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Non-effectiveness of Sodium Rhodanate in Antagonizing Morphine, Ether and Sodium Amytal.

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Bancroft[1, 2, 3] and his collaborators have recently resurrected the old theory of Claude Bernard that narcotic and anesthetic drugs act by causing aggregation of the protein micelles in the cytoplasm. They correctly claim that if this is the correct theory the dispersing ions of the Hofmeister lyotropic series should antagonize this action. They have therefore administered NaSCN intravenously to rabbits and claim to have partly antagonized thereby the effects of morphine sulphate, ether, and sodium amytal. Their experimental series consisted of *one* treated rabbit and *one* control in each group. Disregarding entirely the well known variability of individual animals they have published very far reaching claims for the therapeutic efficacy of sodium thiocyanate (sodium rhodanate) for the treatment of morphine addiction, various forms of insanity and even general nervousness. Henderson[4] and Burkholder[5] independently repeated Bancroft's experiments on larger series of animals and were unable to confirm his results.

As the method described by Hirschfelder and Ridges[6] afforded us a very delicate technique for testing and following the course of

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[3] Bancroft, Wilder D., Gutsell, Robert S., and Rutzler, John E., Jr., *J. Phys. Chem.*, 1932, **36**, 1521, 2011.

[4] Henderson, V. E., and Lucas, G. H. W., *J. Pharm. and Exp. Therap.*, 1932, **44**, 253.

[5] Burkholder, Theodore M., *J. Lab. and Clin. Med.*, 1932, **18**, 29.

[6] Hirschfelder, A. D., and Ridges, A. H., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 958.

analgesia and narcosis we have used it in repeating Bancroft's experiments on a larger series of rabbits.*

Morphine Sulphate. Twenty-four rabbits were given doses of 25 to 50 mg. morphine sulphate per kilo subcutaneously. Three animals were given 150 to 500 mg. sodium rhodanate per kilo intravenously 5 to 10 minutes before the morphine, 11 animals received the same dose 20 to 30 minutes after the morphine. Ten controls received the same doses of morphine sulphate as the treated animals. Narcosis, i. e., the period during which the animals remained lying on their sides when placed in that position was a little longer in the rhodanate animals than in the controls, as was the time necessary before they recommenced coordinated movements, and also the time necessary for complete recovery. Curves of sensation tested in 4 rhodanate animals and 2 controls showed no constant difference between the two groups, except that analgesia lasted longer in the rhodanate animals.

Sodium Amytal. Eleven rabbits received 50 mg. Na Amytal subcutaneously and 6 of these 150 to 200 mg. Na rhodanate intravenously 45 minutes after the Amytal. As in the morphine series narcosis lasted a little longer (average duration 4 hours, 30 minutes) than in the controls (average duration 3 hours, 45 minutes). Five animals received 30 mg. Na Amytal, 3 of which received 150 mg. of Na rhodanate. Average duration of anesthesia was 2 hours, 30 minutes. Average duration of anesthesia of controls was 2 hours, 10 minutes.

Ether Anesthesia. In order to secure as nearly as possible uniform anesthesia of rhodanate animals and controls one treated animal and one control were placed simultaneously in a large etherizing chamber, a cylinder 70 cm. long x 30 cm. diameter into which a stream of air containing ether vapor, thoroughly mixed in baffle chambers was passed. A glass tube containing 2 copper wires inserted through the wall of the chamber was used for testing sensitivity at various stages of anesthesia. Eight rabbits received 150 to 200 mg. per kg. sodium rhodanate intravenously before the anesthetization. An equal number of controls were used.† Here also the

* Since Prof. Bancroft has been awarded the Nichols medal of the New York Chemical Society for these researches, further investigation of his experimental data seemed necessary. Since Prof. Bancroft insists upon the use of Merck's Sodium Thiocyanate (Sodium Rhodanate), we used Merck's Sodium Thiocyanate recrystallized three times.

† After an interval of one week the control rabbit was given the NaSCN and the previous rhodanate animal was used as a control, thus ruling out individual variations.

rhodanate animals showed an average increased depth of anesthesia and retardation of recovery over the controls.

These results confirm the work of Henderson and of Burkholder and are in absolute contradiction to the claims of Bancroft regarding the pharmacological action of sodium rhodanate. Bancroft's therapeutic claims based upon such experiments are therefore unwarranted.

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Thermolability of the Tissue Extract Factor in Extract Activation.

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The writer has found that the addition of one volume of rabbit plasma to 60-100 volumes of chick embryo extract greatly increases the coagulative power of the extract[1]; that the increase of power is due to the appearance of a body which shows the same sensitivity to heparin as thrombin[2]; that the body reacts like thrombin in the presence and absence of ionic calcium[3]; that thermolability studies on the plasma factor indicate that this factor is prothrombin[4]. Mills and Matthews[5] found that mixtures of rabbit serum and lung extract show a temporary increase in coagulative power. Burns, Scharles, and Aitkin[6] have recently restudied the clotting power of extracts and sera from various sources. The papers cited above and some unpublished work made it reasonable to suppose that the cephalin in tissue extracts might be the factor involved in activation.

It is generally accepted that the only coagulation factor surviving boiling is cephalin. Mills[7] uses this as a method of distinguishing between tissue fibrinogen and cephalin in his study of blood platelets.

In this study chick embryo extract is made by extracting a 10 day embryo with Ringer solution. Coagulative power is tested by determining the shortening of the clotting time of a recalcified

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2 King, Joseph T., *Am. J. Physiol.*, 1932, **101**, 64.

3 King, Joseph T., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1112.

4 King, Joseph T., in press.

5 Mills, C. A., and Matthews, Stewart, *Am. J. Physiol.*, 1922, **60**, 193.

6 Burns, E. L., Scharles, F. H., and Aitkin, L. F., *Am. J. Physiol.*, 1931, **97**, 233.

7 Mills, C. A., *Chinese J. Physiol.*, 1927, **1**, 235.