and theophylline for its effects upon the electrocardiogram with and without induced anoxemia. The length of time necessary for the recovery of the electrocardiogram and for the return of the white blood cell count and sedimentation time to normal was roughly proportional to the size of the infarct, and independent of the administration of the papaverine. From our failure to demonstrate any reduction in the size of the infarct after coronary ligation, it cannot be concluded that papaverine hydrochloride has no place in the clinical treatment of coronary occlusion or of angina pectoris.

Conclusion. The daily injection of papaverine hydrochloride (5 mg per kilo) into cats for 2 weeks did not alter significantly the size of the infarct resulting from the ligation of the left branch of the left anterior descending coronary artery.

It is suggested that because of the greatly variable amount of cardiac tissue involved in each ligation this method of study is too crude to detect any "clinical" improvement that the drug may have exerted.

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Anaphylactic Shock and Susceptibility to Histamine Poisoning in the Cotton Rat *Sigmodon hispidus littoralis.**

BEATRICE CARRIER SEEGAL

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

The Eastern cotton rat *Sigmodon hispidus hispidus* and the Florida cotton rat *Sigmodon hispidus littoralis* have come into prominence as laboratory animals because of their reported susceptibility to the virus of poliomyelitis.[1] [2] The cotton rat is a small rodent and apparently it is capable of adaptation to laboratory life. It is therefore of interest to explore its usefulness for other experimental purposes. Reports on a natural trypanosome infection of the Florida cotton rat,[3] on the susceptibility of this animal to diph-

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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**, 375.

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

theric toxin,[4] and to infection with the tubercle bacillus[5] have been made. The present communication describes attempts to produce anaphylactic shock in the Florida cotton rat. In addition to testing for hypersensitivity, the serums of some of the animals, obtained after sensitization, were tested for precipitin content. The animals subsequently were subjected to intravenous injections of histamine.

Sheep serum as an anaphylactogen: One or 2 sensitizing injections of sheep serum were given intravenously to 8 cotton rats. The total amount used for sensitization ranged from 0.05 to 0.6 cc. After an incubation period, varying from 17 to 29 days, the animals were reinjected intravenously with 0.25 to 0.50 cc of sheep serum. In no case was any reaction obtained following the shocking injection of antigen. Six of these animals were retested for sensitivity 17 days later by the intravenous injection of 0.3 to 0.5 cc of sheep serum. The animals were again equally refractory to shock.

Five of the animals were bled 19 or 25 days after the last shocking injection of antigen, and their serums tested for precipitins to sheep serum. In 3 of the serums no precipitins could be demonstrated; in 1 serum there was a trace with antigen diluted 1:20, while the last serum reacted to give a definite precipitate with antigen diluted 1:10, 1:40, and 1:160 and a trace with antigen diluted 1:640.

Whole egg white as an anaphylactogen: Two sensitizing injections of 0.5 cc of 25% whole egg white were given 3 days apart to 9 cotton rats. The first injection was given intravenously, the second intraperitoneally. Five of the 9 animals had previously been used in the sheep serum experiments. After a 21-day incubation period, all 9 animals received 0.5 cc of the same egg white solution intravenously. Seven of the cotton rats failed to show any reaction. One animal was listless for about 20 minutes, sitting in one corner of the cage and responding only sluggishly to prodding. The last animal showed a greatly increased rate of respiration for about 5 minutes after injection. It then appeared normal for about 15 minutes when it was observed that the animal had become limp and could not be aroused to activity. Respirations were slow but not labored. The animal lay on its side, became progressively weaker with slower respiration during another 15 minutes and then stopped breathing, 35 minutes after the injection of egg white. Autopsy revealed no gross lesions in the heart or lungs. Each pleural cavity contained a drop of blood or bloody fluid, and there was a small amount of serosanguinous fluid in the peritoneal cavity. The

[4] Jungeblut, C. W., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 479.

[5] Steinbach, M. M., and Duca, C. J., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 288.

mucosa of the stomach had one area of hemorrhage 4 mm in diameter and one of the Peyer's patches of the small intestine was studded with petechial hemorrhages. The type of death and the paucity of findings at autopsy suggested the picture of anaphylaxis in the rat.

Four of the 9 animals sensitized to egg white were bled from the heart 4 hours before the intravenous shocking injection of antigen. Serums from these bloods were tested for precipitins. Three of the serums contained no demonstrable precipitins, while the fourth showed only a trace of precipitate when tested with antigen diluted 1:20 and 1:100.

Histamine shock: Eight cotton rats were tested for their susceptibility to histamine (ergamine acid phosphate, Burroughs Wellcome & Co.). The drug was dissolved in 0.85% NaCl so that each cubic centimeter contained 1 mg. The cotton rats, weighing between 130 and 175 g, were injected intravenously with 0.4 to 1.5 mg. The minimal lethal dose proved to be roughly 1 mg of histamine for a 130 g cotton rat, or approximately 0.8 mg per 100 g. This amount killed 4 out of 5 animals, whereas 0.6 mg per 100 g respiratory rate in the 3 animals tested. There was considerable of cotton rat failed to produce more than transitory increase in individual variation in the mode of death. In 1 animal (weight 132 g) death occurred in 3 minutes following injection of 1 mg of histamine. It was characterized by frothing at the nose and labored respiration and by tonic and clonic convulsions and opisthotonos. At autopsy the lungs were slightly distended and hemorrhagic. A second animal (weight 175 g) died one hour following the intravenous injection of 1.5 mg. This animal did not show discharge of froth from the nose and the respirations, although rapid, were not labored. It lay on its side, prostrated, for 45 minutes before death. On autopsy the lungs appeared normal. There were many petechial hemorrhages in the Peyer's patches and also scattered through the small intestine. A third rat, also 130 g in weight, died in 3 hours following the injection of 1 mg. In this case, difficulty of respiration was also absent. Periods of complete prostration alternated with periods of violent tonic and clonic convulsions. The only findings at autopsy were petechial hemorrhages in Peyer's patches. A fourth cotton rat, which had also been given 1 mg of histamine, showed only some increase in the rate of respiration for 30 minutes following injection, but looked sick and listless the following day and died 24 hours later without showing any lesions at autopsy.

The potency of the histamine was tested in 3 guinea pigs weighing 700 g. Two of these animals died acutely following the injection of 0.4 mg while the third survived 0.3 mg.

Conclusions: The cotton rat was found relatively refractory to anaphylactic shock. In this respect it resembles the ordinary laboratory rat. Low titered precipitins occurred in 3 of the 9 serums tested after sensitization. The minimal lethal dose of histamine intravenously was approximately 0.8 mg per 100 g for the cotton rat. This is 15 times the quantity required to kill a guinea pig, but is 100 times less than that which has been reported lethal for the rat.

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Relation Between Volume of Vehicle and Chick Comb Response to Androsterone.*

EMANUEL KLEMPNER, FRANKLIN HOLLANDER AND ROBERT T. FRANK.

From the Laboratories of the Mount Sinai Hospital, New York.

It was suggested previously (Frank, Klempner and Hollander[1]) that, in the use of sesame oil as a vehicle in our bioassay method for androgens, a reduction in the volume of vehicle from 0.1 cc to 0.05 cc was one of the factors which contributed to the improvement in response. Subsequently, the possibility presented itself that a further reduction in this volume might effect further improvement, as manifested by increased comb growth for a given dose of androgen. Accordingly, we have investigated the response elicited by the application of various dosages of androsterone in 0.05 cc and in 0.02 cc† of oil, applied daily, in paired experiments run simultaneously. In all other respects, the experimental conditions were exactly the same as in our last report (*loc. cit.*).

The results of such paired experiments are summarized in Table

* This investigation was supported in part by a grant from the Friedsam Foundation.

1 Frank, R. T., Klempner, E., and Hollander, F., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 853.

† In order to facilitate the application of these small volumes, as well as to control accuracy of delivery, a simple mechanical device was attached to the syringes used. This device, constructed by Mr. Vondrak, chief technician of laboratories, Mount Sinai Hospital, will be described elsewhere.