PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 155, 599-601 (1977)

TSH in Serum and Milk of Normal, Thyroidectomized, and Hyperthyroid Lactating Rats[1] (39858)

L. KRULICH, O. KOLDOVSKY,* T. JUMAWAN,* H. LAU,* AND C. HOROWITZ*

*Department of Physiology, University of Texas Health Science Center at Dallas, Southwestern Medical School, Dallas, Texas 75235, and * Department of Pediatrics, University of Pennsylvania, Philadelphia, Pennsylvania 19104*

It has been shown recently that milk of various species contains several hormones. Progesterone and other steroids were detected in cow's milk (1, 2), prolactin in milk of women, goats, and rats (2, 4, 5), and thyroid hormones in milk from human beings, monkeys, and rats, respectively (6-9). The question has arisen whether milk also contains thyrotropin (TSH) and whether its concentration in milk is influenced by changes in serum TSH levels. Therefore, TSH in serum and milk was determined in normal lactating rats, in lactating thyroidectomized animals with elevated TSH levels, as well as in animals treated with large doses of triiodothyronine to suppress TSH secretion.

Materials and Methods. Charles River females of the CD strain were obtained on the 14th day of pregnancy. On the 3rd day postpartum (p.p.) the number of pups per mother was decreased to nine. On the 11th day p.p. half of the litter of one mother was exchanged with half of the litter of another mother. One mixed litter and mother were the experimental group and the other mixed litter and mother served as controls. In some experiments, however, both groups remained untreated, so that the number of controls is larger than the number of experimental animals.

The lactating rats were thyroidectomized, with pentobarbital (Nembutal, 3.5 mg/100 g, ip) used for anesthesia, either 7 or 14 days p.p. In the first case, the experiment was terminated on the 15th day p.p., in the second case, on Day 19 or 22 p.p., respectively. L-Triiodothyronine (T_3-free acid) dissolved in 0.005 *N* NaOH was administered daily (1.2 mg/animal) from Day 11 to Day 15 p.p. Control animals received an equivalent volume of the vehicle.

Collection of blood and milk for TSH determination was performed as follows: At 9 AM the pups were removed from the dams. Between 12:30 and 1:30 PM the females were anesthetized with ether and a blood sample was collected from the retroorbital venous plexus. Immediately thereafter, oxytocin (1 to 2 IU, iv) was injected ip and 5 to 10 min later milk was obtained by manual expression. Serum and milk samples were stored at −20° until assayed.

With the exception of samples from the T_3-treated rats and their controls, all the other samples were determined in a single assay.

TSH in serum and milk was determined by the NIAMDD radioimmunoassay kit for rat TSH. The TSH concentrations are expressed in terms of the R-P-1 standard provided with the kit.

The statistical significance of the results was evaluated by Student's *t* test for unpaired samples.

Results and Discussion. The concentrations of TSH in serum and milk from all the experimental groups are compared in Table I. In euthyroid lactating rats, the mean concentration of TSH in milk appears lower than the concentration in serum. The difference is, however, not statistically significant owing to the large variability of the TSH levels. The serum TSH concentrations in normal lactating females are lower than the TSH levels usually seen in normal cyclic females (Castro-Vasques, Krulich, and McCann, unpublished results) and definitely lower than those seen in normal males (10). There were no significant differences

[1] Supported by PHS Grants AM10073, HD05151, and AM14531.

ISSN 0037-9727

TABLE I. TSH CONCENTRATIONS IN SERUM AND MILK IN NORMAL LACTATING RATS, LACTATING THYROIDECTOMIZED RATS, AND LACTATING RATS TREATED WITH T_3.

Experiment No.	Treatment	Termination of experiment (days p.p.)	TSH (ng/ml ± SE)	
			Serum	Milk
1	Controls	14	163 ± 39.6 (7)[a]	167 ± 18.3 (7)
		19	296 ± 75.6 (8)	145 ± 13.3 (8)
		22	152 ± 58.3 (3)	160 ± 16.6 (2)
	All controls		219 ± 39.8 (18)	156 ± 9.8 (17)
	Thryoidectomy (thx) on p.p. Day			
	7	14	684 ± 89.7* (4)	222 ± 9.6** (4)
	14	19	835 ± 121* (4)	234 ± 14.0* (4)
	14	22	1,156 ± 239* (4)	234 ± 11.4** (3)
	All thx		892 ± 104* (12)	230 ± 6.5* (11)
2	Controls	14	270 ±49.4 (6)	152 ± 12.6 (6)
	T_3	14	72 ± 7.1* (5)	63 ± 6.7* (5)

[a] Numbers in parentheses indicate the number of animals per group.
* Significant at $P < 0.01$ with respect to the appropriate controls.
** Significant at $P < 0.05$.

among the three lactation periods studied. Thyroidectomy was followed by a highly significant fourfold elevation of serum TSH and by a significant increase of TSH concentration in milk by 47%. The magnitude of the elevation of TSH in milk was, however, in no apparent relationship with the magnitude of the elevation in serum TSH. In contrast, administration of T_3 reduced serum TSH as well as TSH in milk to barely detectable values.

The results presented above show (a) that TSH is present in the milk of normal lactating rats, (b) that the TSH concentration in milk can be significantly influenced by the thyroid status of the lactating females, and (c) that the changes of TSH concentration in milk follow the same direction as the changes of serum TSH levels, but that their relative magnitude is smaller in milk than in serum. TSH can, therefore, be added to the list of hormones present in milk; however, the physiological significance, if any, of these findings remains to be explored.

Summary. TSH was determined by radioimmunoassay in serum and milk of euthyroid, hyperthyroid, and thyroidectomized lactating rats. In the normal euthyroid rats, the average serum TSH concentration was 219 ± 39.8 ng/ml, while the average concentration in milk was 156 ± 9.8 ng/ml. Five to seven days after thyroidectomy both values were significantly increased to 892 ± 109 and 230 ± 6.5 ng/ml, respectively. In animals treated with a very large dose of T_3 for 4 days, serum and milk TSH concentrations were conspicuously decreased to 72 ± 7.1 and 63 ± 6.7 ng/ml, respectively.

1. Darling, J. A. B., Laing, A. H., and Harkness, R. A., J. Endocrinol. **62,** 291 (1974).
2. Ginther, O. J., Nuti, L., Wentworth, B. C. and Tyler, W. J., Proc. Soc. Exp. Biol. Med. **146,** 354 (1974).
3. Gala, R. R., Horm. Res. **6,** 310 (1975).
4. McMurtry, J. P., and Malven, P. V., Endocrinology **96,** 559 (1974).
5. McMurtry, J. P., and Malven, P. V., J. Endocrinol. **61,** 211 (1974).
6. Štrbák, V., Macho, L., Knopp, J., and Struhárová, L., Endocrinol. Exp. **8,** (1974).
7. Štrbák, V., Macho, L., Kováč, R., Škultéyová,

M., and Michalicková, J., Endocrinol. Exp. **10,** 167 (1976).
8. Montalvo, J. M., Wahner, H. W., and Christie, R. J., Program of the 56th Meeting of the Endocrine Society, A-91 (1974).
9. Tenore, A., Parks, J. S., and Bongiovanni, A. M., *in* "Symposium on Recent Progress in Pediatric Endocrinology, Milan, 1976." Academic Press, New York (in press).
10. Krulich, L., Giachetti, A., Marchlewska-Koj, A., Hefco, E., and Jameson, H. E., Endocrinology **100,** 496 (1977).

Received March 25, 1977. P.S.E.B.M. 1977, Vol. 155.