

Use of Multiple Mycobacterial Antigens In Skin Testing Among the Navajo

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SINCE the advent of chemotherapy for tuberculosis, the prevalence of a variety of atypical mycobacterial infections has been reported in a variety of populations in different countries. Although many of these studies have been confined to the use of human tuberculin and a single atypical antigen (most often Battey), several researchers have used a spectrum of atypical antigens.

Bjerkedal used nine atypical antigens in his survey of Norwegian school children, and 14 percent of those tested reacted with 6 mm. or more induration to PPD-G as compared with only 0.2 percent who had reactions to PPD-S (1). Using PPD-B and PPD-G in conjunction with the human strain, Katz and co-workers found reaction rates (based on 5 mm. or more of induration) of 57 percent for PPD-S, 31 percent for

PPD-B, and 47 percent for PPD-G among adult mental patients in New York State; however, in only 2 percent were the PPD-G readings greater than the PPD-S, and in none of the patients did the PPD-B reaction exceed the PPD-S (2).

In an early study of Navy recruits throughout the United States, Edwards reported from 8 to 49 percent reaction rates (2 mm. or more) for a wide variety of atypical antigens, compared with 9 percent for PPD-3 (3). Smith and Johnston found high reaction rates for PPD-B and relatively similar rates for PPD-S, PPD-Y, PPD-scotochromogen, and PPD-F among medical and nursing students in North Carolina (4). The status of skin testing for atypical mycobacterial infections up to 1967 is well summarized by Smith (5). Palmer and Edwards recommended the use of another mycobacterial antigen, such as PPD-B, in addition to tuberculin, for distinguishing persons infected with tuberculosis from those infected with other mycobacteria (6).

One population group in the United States for whom tuberculosis remains a major health problem is the American Indian. The death rate from

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tuberculosis among Indians in 1967 was 16.2 per 100,000, or four to six times that for the overall U.S. population (7). For that same year, the incidence rates for tuberculosis in Indians was 169.8 per 100,000, compared with a U.S. rate of 23.0 for all races (7).

Methods

This study was made of Indians of the Shiprock Service Unit in the northeastern portion of the Navajo Reservation. This section covers parts of Arizona and New Mexico, as well as a small part of southern Utah. The Navajo employees of the largest single industry in the service unit, an electrical semiconductor assembly plant, were selected by random sampling to provide a study sample of adults. Students 6-16 years old at two Bureau of Indian Affairs boarding schools in the service unit were studied. Thus the reactions of about 900 children and 429 adults to six antigens were tested and read.

Each person was inoculated intradermally with 0.1 ml. of each of the six antigens, three on the volar surface of each forearm. The reactions to the nearest millimeter of induration were read 48 hours later by a single team of observers, who were unaware of which antigen caused which reaction.

Results

A total of 529 males and 800 females were tested. To maximize specificity at the risk of some loss of sensitivity, the criteria for a positive reading for a particular antigen was set at a reaction size of 5 mm. or more and at least 3 mm. greater than any other reaction. The distribution of the 286 reactions thus defined as positive for a single

infection is shown in table 1. Overall, 16.6 percent were positive for PPD-S, 1.8 percent for PPD-Y, 1.4 percent for PPD-B, 1.5 percent for PPD-G, and 0.6 percent for PPD-A. There was a general increase in the rate of positive reactions to each antigen with age. The rate of single infections among males tested was 15 percent and among females, 22 percent.

In addition, some 79 reactions were greater than 5 mm. but did not fall within the criteria mentioned before. These reactions were classified under "mixed" infections and analyzed as being positive for each of those antigens to which the reactions were greater than 5 mm. and at least 3 mm. or more greater than other reactions. The distribution of these "mixed" infections is shown in table 2. The largest group of "mixed" infections was in reaction to human tuberculin and photochromogen. In all, 16 different combinations of infections were suspected. As with the single infections, the reaction rate increased with age. Some 4 percent of the males and 7 percent of the females were presumed to be multiply infected.

In all, there were 365 reactors (an overall rate of 27 percent) to one or more antigens among the 1,329 Navajos tested. The 220 reactions to PPD-S represented 60 percent of these reactions.

Discussion

More than a third of the positive skin reactions were to antigens other than human tuberculin antigen. Comparative data on the Southwest Indians are scarce. From a compilation of data gathered by the Indian Health Service on Navajo school children ages 10 and 11, Pust reported a

Table 1. Number and percent of persons in each age group with positive reaction to 6 antigens

Age group (years)	Total in group	PPD-S		PPD-B		PPD-Y		PPD-G		PPD-A		PPD-F	
		Number	Per-cent ¹	Number	Per-cent ¹	Number	Per-cent ¹	Number	Per-cent ¹	Number	Per-cent ¹	Number	Per-cent ¹
5-9.....	291	12	4.1	1	0.3	1	0.3	1	0.3	1	0.3	0	0
10-14.....	523	30	5.7	10	1.9	1	.2	4	.8	3	.6	1	.2
15-19.....	93	9	9.6	1	1.1	0	0	0	0	0	0	0	0
20-24.....	139	34	31.0	3	2.2	5	3.6	1	0	1	.7	0	0
25-29.....	127	50	39.4	1	.8	7	5.5	7	5.5	1	.8	0	0
30-34.....	75	38	50.7	0	0	4	5.3	1	1.3	1	1.3	0	0
35-39.....	43	25	58.1	1	2.3	1	2.3	0	0	1	2.3	0	0
40-44.....	27	16	48.1	1	3.7	2	7.4	4	14.8	0	0	0	0
45-49.....	7	4	42.9	0	0	0	0	0	0	0	0	0	0
50 or more.....	4	2	50.0	0	0	1	25.0	0	0	0	0	0	0
Total.....	1,329	220	16.6	17	1.4	22	1.8	18	1.5	8	.6	1	0

¹ A positive reading for a particular antigen was set at a reaction size of 5 mm. or more and at least 3 mm. greater than any other reaction.

Table 2. Number and percent of persons in each age group with positive reactions to more than one antigen at the prescribed level (that is, presumably having "mixed" infections)

Age group (years)	Number	Human tuberculin and photochromogen		Human tuberculin and Battey		Human tuberculin and Gause		Avian and Gause		Battey, avian, and Gause		Other ¹	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
5-9.....	291	2	0.7	0	0	0	0	2	0.7	0	0	4	1.4
10-14.....	523	2	.3	3	.6	2	.3	2	.3	2	.3	6	1.1
15-19.....	93	1	1.1	1	1.0	0	0	0	0	0	0	2	2.1
20-24.....	139	8	5.8	0	0	0	0	0	0	1	.7	0	0
25-29.....	127	8	6.3	0	0	0	0	0	0	1	.8	7	5.0
30-34.....	75	6	8.0	0	0	1	1.3	0	0	0	0	7	9.3
35-39.....	43	4	9.3	1	2.3	0	0	0	0	0	0	4	9.3
40-44.....	27	1	3.7	0	0	0	0	0	0	0	0	0	0
45-49.....	7	0	0	0	0	0	0	0	0	0	0	0	0
50 or more.....	4	0	0	0	0	1	25.0	0	0	0	0	0	0
Total.....	1,329	32	2.4	5	.4	4	.3	4	.3	4	.3	30	2.3

¹ Includes: Gause and Battey; avian and fortuitum; human tuberculin and avian; Battey and fortuitum; photochromogen, avian, and Battey; human tuberculin, photochromogen, and Gause; human tuberculin, Gause, and fortuitum; human tuberculin, avian, and Gause; human tuberculin, photochromogen, and avian; human tuberculin, photochromogen, and Battey; photochromogen, avian, and Gause. Each occurred at a frequency of 3 or less.

positive skin reaction to PPD-S or PPD-B in only 6.4 percent, of whom 5.3 percent tested positive to human antigens and 1.1 percent to Battey antigen (8). Brigham reported skin tests on 201 isolated Havasupai Indians in a remote village in the Grand Canyon. He found 19 percent with 10 mm. or more reaction to PPD-S, 10 percent with 5 mm. or more to PPD-B, 13 percent with reactions to PPD-G, and 12 percent with reactions to PPD-Y. Among a group of Arizona Indians from several tribes, the majority under 20 years of age, he found 16 percent with 10 mm. or more reaction to PPD-S, 8 percent with 5 mm. or more reaction to PPD-B, 5 percent with 5 mm. or more reaction to PPD-G, and 10 percent with 5 mm. or more reaction to PPD-Y (9).

The studies by Edwards and co-workers of Navy recruits who were white males and lifetime residents of one county provide some additional data. Among those from Arizona 2.6 percent had 10 mm. or greater reactions to PPD-S, and 41.3 percent had 4 mm. or greater reaction to PPD-B. For New Mexico, the figures were 6.8 percent to PPD-S and 18.7 percent to PPD-B (10).

In the present study the overall reaction rate was 27 percent, although the rate for infections to human tuberculin antigens was only 17 percent. Approximately one-third of the positive reactions probably were caused at least in part by other infections. In terms of the effects of these infections on a tuberculosis detection program, it is

useful to compare the potential rates if one were to use only the PPD-S reading. With 5 mm. as the minimum criterion for a positive test, 23 percent would be detected. With 10 mm. or more, 21 percent would be noted. We can then assume that the 5 mm. rate would include as many as 6 percent false positives and the 10 mm., 4 percent.

Previous experimental work suggests that the specificity and sensitivity of multiple antigen skin testing are maximal when a simple criterion of 5 mm. or more reaction to human tuberculin is used (11). The labeling of the presumed "mixed" infections represents only one possible interpretation of that portion of the data. Edwards and co-workers have stressed the need for caution in interpreting multiple antigen reactions in various populations, given the products available for skin testing today (12). Certainly any definition of a positive reactor, particularly with a presumed infection by more than one organism, is arbitrary. Although data are available to support the interpretation of presumed single infections, knowledge of the pattern of reactions in multiply infected persons is far less complete; the role of cross-reactions must be studied more before definitive interpretations are feasible. Until then a more cautious approach might be to speak of "mixed" reactors instead of "mixed" infections.

Although the groups studied were not selected by random sampling of the reservation population, there is no reason to believe that the rates are

atypical. Any bias should be in the direction of lower rates in the study group, which represents persons who are either employees or students. Both the employees and the students had been given routine screening for tuberculosis before the present study.

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Some 1,329 Navajos were simultaneously skin tested with six tuberculin antigens. Among the 365 reactors, 220 (or 27 percent) reacted to human tuberculin. More than 2 percent of the groups tested were classified as

“mixed” reactors to two or more antigens.

Reaction rates increased with age, and females were more frequently reactors than were males. Approximately one-third of the positive reactions could be attrib-

uted, at least in part, to infections by strains other than the human tuberculin antigens. These data were compared with those available for other American Indian populations.