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Experimental Tuberculosis in the Cotton Rat (*Sigmodon hispidus littoralis*).*

M. Maxim Steinbach and Charles J. Duca.

From the Department of Bacteriology, College of Physicians and Surgeons, Columbia University, New York.

Armstrong[1] was the first to discover that the Eastern cotton rat differs from other rodents in that it proved susceptible to the virus of poliomyelitis. Similar results were recently obtained by Jungeblut and Sanders[2] with another strain of monkey poliomyelitis virus. Since then there has been carried out in this department a systematic study of the reaction of cotton rats to other infections and toxic agents. It was found that this animal *(Sigmodon hispidus littoralis)* resembles the guinea pig in its susceptibility to diphtheritic toxin and bacillary infection with *C. diphtheriæ*.[3] This resemblance between the two species was also shown to exist with respect to their susceptibility to infection with *Trypanosoma equiperdum*.[4] It seemed of interest to determine how this animal compares with the guinea pig and the albino rat in its susceptibility to infection with tubercle bacilli.

Experimental Methods. Seven albino rats (averaging 100 g in weight), 7 cotton rats (averaging 80 g), and 7 guinea pigs (averaging 350 g) were tested intracutaneously with 1 mg O.T. and found to be negative. All animals were then infected intravenously with 1 mg of bovine tubercle bacilli (B1). In some instances part of the inoculum escaped into the surrounding tissue as evidenced by the occurrence of infection of the regional glands. Two weeks after infection all animals in the 3 groups were again tested intracutaneously with 1 mg O.T. Half of the survivors in each group were sacrificed for pathological studies 46 days following infection; at the end of 2 months the remaining animals were tested for susceptibility to tuberculin-shock.

Results. Guinea Pigs: Six animals which survived longer than 2 weeks were found to be highly sensitive to intracutaneous doses of

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1 Armstrong, C., *Pub. Health Rep.*, 1939, **34**, 1719.

2 Jungeblut, C. W., and Sanders, M., Proc. Soc. Exp. Biol. and Med., 1940, **44**, in press.

3 Jungeblut, C. W., Proc. Soc. Exp. Biol. and Med., 1940, **43**, 479.

4 Culbertson, J. T., *J. Parasit.*, in press.

1 mg O.T. All 7 died within 12 to 37 days after infection and showed extensive parenchymatous tuberculosis with caseation. It was interesting to note that 5 of these guinea pigs had miliary tuberculosis of the kidneys, a condition not encountered with subcutaneous or intraäbdominal infection.

Albino Rats: All of these rats were negative to intracutaneous doses of 1 mg O.T., and tolerated 500 mg of O.T., injected subcutaneously, without noticeable symptoms. At necropsy, 46 days after infection, 3 of 4 animals showed a sparse scattering of tubercles in the lungs, and some suspicious areas in the spleen. No other macroscopic evidence of tuberculosis was found. The 3 remaining animals were sacrificed 65 days after infection, subsequent to unsuccessful attempts at shocking them with 1 g O.T. These rats showed the same scant tuberculous involvement as those sacrificed earlier.

Cotton Rats: All of the cotton rats reacted negatively to the intracutaneous injection of 1 mg O.T. 2 weeks after infection. All 4 animals which had been sacrificed at 46 days showed miliary tuberculosis of the lungs, spleen, and lymph glands. One cotton rat had miliary tuberculosis of the liver, and 3 showed tubercles in the kidneys. In all 4 cotton rats definite tissue-destruction and caseation was observed at the site of infection.

Of the 3 surviving animals, one died 65 days after infection, and showed extensive tuberculosis in the lungs, liver, and kidneys. The 2 remaining cotton rats were given 250 mg O.T. subcutaneously at the same time. One died the following day with no evidence of tuberculin shock. The other cotton rat showed no symptoms. It was then injected subcutaneously with 500 mg O.T. No evidence of tuberculin-intoxication was observed during the next 24 hours. The same animal was then injected intraäbdominally with 1 g O.T. Within 5 minutes after injection, the animal became restless and dyspneic, and died within 40 minutes. At necropsy, there was serous fluid in the thoracic and abdominal cavities, and focal hemorrhages were found about the tubercles in the various organs. Both of the last 2 cotton rats showed miliary tuberculosis of the lungs, liver, spleen, glands, and kidneys.

Histopathology: Histological study of the tissues confirmed and further emphasized the differences found at autopsy. The tubercles in the cotton rat are predominantly epithelioid in type, some showing caseation, but no giant cells were observed. In most sections the tubercles were conglomerated. Acid-fast bacilli are easily demonstrated in the tubercles. A more complete description of the histopathology will be given in a later communication.

Summary and Conclusions. A comparative study of the Eastern

cotton rat, the albino rat, and the guinea pig suggests that the cotton rat occupies a position midway between the other two species regarding its susceptibility to infection with pathogenic bovine tubercle bacilli. It is definitely more susceptible than the naturally resistant albino rat but not as highly susceptible as the guinea pig. Like the albino rat, the tuberculous cotton rat is insensitive to skin-test doses of tuberculin, and tolerates large amounts injected subcutaneously. Since the observations on tuberculin shock are based upon findings obtained from only one animal, further work is necessary to confirm this point.

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Hypoaminoacidemia in Patients with Pneumococcal Pneumonia.

LEE E. FARR, COLIN M. MACLEOD, PALMER H. FUTCHER, KENDALL EMERSON, GEORGE S. MIRICK AND EDWARD C. CURNEN.

From the Hospital of the Rockefeller Institute for Medical Research, New York.

The observations by Farr and MacFadyen[1] and Farr[2] on the incidence and duration of hypoaminoacidemia in children with the nephrotic syndrome have reopened the question of the constancy of blood amino acid concentration in other disease states. Because of certain clinical similarities between the onset of recovery in pneumococcal pneumonia and that of children from nephrotic crises, as well as the prevalence of pneumococcal infections in nephrotic children, we believed that extension of studies on blood amino acids to diseases other than Bright's disease might profitably begin with pneumonia.

Studies of plasma amino acids on all patients admitted to the pneumonia service in this hospital have been made. While these are not yet completed, the results thus far have been sufficiently striking and uniform to warrant reporting them.

Methods. Blood was drawn from each patient immediately upon admission to the hospital and before any therapy was begun. Subsequently, blood was drawn at selected intervals, when possible after an overnight fast, otherwise after an interval of at least 4 hours had elapsed from the time when the last protein-containing food was given. The blood was drawn with care to prevent hemolysis, ox-

1 Farr, L. E., and MacFadyen, D. A., *Am. J. Dis. Child.*, 1940, **59**, 782.

2 Farr, L. E., *J. Ped.*, in press.