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Relative Spread of Particulate and Diffusible Substances in the Skin of Male and Female Rabbits.*

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In an endeavor to elucidate the physiological basis for the varying inherited, natural resistance to tuberculosis demonstrated in certain inbred rabbit families,¹ it was found that among the factors determining this resistance, the spread of particulate matter in the skin played a prominent rôle.² In general, rabbits belonging to the susceptible families spread intracutaneously injected India ink over a wider area than rabbits belonging to the resistant strains. This observation was considered of significance, for the following reasons. In the resistant families tuberculosis naturally acquired by respiratory contagion, was limited to the lungs, and the rabbits died after a prolonged illness from a strictly localized ulcerative phthisis without spread to the draining lymph nodes and internal organs, a picture resembling in its essential characteristics the reinfection type of adult pulmonary tuberculosis in man. Rabbits of the susceptible families, on the other hand, died of a more rapidly fatal disease, originating in a primary focus in the lungs, soon spreading to the draining tracheobronchial lymph nodes, which became massively enlarged and caseous. Extensive caseous pneumonia without cavity formation developed forthwith and large nodular destructive lesions occurred in many organs from bacilli disseminated by the blood. The disease had the characteristics of a first infection and resembled the childhood type of tuberculosis in man.

There was thus a correspondence between the spread of carbon particles and the spread of tuberculosis in the tissues of these rabbit families.

It is well known that the mortality from tuberculosis is much greater in young women than in young men. In view of the parallel existing between the spread of India ink and resistance to tuberculosis, it seemed of interest to determine if sex differences can be observed experimentally in the spread of particulate matter. The

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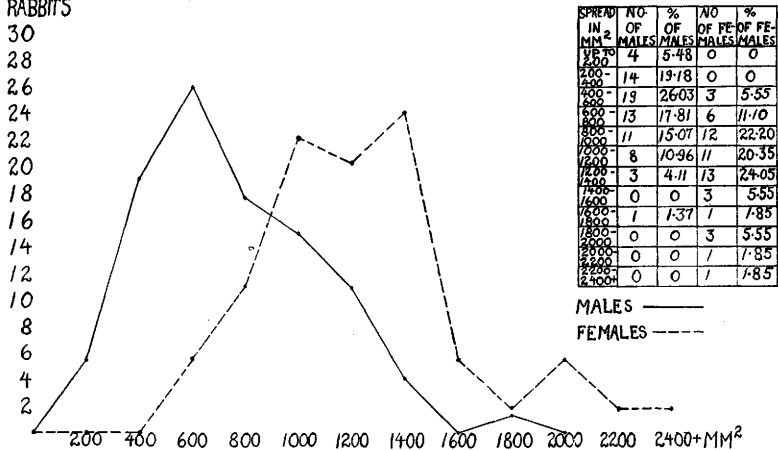
¹ Lurie, M. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **39**, 176.

² Lurie, M. B., *Ibid.*, 1938, **39**, 181.

spread of India ink was therefore studied in a series of male and female rabbits of the different families in our possession. Five-tenths of a cubic centimeter of an autoclaved 1:5 dilution of Higgins waterproof India ink in saline was injected intracutaneously in the flank. The approximate spread of the ink, in square millimeters, was determined on the next day by measuring with accurate calipers the 2 largest diameters of the stained area at right angles to each other. The product of these diameters was regarded as the area of spread. A total of 73 males and 54 females were tested. Seven rabbit families, each varying considerably in its capacity to spread India ink, were used. From 3 to 20 individuals of each sex from each family were examined. The age of the rabbits varied from 4 to 18 months. The mean age of the males was 7.2, with a standard deviation of the mean of 0.3. The mean age of the females was also 7.2 months with a standard deviation of the mean of 0.4. It is obvious that there was no difference in the age distribution of these males and females.

In Chart I are presented the data as well as the graphic curves of the distribution of the spread of India ink in the skin of these male and female rabbits. The mean spread in the males was 650 mm² with a standard deviation of the mean of ± 39 . The mean spread in the females was 1155, with a standard deviation of the mean of ± 58 . The critical ratio of the difference equals 7.7, which shows that this difference is beyond question statistically significant. This greater spreading power of the skin of females was evident in each of the 7 families tested, despite the very great range in the spread of India

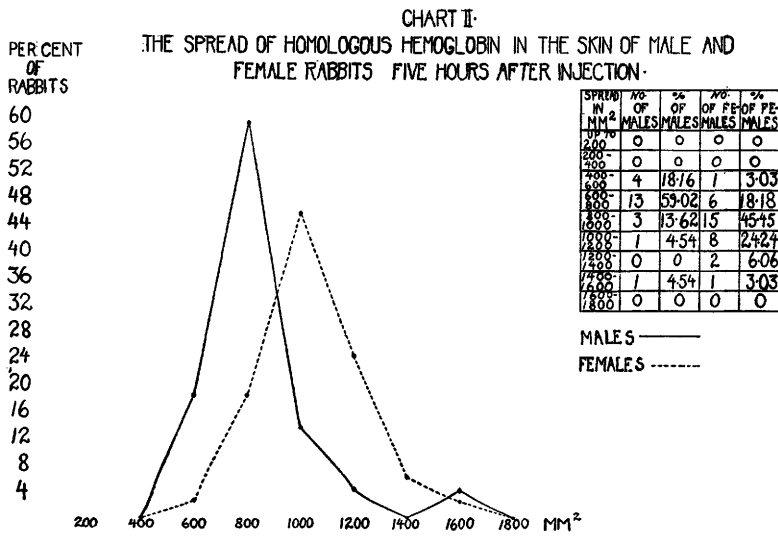
CHART I.
THE SPREAD OF INDIA INK IN THE SKIN OF MALE AND FEMALE RABBITS
ONE DAY AFTER INJECTION



ink in the different families. For example, the average spread in the males of the resistant family "A" was 441 mm². The spread in "A" females was 819. Likewise the average spread of India ink in the susceptible "F" family was 720 for the males and 1077 for the females.

Similar determinations were made of the spread of a diffusible substance in the skin of many of the rabbits tested above with the particulate carbon. The use of rabbit hemoglobin for this purpose was suggested by Madinaveitia.³ The hemoglobin was prepared as outlined by this investigator and 0.3 cc was injected intracutaneously in the flank of the males and females. The spread of hemoglobin in the skin was determined as described above for India ink, 5 hours after the injection. At this time the margins of the hemoglobin-stained skin are very sharp. The next day, however, the margins are indistinct. Twenty-two males and 33 females were used. Members of all the 7 families previously tested with India ink were included. The age of the rabbits ranged from 4 to 18 months. The average age of the male rabbits was 8.9 with a standard deviation of the mean of 0.7. The average age of the female rabbits was 7.1 with a standard deviation of the mean of 0.6. The difference between the ages of the male and female rabbits was, however, not statistically significant.

In Chart II are presented the data as well as the graphic curves of the distribution of the spread of rabbit hemoglobin in the skin of



³ Madinaveitia, J., *Biochem. J.*, 1938, **32**, 1806.

these males and females. It is interesting to note that the range of spread of hemoglobin is much smaller than that of India ink. This is probably due to the shorter interval between the injection of the hemoglobin and the reading of the spread. Nevertheless, the mean spread of hemoglobin in the males was 728 mm², with a standard deviation of the mean of ± 47 , while the average spread in the females was 937 with a standard deviation of the mean of ± 35 . The critical ratio of the difference is 3.6, which places it in the realm of definite statistical significance. Not enough observations were obtained on each individual family to show a significant difference between the males and females of some families.

It is plain, therefore, that the spread of particulate and diffusible substances in the skin of rabbits is a sex limited character; the females spreading both to a greater degree. The age of the rabbits tested was in all instances above 3 months and reached up to 18 months. In this age range no difference was noted in the spreading capacity of younger and older rabbits.

The sex limited nature of the difference suggested trial of the effect of sex hormones on the spread of these substances. In a few experiments, the addition of as much as 50 international units of theelin to the standard dose of India ink or hemoglobin had no significant enhancing effect on their spread in the skin of male rabbits. Whether the greater spreading capacity of the skin of female rabbits for these substances is associated with a lower resistance to tuberculosis has not yet been determined.

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Oxygen Consumption of the Parts of the Amphibian Gastrula.*

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Interest in the organizer has led to the determination of its oxygen consumption and the results of various investigators do not agree. Brachet,¹ Brachet and Shapiro,² and Fischer and Hartwig,³ agree that the dorsal lip exhibits a higher rate, while Waddington, Need-

* Aided by a grant from the Rockefeller Foundation.

¹ Brachet, J., *Arch. de Biol.*, 1934, **46**, 25.

² Brachet, J., and Shapiro, H., *J. Cell. Comp. Physiol.*, 1936, **10**, 133.

³ Fischer, F. G., and Hartwig, H., *Biol. Zent.*, 1938, **58**, 567.