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The Possible Oestrus-Inducing Effect of Commercial Taurocholate.*

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(Introduced by W. W. Swingle.)

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Gsell-Busse[1] has recently reported the production of oestrus in the rat and mouse through the administration of commercial preparations of sodium taurocholate—a subcutaneous dosage of 30 mg. bringing about oestrus in about 60 cases, tested according to the method of Allen and Doisy.[2]

Striking results were also obtained in the promotion of uterine hypertrophy, both in immature and in spayed adult rats. The uteri in sexually immature rats increased from 2½ to 5½ times the size of controls, following 14 days' subcutaneous injection of 25 mg. commercial taurocholate daily. Similar results were obtained in young rabbits and guinea pigs. Precocious sexual maturity was induced in immature rats by administration of 20 mg. of taurocholate in two doses, oestrus appearing at the end of two days.

The same author also reported the prolongation of the oestrous phase in rats by repeated daily injections of 25 gm. of taurocholate. Oestrus appeared in two days and persisted throughout the period of injection—from three to six weeks in some instances.

In attempting to repeat this work the authors have been unable to confirm Gsell-Busse. Following is a brief summary of results obtained.

Production of oestrus: Five spayed adult female rats received subcutaneously 30 mg. of commercial sodium taurocholate (Merck) daily. No animal came into oestrus (tested by the vaginal smear technique)even though the injections were continued for one week. On the contrary, severe diarrhea set in on the third day and lasted throughout the course of injection. The animals developed severe local reactions at the site of injection, became "droopy", and were found upon autopsy at the end of seven days' injection to have the typical genital atrophy of castration. Another commercial preparation of sodium taurocholate (Eastman) was tried on five experimental animals, with the same results. A similar series treated with sodium glycocholate (Merck) also failed to respond.

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[1] Gsell-Busse, A. A., *Arch. f. d. ges. Physiol.*, 1928, ccxix, 626.

[2] Allen, E., and Doisy, E. A., *Am. J. Anat.*, 1922, xxx, 297.

Induction of precocious sexual maturity: A litter of eight immature (30 day) female rats was utilized; two being given sodium taurocholate, two sodium glycocholate, and four kept as controls. Subcutaneous injection twice daily of 15 mg. each failed to produce precocious sexual development, although injections were continued for eight days. Severe diarrhea set in on the third or fourth day and the rats suffered some degree of general emaciation. At the end of eight days they were appreciably smaller than the controls. Injections produced severe local reactions.

Gsell-Busse also reported an "antimasculine" effect of sodium taurocholate. He found that injections of 20 mg. daily for 19 days resulted in a marked retardation of development of the testes in young experimental animals. In attempting to repeat this experiment on rats the authors obtained essentially the same results, but the disparity in weight between experimental animals and litter controls was found not to be confined to the genitalia but was true for the animal as a whole. Typical data are tabulated below.

Four litter mate males (35 days old); two on taurocholate (Merck), two as controls. At the end of 14 days' injection of 20 mg. per day the following weights were recorded at autopsy:

Injected	body weight	left testicle	right testicle	kidney
Rat No. I	130 gm.	0.382 gm.	0.830 gm.	1.222
Rat No. II	127 gm.	0.615 gm.	0.430 gm.	
Controls				
Rat No. I	205 gm.	1.248 gm.	1.683 gm.	1.857
Rat No. II	203.5 gm.	1.133 gm.	1.135 gm.	

Essentially the same results were obtained with commercial sodium glycocholate.

It appeared obvious from the foregoing results, and also from the work of Horrall and Carlson[3] that cholate salts, instead of promoting oestrus, were actually inimical in their effect upon the animal. This suggested the following experiment.

Antagonistic effect of taurocholate to Estrogen. (Estrogen supplied by Parke, Davis & Company.) Three spayed females were given three subcutaneous injections six hours apart of Estrogen (a total of 2 rat units), along with three 15 mg. subcutaneous injections of taurocholate (Merck). Three controls received the same amount of Estrogen without being given taurocholate. The controls came into typical oestrus on the third day, whereas those which received both Estrogen and taurocholate failed to display any change.

[3] Horrall, O. H., and Carlson, A. A., *Am. J. Physiol.*, 1928, lxxxv, 591.

It is to be concluded that the commercial preparations of sodium taurocholate used in this study do not contain a principle similar in action to the ovarian hormone.

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Studies on Simple Goiter Produced by Cabbage and Other Vegetables.

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Chesney, Webster and Clawson[1, 2, 3] have shown that when fresh cabbage *(Brassica oleracea)* is fed to rabbits as the principal food, clinically detectable thyroid hyperplasia occurs in 2 or 3 months, and with continued cabbage feeding very large goiters (up to 45 gm.) have been produced. They further showed that the development of goiter was associated with a lowering of the metabolism and that the administration of small amounts of iodine readily raises the metabolic rate in goiterous rabbits and prevents thyroid hyperplasia. In these respects, as well as histologically, the thyroid hyperplasia produced by feeding cabbage is identical with that of simple or endemic goiter.

We have confirmed these findings.

Boiling or steaming cabbage for 30 minutes increases its capacity to produce thyroid hyperplasia. Steaming for 15 minutes is less effective and steaming for 60 minutes renders it neither more nor less potent than for 30 minutes. Steamed cabbage from which 60% of the weight is removed as press juice is practically as effective as whole cabbage when fed in calori-equivalent amounts. Hashed fresh cabbage has very little capacity to produce thyroid hyperplasia, while hashed steamed cabbage fully retains this quality. In our hands the press juice of 500 gm. of steamed cabbage (300 cc.) when fed daily to rabbits whether whole or concentrated *in vacuo* was only slightly effective.

Rabbits previously iodized and fed with fresh cabbage up to 75 calories per kg. per day (3 gm. of cabbage are equivalent to approx-

[1] Chesney, A. M., Clawson, T. A., and Webster, B., *Johns Hopkins Hosp. Bull.*, 1928, xliii, 261.

[2] Webster, B., Clawson, T. A., and Chesney, A. M., *Johns Hopkins Hosp. Bull.*, 1928, xliii, 278.

[3] Webster, B., and Chesney, A. M., *Johns Hopkins Hosp. Bull.*, 1928, xliii, 291.