

each rat thrived normally until about the 15th to 21st day when the young began to exhibit weakness, with spasms, and were destroyed by their mothers. In the case of the second litter this result was prevented by giving one mother 0.2 gram of dry whole yeast daily and the other mother 0.2 gram of dry alfalfa meal in the form of a pellet. Five of these second generation rats, representing both litters, are at present doing well on the "artificial" milk," without the additions mentioned.

It is not possible, at present, to reconcile the results of this experiment with those of Mattill or with our own on whole milk. There seems to be evidence that milk only as the sole diet lacks something for the attainment of normal sexual maturity in the female rat. Our results might also be interpreted to indicate a lack of something required for normal lactation, were it not for extensive unpublished data which we have showing that the addition of 10 c.c. of whole milk (1.25 grams of milk solids) to the diet of rats which fail to grow normally, as well as reproduce, has resulted in the securing of normal rats in experiments which have, to date, reached the third generation.

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### The effect of local anaesthetics upon the conjunctivitis caused by mustard oil.

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Spiess<sup>1</sup> and Ninian Bruce<sup>2</sup> have shown that the oedema of the conjunctiva which can be produced by instilling mustard oil into the conjunctival sac of a rabbit, can be prevented by the instillation of 10 per cent. cocaine. Bruce interprets this action as being due to the inhibition of vasdilator axon reflexes to the capillaries

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<sup>1</sup> Spiess, G., *Muenchen Med. Woch.*, 1906, 345.

<sup>2</sup> Bruce, A. Ninian, *Arch. f. Exper. Path. u. Pharmacol.*, 1910, lxxiii, 424.

and smaller arterioles, and he found that if the ophthalmic nerve was cut before applying mustard oil oedema could then be produced only during the period in which the vasodilator fibers were still undegenerated, and a sufficient time were allowed for the vasodilator nerves to degenerate completely before the mustard oil was applied, oedema did not result after the instillation of mustard oil. Bruce's results have been confirmed by Bardy.<sup>1</sup>

In 1917 I<sup>2</sup> was able to demonstrate the following facts: (1) That the application of epinephrin, producing a local vasoconstriction of the conjunctival vessels, inhibited the development of the oedema, for about an hour, but that after the epinephrin effect had worn off oedema developed subsequently. (2) That any continued lowering of the general blood pressure to less than 50 mm. Hg. prevented or greatly retarded the development of the oedema, even if the conjunctival vessels were dilated by the local administration of 1 per cent. sodium nitrite or if lymph secretion were increased by the intravenous injection of "Witte's peptone." (3) That intravenous lowering of the general blood pressure by the continuous intravenous injection of dilute hydrochloric acid, in spite of the acidosis produced, diminished or entirely prevented the development of the oedema from mustard oil. (4) That ligation of the carotid artery greatly reduced the development of oedema in the eye upon the side corresponding to the ligated artery; and that in the peripheral end of the ligated artery the blood pressure was less than 40 mm. Hg.

These experiments would lead to the conclusion that the oedema develops only when there is a sufficiently high pressure in the arterioles and capillaries to bring about a sufficient filtration after the walls of the blood vessels have been injured; and that if an adequate pressure is not present, the oedema does not develop whether the smaller vessels are dilated or not.

Since Krogh<sup>3,4</sup> in his studies upon the capillary circulation lays a great deal of emphasis on the functional importance of axon reflexes and upon Ninian Bruce's studies, it seemed of interest to determine the effect that local anaesthetics other than

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<sup>1</sup> Bardy, H., *Skand. Arch. f. Physiol.*, 1914-15, xxxii, 198.

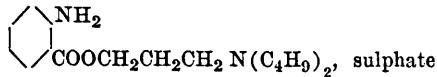
<sup>2</sup> Hirschfelder, A. D., *Jour. A. M. A.*, 1916, lxxvii, 1891; and *Trans. Sec. Pharmacol. and Therap. A. M. A.*, 1917, 182.

<sup>3</sup> Krogh, A., *Jour. Physiol.*, 1919-1920, liii, 398; 1921, lv, 412.

<sup>4</sup> Krogh, A., Harrop, G. A., and Rehberg, P. B., *Ibid*, 1922, lvi, 179.

Rabbit	Anæsthetic	Treated Eye	Reaction	Control Eye
1	Cocaine	No œdema		Oedema
2	Cocaine } 10 min.	Oedema		Oedema
3	Cocaine } before mus-	Oedema		Oedema
4	Cocaine } tard oil.	Oedema		Oedema
5	Procaine	Slight œdema		Marked œdema
6	Procaine } 10 min.	Marked œdema		Less œdema
7	Procaine } before mus-	Marked œdema	Same in both eyes	
8	Procaine } tard oil.	Marked œdema	Same in both eyes	
9	Saligenin	Marked œdema		Oedema
10	Saligenin } 10 min.	Marked œdema		Oedema
11	Saligenin } before mus-	Marked œdema	Same in both eyes	
12	Saligenin } tard oil.	Less œdema		Marked œdema
13	Butyn		Marked œdema in both eyes	
14	Butyn } 10 min.		Marked œdema in both eyes	
15	Butyn } before mus-		Marked œdema in both eyes	
16	Butyn } tard oil.		Marked œdema in both eyes	

cocaine might produce upon the development of oedema from mustard oil. We tested the effects of instilling the following solutions upon the development of mustard oil conjunctival oedema: (1) 4 per cent. cocaine solution in 0.9 per cent. NaCl; (2) 4 per cent. procaine (novocaine) in 0.9 per cent. NaCl; (3) 4 per cent. saligenin in 0.9 per cent. NaCl; and (4) 2 per cent. butyn



dissolved in distilled water.

These substances produced complete sensory anaesthesia of the conjunctiva so that the corneal conjunctiva would be scratched with a thin copper wire without causing any winking reflex or any other movements of the rabbit.

Procaine and butyn seem to have no marked effect on blood vessels; saligenin definitely dilates them.

It will be seen that the oedema developed in the same manner and degree and with the same rapidity in the anaesthetized as in the unanaesthetized eye, in all the experiments with the exception of one in which the oil was instilled almost immediately after the 4 per cent. cocaine. This exception may be due to some vaso constrictor action of the cocaine.

These experiments seem to indicate that mere sensory anaesthesia does not prevent or inhibit the development of oedema from mustard oil, and that the maintenance of a high filtration pressure in the vessels of the eyelid is the most important factor in the development of oedema in an area, the walls of whose blood vessels have been injured by this agent.

It is possible that in Bruce's employment of 10 per cent. alypine and 10 per cent. cocaine to inhibit the oedema, the hypertonic solution of the drug acted to constrict the vessels; and that, in his experiments on cutting the ophthalmic nerves, the still intact vasoconstrictor fibers may have brought about a predominant constrictor response after the vasodilator nerves had degenerated.