ever this may be, it is certain that the dyes move through the tissues along tracks, as it were, determined by the form and situation of the connective tissue fibers.

9704 P

Role of Histamine in Circulatory Effects of Rattlesnake Venom (Crotalin).

CARL A. DRAGSTEDT, FRANKLIN B. MEAD AND SIMON W. EYER.

From the Department of Physiology and Pharmacology, Northwestern University Medical School, Chicago.

Essex and Markowitz[1] have made an extensive study of the physiologic action of crotalin and have pointed out a number of similarities to the action of histamine. Feldberg and Kellaway[2] have recently shown that crotalin has the property of liberating histamine into the perfusate when it is added to the perfusion fluid with which the lungs of cats or guinea pigs are being perfused. Their studies demonstrate a mechanism whereby the characteristic action of histamine can be superimposed upon the direct effects of the venom. The extent to which the added action of histamine influences the action of the venom in intact animals is not indicated by these experiments. In a series of studies on anaphylactic shock[3] and peptone shock[4] in the dog, we have been able to show that the degree of the vascular reaction is correlated with and dependent upon the amount of histamine liberated from the dog's tissues in these reactions. We were, therefore interested in determining whether histamine is liberated when venom is administered to the intact dog and whether the amount of histamine liberated is adequate to account for the degree of the vascular effect produced.

Crotalin* (from *Crotalus atrox*) was injected intravenously into 5 anesthetized dogs, in doses of 0.5 to 1.3 mg. per kilo, and samples of blood and thoracic duct lymph were collected during the ensuing reaction and tested for histamine. All of the reactions were severe, 2 being fatal within 20 minutes. Histamine was found

1 Essex, H. E., and Markowitz, J., *Am. J. Physiol.*, 1930, **92**, 705.

2 Feldberg, W., and Kellaway, C. H., *J. Physiol.*, 1937, **90**, 257.

3 Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Therap.*, 1936, **57**, 419.

4 Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Therap.*, 1937, **59**, 429.

* We are indebted to Mr. R. H. Hutchison of the Antivenine Institute of America for the venom used in these experiments.

in the blood in 2 experiments and also in the lymph in one of these. The identification of histamine was based upon the presence in extracts made by Code's[5] method for the determination of histamine, of a physiologically active substance which lowered the blood pressure of the atropinized cat, contracted the guinea pig intestine, and was inactivated by diazotized sulfanilic acid. The amounts of histamine determined in the 2 positive experiments were inadequate to account for the degree of the vascular reactions, and as there were no significant quantities of histamine detected in 3 experiments, it is our belief that histamine plays only a contributory and subsidiary rôle in the vascular effects of intravenously injected venom.

Conclusions. The observation of Feldberg and Kellaway, that crotalin may liberate histamine from perfused tissues is confirmed by showing that it may also liberate histamine when injected intravenously into an intact animal. Preliminary studies indicate that the amount of histamine liberated is inadequate to account for the degree of the vascular reaction produced and that it therefore plays a contributory and subsidiary rôle to the total effect of the venom.

9705 P

Effects of Alizarine Red S Injections on the Teeth and Bones of *Macacus rhesus* Monkey.*

I. SCHOUR AND M. M. HOFFMAN.

From the Department of Dental Histology, University of Illinois College of Dentistry.

Seventeen *Macacus rhesus* monkeys of mixed or adult dentition, ranging in age from 1½ to 7 years,[1] were given multiple intravenous, intraperitoneal or subcutaneous injections of 5-10 cc. of 2% Alizarine Red S (Sodium Sulphalizarate) of color index 1034 (Coleman and Bell Company) at 5- to 30-day intervals. The time between the last injection and death ranged from 3 hours to 125 days. The dosage ranged from 40 to 60.5 mg. per kilo.

[5] Code, C. F., *J. Physiol.*, 1937, **89**, 257.

* This investigation was aided in part by a grant from the Carnegie Corporation. The animals of this investigation were made available through the kind coöperation of Dr. George W. Bartelmez of the Anatomy Department and Dr. E. H. Lennette of the Bacteriology Department of the University of Chicago.

[1] Schultz, A. H., *Am. J. Phys. Anthrop.*, 1935, **19**, 489.