the importance of detailed geologic interpretation and correlation of archeological sites were considered.

The success of the meeting as an open forum for the discussion of problems relating to Early Man has made all who attended hope for the establishment of an annual summer meeting, for which Santa Fe seems so admirably situated. Especial thanks for the success of this meeting are due Dr. E. B. Howard, of the University Museum, Philadelphia, Pa., who was responsible for the planning and organization, and to the staff of the Laboratory of Anthropology at Santa Fe, who acted as hosts.

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SPECIAL ARTICLES

THE SUSCEPTIBILITY OF THE EASTERN COTTON RAT, SIGMODON HISPIDUS HISPIDUS, TO EUROPEAN TYPHUS

ONE of the outstanding difficulties in the study of typhus fever has been the lack of an animal in which the disease could be reproduced as it occurs in man. With this in mind, a search for more suitable experimental animals for the study of typhus was undertaken, and our results obtained with the eastern cotton rat, *Sigmodon hispidus hispidus,* are presented below. After these studies were under way, we discovered that Gerardo Varela[1] had already tested the susceptibility of these rodents to murine typhus. Although Varela was able to demonstrate the infectivity of the cotton rat brain as late as 5 days after inoculation, the rats themselves apparently remained healthy.

In our experiments the European typhus rickettsiae used were the well-known old Breinl strain and also three new strains isolated from patients in Madrid about 6 months ago during a recent epidemic of typhus.

Yolk sac membranes of developing chick embryos inoculated with typhus rickettsiae according to Cox's technique[2] served as the source of the infectious material for this study. In an experiment using cotton rats between 25 and 30 gm in weight, the smallest volume of a 10 per cent. yolk sac suspension given intraperitoneally which resulted in death was between 0.05 and 0.5 cc. By the intracardial and intranasal routes the minimal lethal dose was approximately 0.01 cc. At autopsy, rickettsiae were found in great abundance in the peritoneal exudate of the rats inoculated intraperitoneally; in the pericardial and mediastinal exudate of those injected intracardially; and in the lungs of those infected intranasally.

A striking relation between age of rats and their susceptibility to typhus was observed. In an experiment with eight cotton rats of different sizes given 0.1 cc of a 10 per cent. yolk sac suspension intracardially, those weighing 20 to 30 gm died in 3 or 4 days, whereas those weighing from 46 to 66 gm recovered from the infection after several days of experimental disease.

To determine whether the fatal infection in young rats could be prevented by a specific immune serum, samples of normal and convalescent human serum were mixed with equal volumes of a 20 per cent. infected yolk sac suspension. The mixtures were incubated for 1 hour at 38° C. and a group of the rats inoculated intracardially with each mixture. The convalescent serum used in this experiment had been obtained from patients 2 weeks after recovery from typical typhus. A portion of the 20 per cent. yolk sac suspension alone was similarly heated for 1 hour at 38° C., after which tenfold dilutions were made and groups of rats inoculated intracardially to serve as infectivity controls. The six rats receiving the convalescent serum survived, whereas the six which received normal serum succumbed 3 or 4 days after inoculation. The titration of the yolk suspension alone showed that the number of minimal lethal doses given each rat in this test with normal or convalescent serum was somewhere between 5 and 50.

In the cotton rats that succumbed to the intracardial injection of infected yolk sac the greatest number of rickettsiae was observed in the mediastinal exudate. The rickettsiae were also numerous in the liver. This organ was chosen as a source material for the serial passages of the infection in the rats. The Madrid-1 strain has now been carried through five passages. After four serial passages it produced fatal infection in all of three rats inoculated intracardially with 0.2 cc of a 10 per cent. liver suspension. The same volume of a 1 per cent. suspension likewise resulted in the death of all rats, whereas the animals given 0.1 per cent. suspension showed only slight evidence of experimental disease. By routes other than the intracardial a fatal infection in serial passage was not obtained.

Although it is obvious that a still more susceptible animal is needed, the results above indicate that the cotton rat is much more suitable than the guinea pig for the investigation of many problems in typhus fever which urgently await solution.

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[1] Gerardo Varela, *Medicina* (Mexico), 13: 171, 1933.
[2] H. R. Cox, *Public Health Reports, U.S.P.H.S.*, 53: 2241, 1938; 55: 110, 1940.