# COMPARISON OF REACTIONS TO HUMAN AND AVIAN TUBERCULINS IN LEPROSY PATIENTS

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A large proportion of tuberculin tests in tropical countries yield weak or doubtful reactions. Since leprosy is common in many of the countries where this phenomenon has been observed, it has been suggested that some of these anomalous reactions may be due to nonspecific sensitization to mycobacterial antigens common to both the leprosy and the tubercle bacilli. The positive tuberculin hemagglutination reaction usually encountered with sera from leprosy patients, and the positive lepromin reaction resulting from vaccination with BCG, support the belief in such common antigens.

Not all patients with leprosy, however, react to tuberculin, and the positive tuberculin reactions among them are generally ascribed to an associated infection by the tubercle bacillus. Leprosy affords no protection against tuberculosis; instead, tuberculosis is a frequently fatal complication among patients in leprosaria. The widely held belief that tuberculosis infection, or vaccination with BCG, affords protection against leprosy is similarly quite questionable. Nonspecific sensitization to tuberculin resulting from infection with leprosy may not, accordingly, be inferred merely from the high incidence of positive tuberculin reactions in leprosy populations.

Differential tuberculin tests with a variety of antigens may be more informative. Such differential reactions to mycobacteria have been well established in connection with Johne's disease in cattle, which produces much stronger reactivity to avian tuberculin, as well as to johnin itself, than to mammalian tuberculin ([3]). The so-called "Battey" bacillus, which is held responsible for the high frequency of weak reactions to human tuberculin in the southeastern United States, also produces greater sensitivity to avian than to human tuberculin ([2]). On the other hand, bovine and human tubercle bacilli, as well as the photochromogenic acid-fast bacilli, produce sensitization to mammalian tuberculin much greater than to the avian preparation. Greater sensitivity to avian than to human tuberculin has also been reported in India ([5]) and in Africa ([4]), were leprosy is frequent.

Data on the relative sensitivity of leprosy patients to these two tuberculins has not, however, been found in the available literature. Accordingly, a special survey of patients at the U. S. Public Health Service Hospital at Carville, Louisiana, was carried out in July 1960.

## MATERIAL AND METHOD

More than a hundred patients were each injected on the volar surface of the right forearm with 5 international units of PPD-S, the human tuberculin prepared by Seibert from the virulent human culture H37Rv, while 5 international units of PPD-A, prepared at Weybridge, England, from avian tubercle bacilli was similarly injected intradermally in the left forearm.

These preparations had been provided through the kindness of Dr. L. B. Edwards of the United States Public Health Service, and had previously been used in similar studies in California (1), Louisiana, and India, and results with similar materials had been reported by other workers. Tuberculous patients and animals generally respond with larger areas of induration and redness to the human tuberculin, while those infected by the "Battey" bacillus or by avian tubercle bacilli react more to the avian preparation.

There were 32 females and 72 males in the group tested. Their average age was more than 45 years, and only 2 patients were under 20 years of age. The majority still had active (i.e., bacteriologically positive) leprosy lesions, although 40 were recorded as arrested or inactive, and many of them had deformities resulting from the disease. There were altogether 24 white and 10 Negro Americans, 31 Mexicans, 2 South Americans, 15 West Indians, 1 East Indian, 10 Filipinos, 10 Chinese and 1 Syrian, by nativity or parentage, but most had been in America for a long time.

## RESULTS

In general, these patients showed a high sensitivity to human tuberculin, 68, or more than two-thirds of them, giving areas of induration more than 6 mm. in diameter, as shown in Table 1. This is about double the incidence of positive reactors to be expected for the United States as a whole, but the difference is readily explained by the age, sex, and race distribution, since two-thirds of these patients were males, over 40 years of age, and foreign-born, and most of them had come from places where tuberculosis prevalence is high.

TABLE 1.—*Relation of number of reactors and size of reactions to human and avian tuberculins.*

| Human tuberculin | | Avian tuberculin | | | |
|---|---|---|---|---|---|
| Size of reaction (mm.) | No. of patients | 0 | 1-6 mm. | 7-15 mm. | 16+ mm. |
| 0 | 34 | 28 | 4 | 2 | — |
| 1- 6 | 3 | 2 | 1 | — | — |
| 7-15 | 22 | 4 | 1 | 13 | 4 |
| 16+ | 45 | 4 | 2 | 18 | 21 |
| Total | 104 | 38 | 8 | 33 | 25 |

Weak reactions of 1 to 6 mm. in diameter, such as have been reported common in India and other tropical countries, and in the southeastern part of the United States, were surprisingly scarce in this series. The

puncture mark, or a small area of hemorrhage or erythema, was noted in many of those without any edema or induration, but often it was impossible to see where the injection had been given. The majority of these patients had dark skins, and more erythema might be encountered in a blond population, but the area was palpated for induration in each instance.

There was a much lower sensitivity to avian than to human tuberculin in this series. Among the 104 patients tested, 28 were entirely negative to both preparations; 6 reacted only to the avian tuberculin, of which only 2 were more than 6 mm. in diameter (8 and 14 mm. respectively); and 10 reacted only to the human tuberculin, of which 8 were more than 6 mm. in diameter, averaging 16 mm. Among the 60 who reacted to both preparations, there were 30, or 50 per cent, which were practically the same or within 4 mm. of each other, 4 larger with the avian, and 26 larger with the human tuberculin. Among those who did respond, the mean diameter of induration with avian tuberclin was 12 mm., that to human tuberculin was 18 mm. The mean difference in the reactions was 6 mm., but it tended to increase with the size of the reaction, the human averaging about double the diameter of the reaction to the avian tuberculin.

Among 8 leprosy patients who also had been diagnosed as having had tuberculosis, one appeared negative to both agents, while the others all gave reactions of more than 12 mm. to the human tuberculin, of whom 5 gave similar and 2 gave smaller reactions to the avian preparation.

The low incidence of weak reactions, and rarity of greater sensitivity to avian tuberculin encountered among these 104 patients who live less than a hundred miles from New Orleans—in an area where such reactions had been reported as frequent in other studies—may be attributed to the fact that most of these patients had come from abroad, where the tuberculosis infection rates are high but nonspecific sensitization is uncommon, and that the institution is relatively isolated. There are relatively few direct contacts between the patients and the neighboring inhabitants. A similar situation was encountered among the patients at the Veterans Hospital in Alexandria, Louisiana, where nonspecific sensitization seemed rare and greater reactions to avian tuberculin were seen in only 4 patients out of about 200, and 2 of those avian reactors were known to have had "Battey" bacillus infection.

## CONCLUSION

Weak sensitivity to tuberculin was found not to be frequent in more than a hundred patients with leprosy who were tested at the Carville leprosarium. The sensitivity that was found was greater to human than to avian tuberculin. Leprosy is therefore probably not responsible for the weak tuberculin reactions observed in tropical countries.

RESUMEN

Una sensibilidad débil a la tuberculina no resultó ser frecuente en más de 100 leprosos comprobados en el Leprosario de Carville. La sensibilidad observada fué mayor a la tuberculina humana que a la aviaria. La lepra no es por lo tanto probablemente la causa de las reacciones débiles a la tuberculina que se observan en los países tropicales.

RESUMÉ

Chez plus de cent malades atteints de lèpre et testés à la léproserie de Carville, il a été constaté qu'une faible réactivité à la tuberculine n'était pas fréquente. La sensibilité notée a été plus marquée à l'égard de la tuberculine humaine qu'à l'égard de la tuberculine aviaire. Dès lors, il est probable que la lèpre n'est pas responsable des faibles réactions à la tuberculine constatées dans les pays tropicaux.

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