

ALLERGY AND DESENSITIZATION IN TUBERCULOSIS¹

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When guinea pigs are infected with tubercle bacilli they become allergic. Also, they develop a demonstrable degree of immunity. This, all workers in tuberculosis know. Indeed, the association of allergy and immunity is so close that many have postulated a necessary bond between them. In recent years, however, Rich (1) and several other observers (2) have done work which purports to show that allergy and immunity to tuberculosis have no obligate relation and can be separated—the animal may be deprived of its allergy, without suffering any loss of immunity. These investigators have desensitized allergic guinea pigs by repeated injections of tuberculin, have rendered them non-allergic, and have shown that such animals seem to be immune for several weeks (up to 65 days) after re-infection with virulent tubercle bacilli.

Our observations on this question embrace the use of approximately 500 guinea pigs in several series of experiments which have been of two varieties: (1) The desensitization of allergic animals and the study of their immunity and (2) the prevention of the development of allergy by daily injection of tuberculin² made prior to infection with virulent bacilli, and continued until the termination of the experiments. The development of tuberculosis in these latter, unsensitized animals was then compared with its development in the normal and the allergic control animals.

Tuberculosis in allergic-desensitized animals

Briefly and without elaboration of the data, it may be stated that our first and larger group of experiments confirmed in part the impression gained by other workers that immunity persists

in desensitized animals for several weeks after re-infection. However, we learned that this protection is but temporary, for when such animals, continued in complete desensitization, live four months or more after re-infection, they no longer show such immunity but die of extensive tuberculosis of the lungs—this at a time when the allergic control animals show but an occasional, scattered tubercle here and there in the body. And when six months have passed after re-infection, all the desensitized animals have invariably died of tuberculosis, while most of the allergic animals remain relatively free from this disease.

Tuberculosis in normal-desensitized³ animals

The question then arose as to what would happen if normal guinea pigs were prevented from ever developing allergy after they had been infected, and our most significant results occurred in animals thus treated. The details in one series of these experiments may be given as representative. In this experiment 48 animals were used. Sixteen of these had had preliminary infection with R₁ (strain of low virulence) for three weeks. Sixteen were normal controls. The remaining sixteen were normal, but, in each one, daily injection of 1 cc. of Old Tuberculin had been started three days before all 48 were infected subcutaneously with a large dose⁴ of virulent tubercle bacilli of the human type. The daily injections of tuberculin were continued in the third group. All animals were skin tested with tuberculin at the third, the sixth and the tenth week after infection. The previously allergic animals remained allergic and gave tuberculin reaction; the normal animals became allergic at the third week and remained so; the third group—the normal-desensitized group

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² The tuberculin used in our experimental work was very kindly furnished by Parke, Davis & Co.

³ "Normal-desensitized" may seem a contradiction of terms. However, it expresses better than any other phrase the actual status of these animals.

⁴ Four-tenths milligram moist weight inoculated in 0.4 cc. saline in each pig.

| WEEK AFTER VIRULENT INFECTION | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|-------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|
| NORMAL | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | ■ |
| NORMAL-DESENSITIZED | □ | | | □ | ■ | ■ | | ■ | ■ | ■ | ■ | |
| ALLERGIC | | □ | | | | | | | ■ | ■ | | ■ |

□ DEATH DUE TO NON-SPECIFIC CAUSES
 ■ MODERATE TUBERCULOSIS
 ■ EXTENSIVE TUBERCULOSIS
 S SACRIFICED

FIG. 1. MORTALITY RECORD FOR THE THREE GROUPS OF ANIMALS

The animals died in the week indicated except that in the 12th week two animals were sacrificed.

which received daily injections of tuberculin—never developed allergy.

Briefly stated, the results were as follows for the normal control group (Figure 1). In the fourth, fifth and sixth week following infection, six animals died of nonspecific pneumonia, but each one had tubercles in the lungs. From the seventh to the tenth week, nine of the animals succumbed to tuberculosis. The last one was killed in the twelfth week and was found to have miliary tuberculosis.

Of the 16 animals in the normal-desensitized group, one died in the first week and two in the fourth week with nonspecific pneumonia. In the fifth and sixth weeks 4 animals died due to non-specific pneumonia, but they also showed tubercles in the lungs. All animals in this group

which lived as long as eight weeks after infection were found to show, at autopsy, an unusual degree of tuberculous pneumonia, characterized by absence of ordinary tubercles and by marked increase in the volume of the lungs, which were almost completely hepatized by the pneumonic process, (Figure 2). Smears made from the cut surface of these lungs showed innumerable acid fast bacilli (Figure 3).

Of the 16 guinea pigs in the allergic group, two died in the second week after reinfection, two in the ninth and three in the tenth, all with non-specific pneumonia, but the latter 5 animals showed an occasional tubercle. One was killed in the twelfth week and showed scattered tubercles in the viscera. Eight remained alive and well after twelve weeks.

It may be stated further that this striking and extensive involvement of the lung is but a part of the characteristic picture, for, as the tuberculous process develops in the lungs of these animals, the disease spares the other viscera so that the spleen and liver remain of practically normal size and appearance.

Whatever else may be deduced from the factors contributing to these results, it is clear at least that normal-desensitized (non-allergic) guinea pigs provide fertile soil for the tubercle bacillus; that such animals, without allergy, are without immunity.

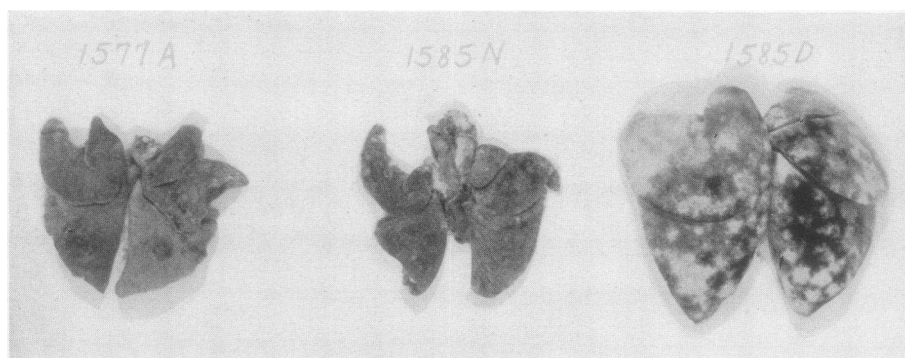


FIG. 2. LUNGS FROM ANIMALS REPRESENTATIVE OF THE THREE GROUPS, IN THE THIRD MONTH AFTER THE VIRULENT INFECTION

To the left, lung from an allergic, reinfected pig. No definite tubercles can be identified in the gross. Middle, lung from normal control animal. Scattered tubercles can be seen. Right, lung from normal-desensitized pig. All lobes are distended with tuberculous bronchopneumonia. Smears from these lungs show innumerable acid-fast bacilli. Photograph $\frac{2}{3}$ natural size.

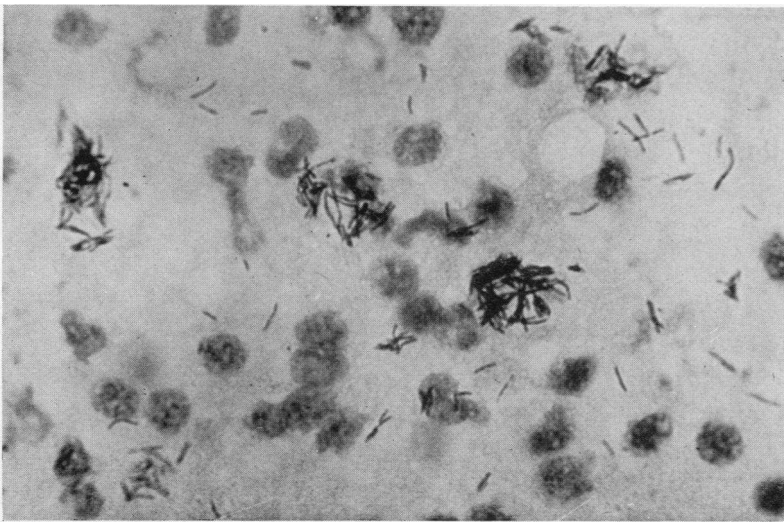


FIG. 3. IMPRESSION SMEAR FROM LUNG OF DESENSITIZED GUINEA PIG SHOWING THE GREAT NUMBER OF ACID-FAST BACILLI

Ziehl-Neelsen stain. Photograph taken with blue light. $\times 1200$.

SUMMARY

(1) Allergic-desensitized guinea pigs experience a delay of several weeks (after reinfection) in the development of tuberculosis. This delay has been mistaken for retained immunity.

(2) Animals which have been prevented from developing allergy by injection of tuberculin are unusually susceptible to tuberculosis and develop what is probably the most marked degree of tuberculous pneumonia yet produced in experimental animals.

(3) These observations indicate that it is unsafe as yet to conclude that the phenomena of al-

lergy are an unessential part of the mechanism of defense against tuberculosis.

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