actually exposed to 400 R of X-irradiation while the control group received only sham exposure. The Figure shows the average daily liquid consumption of these 2 groups. From the upper graph one observes a difference of about 35% between daily water and saccharin consumption. The animals in this group definitely prefer sodium saccharin solution to plain tap water as usually observed. In the lower graphs, however, this trend is just reversed. The average daily water consumption exceeds that of sodium saccharin almost 2 to 1.

SCARBOROUGH and MCLAURIN[13] have reported that saccharin solutions, when injected i.p. prior to radiation exposure, does not produce a conditioned aversion. Neither have we observed any avoidance when H_2O_2, a confirmed radiolytic product of irradiated solutions, was injected into the peritoneal cavity of the animals. Since over a decade ago when the first investigators reported that information could be transferred, a number of experiments have been performed but a conclusive demonstration is still yet to be presented. New models were offered to explain the possible mechanism of 'information' or 'learning' transfer, ranging from the idea that neurons may have high chemical specificity[14] to electron-microscope evidence of the existence of intrasynaptic protein filament[15].

The learning and/or behavioral aspect of post-irradiation aversion in mice is still being questioned. Whether the effect of irradiation really changes the composition of the brain in the animals trained to prefer sodium saccharin is a difficult question to answer. P^{32}-labeled RNA, according to LUTTGES et al.[16], was not traceable in the brain after i.p. injection; and nucleic acid extracted from the brains of trained animals does not produce 'transfer of learning' when injected i.p. or intraventricularly. REINIS[17], however, found significant 'transfer effect' by i.p. injection of brain extracts. As we mentioned earlier, we are still very far from being in a position where we can offer any acceptable hypothesis.

Zusammenfassung. Man kann «post-irradiation»-bedingtes Ablehnungsverhalten indirekt herbeifuhren, indem man Hirngewebe von abgerichteten Mäusen in den Peritonealraum der unabgerichteten Mause injiziert. Die «Empfänger» verhalten sich, als seien sie selbst dem Saccharinbevorzugungs-Test und anschliessend ionisierender Bestrahlung ausgesetzt worden. Wir haben zur Zeit noch keine stichhaltige Erklärung für diese interessante Beobachtung.

H. LEVAN[18], D. L. HEBRON[18], W. S. MOOS[19] and H. C. MASON[20]

Veterans Administration Hospital, Section of Radiation Physics, Therapeutic Radiology Service, Hines (Illinois 60141, USA), 14 January 1970.

[13] B. B. SCARBOROUGH and W. S. MCLAURIN, Radiat. Res. *15*, 829 (1961).
[14] R. B. HARRIS and L. B. FLEXNER, Am. Scient. *54*, 174 (1966).
[15] R. ROSENBLATT, *Computer and Information Science* (Academic Press, New York 1967), p. 33.
[16] M. LUTTGES, T. JOHNSON, C. BUCK, J. HOLLAND and J. MCGAUGH, Science *151*, 834 (1966).
[17] S. REINIS, Nature *220*, 177 (1968).
[18] Present address: Department of Therapeutic Radiology, V. A. Hospital, Hines, Illinois 60141; and Department of Radiology, The Chicago Medical School, Chicago (Illinois, USA).
[19] International Atomic Energy Agency, Kärntnerring 11, Wien 1 (Austria).
[20] Arkansas State Hospital, Little Rock (Arkansas 72202, USA).

Effects of Ergocornine and 2-Br-α-Ergokryptin (CB-154) on the Formation of Mammary Hyperplastic Alveolar Nodules and the Pituitary Prolactin Levels in Mice

Several investigations have demonstrated that ergocornine suppresses deciduoma formation[1] and implantation[1], terminates pseudopregnancy[2], early pregnancy[2] and lactation[3], inhibits the growth of prolactin responsive carcinogen-induced mammary tumor[4] and causes endogenous estrogen-progesterone imbalance[5]. The other ergot alkaloids, α-ergokryptin and 2-Br-α-ergokryptin (CB-154), were also reported to inhibit fertility and lactation in rat[6]. SHELESNYAK[7] found that the pregnancy was protected against ergocornine interference by the additional treatment of prolactin. All these results infer that these ergot alkaloids would inhibit the anterior pituitary secretion.

It is well known that hyperplastic alveolar nodules (HAN) of the mammary gland in mice represent the preneoplastic state in mammary tumorigenesis and that prolactin has a prominent role in the formation of HAN[8]. The present experiment was carried out in order to investigate whether or not ergocornine and CB-154 suppress the formation of HAN, and the pituitary prolactin levels of these ergot alkaloids treated mice were also determined.

Materials and methods. Animals used were 7- to 8-month-old multiparous female mice of C3H/He strain more than 1 month after the last lactation. They were divided into 3 groups consisting of 10–11 mice each. Groups I and II were given s.c. injections of 0.2 mg of ergocornine methanesulfonate and CB-154 suspended in 0.1 ml of physiological saline daily for 20–23 days, respectively. Group III received no treatment and was served as control. All mice were examined by vaginal smears once a day throughout the experiment, beginning 10 days before the start of injections. They were killed by decapitation at 20–23 days after the start of injections when they showed the proestrous to estrous smears. The anterior pituitary was immediately removed, weighed and kept at −20 °C until assayed. Prolactin and growth hormone (GH) levels in the anterior pituitary were determined by recently developed disc electrophoretic method

[1] M. C. SHELESNYAK, Am. J. Physiol. *179*, 301 (1954).
[2] R. A. CARLSEN, G. H. ZEILMAKER and M. C. SHELESNYAK, J. Reprod. Fert. *2*, 369 (1961).
[3] G. H. ZEILMAKER and R. A. CARLSEN, Acta endocrin. *41*, 321 (1962).
[4] H. NAGASAWA and J. MEITES, unpublished data.
[5] M. C. SHELESNYAK, Am. J. Physiol. *180*, 47 (1955).
[6] E. FLÜCKIGER and H. R. WAGNER, Experientia *24*, 1130 (1968).
[7] M. C. SHELESNYAK, Acta endocrin. *27*, 99 (1958).
[8] H. A. BERN and S. NANDI, Prog. exp. Tumor. Res. *2*, 99 (1961).

Table I. Inhibitory effects of ergocornine and CB-154 on the formations of lobulo-alveoli (L-A) and hyperplastic alveolar nodules (HAN) in the mammary gland of mice

Group	Treatment	No. of mice	Average rating of L-A formation[a]	Total No. of HAN per mouse[b]	Average size of HAN (mm)
I	Ergocornine (0.2 mg/day)	11	1.6 ± 0.3[c]	9.9 ± 3.5	0.52 ± 0.02
II	CB-154 (0.2 mg/day)	10	1.5 ± 0.2	5.6 ± 1.7	0.47 ± 0.03
III	–	11	2.5 ± 0.2	22.5 ± 3.9	0.54 ± 0.02

[a] Average in bilateral thoracic third mammary glands. [b] Sum in bilateral thoracic third mammary glands. [c] Mean ± S.E. of mean.

Table II. Effects of ergocornine and CB-154 on pituitary weight and pituitary prolactin and growth hormone (GH) levels

Group	Treatment	No. of mice	Anterior pituitary weight (mg)	Prolactin[a] Content (cm^2/AP)	Concentration (cm^2/mg AP)	GH[a] Content (cm^2/AP)	Concentration (cm^2/mg AP)
I	Ergocornine (0.2 mg/day)	11	2.17 ± 0.06[b]	1.6 ± 0.1	0.7 ± 0.1	11.0 ± 0.5	5.1 ± 0.1
II	CB-154 (0.2 mg/day)	10	2.05 ± 0.08	1.6 ± 0.1	0.8 ± 0.0	11.0 ± 0.2	5.4 ± 0.2
III	–	11	2.58 ± 0.09	2.9 ± 0.2	1.2 ± 0.0	12.6 ± 0.5	4.9 ± 0.2

[a] Contents and concentrations of prolactin and GH are expressed as optical density (cm^2). [b] Mean ± S.E. of mean. AP: anterior pituitary.

on polyacrylamide gel by CHEEVER et al.[9]. The densities of these hormone bands were measured with microdensitometer (Canalco, Model E). It has been confirmed that the doses of the standard preparations of these hormones (prolactin, NIH-P-B_2; GH, NIH-GH-B_{12}) had the linear relations with their optical densities[10,11]. The bilateral thoracic third mammary glands were used for whole mount preparations. The number of HAN was counted and its size was measured under 10-fold magnification. The degree of lobulo-alveolar (L-A) formation of the gland was rated from 1–7 in increments of 1 by the standard of WRENN et al.[12] with a little simplification.

Results and discussion. The number and size of HAN and the degree of L-A formation in mammary glands are presented in Table I. The number of HAN and the degree of L-A formation were significantly less in groups I and II than in group III, whereas the size of HAN was nearly the same in all groups. The ghosts of HAN were sporadically observed in the glands of groups I and II. This suggests that the administrations of these ergot alkaloids induced involution of the already established HAN as well as inhibition of development of new HAN.

The anterior pituitary weight and pituitary levels of prolactin and GH in each group are shown in Table II. Both pituitary prolactin contents and concentrations in groups I and II were significantly lower than those in group III. These findings clearly indicate that these ergot alkaloids suppress the pituitary prolactin secretion, because it has been found that both pituitary and serum prolactin levels of rat decreased not only on single[13] but also on chronic[14] administration of ergocornine. Remarkable inhibition of development and growth of HAN by ergocornine and CB-154 could be ascribed to their inhibitory actions on pituitary prolactin secretion.

The estrous cycles of ergot alkaloids treated mice did not show the rather long diestrus often observed in the estrous cycles of normal C3H/He mice[15]. This could also be accounted for by the inhibitory actions of ergot alkaloids on pituitary prolactin secretion, which in turn affected the ovarian progesterone secretion as suggested by VALAVUDHI et al.[16].

GH contents of whole pituitary were slightly lower in groups I and II than in group III, but GH concentration per mg of pituitary was not different among groups, indicating that ergocornine and CB-154 had little effects on the pituitary GH secretion (Table II).

The body weight changes during the experiment were −7, −2 and −1% in groups I, II and III respectively. The body weight was slightly decreased by ergocornine, but not by CB-154.

Zusammenfassung. Ergocornin und 2-Br-α-Ergokryptin (CB-154) unterdrücken die Formation von hyperplastischen alveolaren Noduli der Milchdrüse und vermindern Prolactin-Sekretion aus dem Hirnanhang in der Maus.

R. YANAI and H. NAGASAWA[17]

Pharmacology Division,
National Cancer Center Research Institute,
Tsukiji 5-1-1, Chuo-ku,
Tokyo (Japan), 10 February 1970.

[9] E. V. CHEEVER, B. K. SEAVEY and U. J. LEWIS, Endocrinology *85*, 698 (1969).
[10] R. YANAI, H. NAGASAWA and K. KURETANI, Endocrinol. Jap. *15*, 365 (1969).
[11] R. YANAI and H. NAGASAWA, Proc. Soc. exptl. Biol. Med. *131*, 167 (1969).
[12] T. R. WRENN, J. BITMAN, W. R. DELANDER and M. L. MENCH, J. Dairy Sci. *49*, 183 (1966).
[13] K-H. LU and J. MEITES, personal communication.
[14] H. NAGASAWA and J. MEITES, unpublished data.
[15] H. NAGASAWA, M. FUJIMOTO, H. IWAHASHI and K. KURETANI, Gann *58*, 115 (1967).
[16] P. VALAVUDHI, B. L. LOBEL and M. C. SHELESNYAK, J. Endocrin. *34*, 425 (1966).
[17] The authors wish to express their heartiest thanks to Drs. M. TAESCHLER and E. FLÜCKIGER, Sandoz Ltd., Basel, for their kind donation of ergocornine and CB-154.