Summary. Testosterone propionate, introduced in pellet form into intact, castrated or partially hypophysectomized immature male *Anolis carolinensis,* elicits both male and female sexual behavior, the latter including submission to copulation and display of a distinctive neck reflex. Testosterone-treated males fight more actively than controls, and the assumption of male or female behavior is apparently related to position as dominant or subordinate in fights among the group. Testosterone affects the reflexes involved in the copulation posture so that they are maintained in exaggerated form after the escape of the partner.

13029 P

Bile Acids and the Pulmonary Tumor Incidence in A Strain Mice.

L. W. LAW.* (Introduced by C. C. Little.)

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The principal bile acids of the higher vertebrates are hydroxy derivatives of cholanic acid, a compound which can be obtained *in vitro* from sterols by degradation. The bile acids as well as sterols have condensed carbon ring molecules to which are attached side-chains in a position such that a new 6-membered ring can be formed so as to give the carcinogenic 1:2-benzanthracene ring system without any molecular rearrangement or migration of groups within the molecule. In 1934 it was shown[1] that such a ring closure to the 1:2-benzanthracene system had occurred in the formation of dehydronorcholene from desoxycholic acid. Upon dehydrogenation of this product methylcholanthrene, a highly carcinogenic substance, was formed. Later[2] it was shown that methylcholanthrene could be obtained from cholic acid, the chief acid of human bile.

These discoveries led to tests for carcinogenic properties of the bile acids with conflicting results. Application of desoxycholic acid in alcohol or benzene to the skin in a large series of mice gave completely negative results. Injections *sub cutem* of 70 mg desoxycholic acid in sesame oil produced sarcomata in 3 of 10 mice at a late date.[3] This experiment was repeated using the C3H strain of

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1 Cook, J. W., and Haslewood, G. A. D., *J. Chem. Soc.,* 1934, 428.

2 Fieser, L. F., and Newman, M. S., *J. Am. Chem. Soc.,* 1935, **57**, 961.

3 Cook, J. W., Kennaway, E. L., and Kennaway, N. M., *Nature,* 1940, **145**, 627.

mice, a very suceptible strain to induction of subcutaneous tumors by carcinogens. Seven spindle-cell tumors were obtained in 208 days, the first appearing 155 days after receiving a total of 28 mg in 6 injections. Shear obtained completely negative results following injections *sub cutem* of both cholic and desoxycholic acids. Ghiron reported that transplantable fibrosarcomata were induced in a high percentage of rats and mice following injections of desoxycholic acid, however no further details of this work have been published.

The purpose of this preliminary report is to record the response of lungs of A strain mice to 2 bile acids† injected subcutaneously. The Jackson Laboratory A strain has a high incidence of pulmonary tumors.[4] Spontaneous tumors in mice under 9 months of age usually appear as single nodules just underneath the pleura, whereas multiple nodules appear very early in mice treated with carcinogens.[5] Equal numbers of pedigreed males and females were used and kept separate. One experimental group was given a total dosage of 10 mg cholic acid dissolved in olive oil. The first injection was given at the age of one month and 3 subsequent injections were given within the following 2 months. A second experimental group was given the same dosage of sodium desoxycholate. The animals were killed at 9 months of age, 8 months following initial injections. Lung nodules were looked for grossly under the dissecting microscope and histological confirmation was made of nodules.

From Table I it can be seen that sodium desoxycholate has increased the pulmonary tumor incidence ($P < .01$) and increased the number of nodules found in the lung. In this experimental group there appeared a fibrosarcoma in an animal 7 months of age. Spontaneous sarcomata are rare in A strain mice and none have been recorded as appearing at this age. There was no effect of cholic acid on the pulmonary tumor incidence.

TABLE I.
Response of Lungs of Strain A Mice to Bile Acids.

Treatment	No. mice	No. lung tumors	% lung tumors	Mean No. nodules in lung
Sodium desoxycholate	20	16*	80.0	3.0
Cholic acid	30	14	46.7	1.4
Controls	38	18	47.3	1.9

*One mouse killed at 8 months—fibrosarcoma.

† Supplied through the courtesy of Dr. Oliver Kamm, Parke, Davis & Co.

[4] Bittner, J. J., *Pub. Health Rep.*, 1939, **54**, 380.

[5] Andervont, H. B., *Pub. Health Rep.*, 1937, **52**, 304.

Mice of strains C3H, C57 black, and A^W, known to be among the most susceptible to subcutaneous growths after application of carcinogens, have not as yet (10 months) given any subcutaneous tumors following similar treatment with cholic acid and sodium desoxycholate.

A study of the effect of larger doses of desoxycholic acid on pulmonary tumor incidence in A strain mice is being continued.

Summary. A significant increase in the incidence of pulmonary tumors is recorded in A strain mice following subcutaneous injection of 10 mg sodium desoxycholate. No such response was indicated following similar treatment with cholic acid.

13030 P

Histophysiological Study on Activity of Stellate Cells of Frog Liver.*

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Activity of stellate cells in the liver ordinarily is tested by their capacity to incorporate microscopic or submicroscopic particles, e. g., colloidal trypan blue. In isolated perfused frog liver this uptake is shown to be an active process by the fact that it is reversibly suppressed by addition to the perfusion fluid of an anesthetic or of iodoacetic acid.[1] Also, the color uptake is stopped by perfusing, for a short time, with Ringer's solution, but reappears upon the addition of serum or of various protein bodies.[2, 3, 1] While studying the influence of surface-active and nonpolar-polar organic compounds on erythrocytes, muscles, nerves, liver, kidney,[4] we were reminded of the statement of A. J. Clark[5] that the strikingly beneficial effect of serum on the heart of a frog, which has become

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1 Ferrari, R., and Höber, R., *Pflüger's Arch.*, 1933, **232**, 299.

2 von Jansco, N., *Z. Exp. Med.*, 1928, **61**, 63.

3 Höber, R., and Titajew, A., *Pflüger's Arch.*, 1929, **223**, 180.

4 Höber, R., *Cold Spring Harbor Symposia*, 1940, **8**, 40.

5 Clark, A. J., *J. Physiol.*, 1913, **47**, 66.