further studies. In a rather similar vein, Comstock and Wolpert have recently summarized the problems involved in cutaneous testing and have suggested an initial two-stage procedure as a baseline, in order to decrease subsequent conversions due to the booster effect.

REFERENCES
1. The Tuberculin Skin Test. New York, American Lung Association, 1974
2. Diagnostic Standards and Classification of Tuberculosis and Other Mycobacterial Diseases. New York, American Lung Association, 1974