Variations in Thyroid Morphology of Mice.* (23662)

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Variations in epithelial height and in the amount of stored colloid in the follicles have been associated with changes in the degree of activity of the thyroid gland. A high follicular epithelium and a small amount of stored colloid are characteristic of actively secreting glands, while a low epithelium and a large amount of colloid within the follicles are characteristic of less actively secreting glands(1). The rate of secretion of the thyroid hormones is controlled to a large extent by the production of thyroid stimulating hormone (TSH) by the pituitary, and observations of changes in thyroid morphology have been employed in various methods for TSH assay(2-4).

This investigation was initiated in order to determine if aging and parity might be associated with changes in thyroid morphology in 2 inbred strains of mice. The occurrence of spontaneous mammary tumors in some of the older C3H mice used in this study also enabled a comparison of the thyroids of these mice with those of tumor-free mice of corresponding ages.

Methods. Inbred Z(C3H)/Bittner/Lawrence and C57 Bl/6/JAX mice were used in this study. The mice were housed in transparent plastic cages and fed Purina Laboratory Chow *ad libitum* with an oat supplement. The temperature was rigidly controlled between 78-80°F without specific humidity control. Female littermates were randomized between the breeding and non-breeding study groups. Pregnant females were not isolated, but their litters were removed from the cage within 3 days after birth. However, about one month before sacrifice, most of the pregnant mice were isolated and were allowed to nurse their last litter for 20-30 days, this last litter being weaned at least two days prior to sacrifice of the mother. Because of time considerations it was not possible to allow all of the animals of the 3 and 4 month groups to have such a period of lactation. Animals with tumors were isolated until they were sacrificed and those with ulcerated tumors were discarded. Animals were killed by cervical dislocation at monthly age intervals ($\pm$ 5 days). They were sacrificed in several large batches, each of which included representatives from many of the groups. The trachea was used to handle the tissue and to enable consistent orientation of the thyroids for sectioning. The tissues were fixed in Bouin's fluid, dehydrated in alcohol, cut at 5 μ and stained with haematoxylin and eosin. The slides were coded to assure objectivity of the measurements. The mean of the measurements of 10 follicles in each of the 863 glands was recorded. The selection of the section to be measured was based on the clarity of the section as well as on the width of the thyroid lobe. Whenever possible, that section having the greatest width from its medial to its lateral aspect was selected. Ten representative follicles, which were midway between the anterior and posterior poles of the thyroid lobe and on a line extending from its medial to its lateral aspect, were measured.

Results. Sex. Analyses of measurements of both epithelial height and diameter of follicles revealed that there were no consistent differences between values obtained for males and for virgin females when animals of corresponding ages were compared. Therefore, the data from these 2 groups were pooled for all further analyses. This pooled sample of 652 mice hereafter will be referred to as the non-parous group.

Age. In both strains the non-parous mice showed a sharp decrease in thyroid epithelial height during the early months of life; from 1 through 3 months in the C3H strain and through 5 months in the C57, (Fig. 1). These

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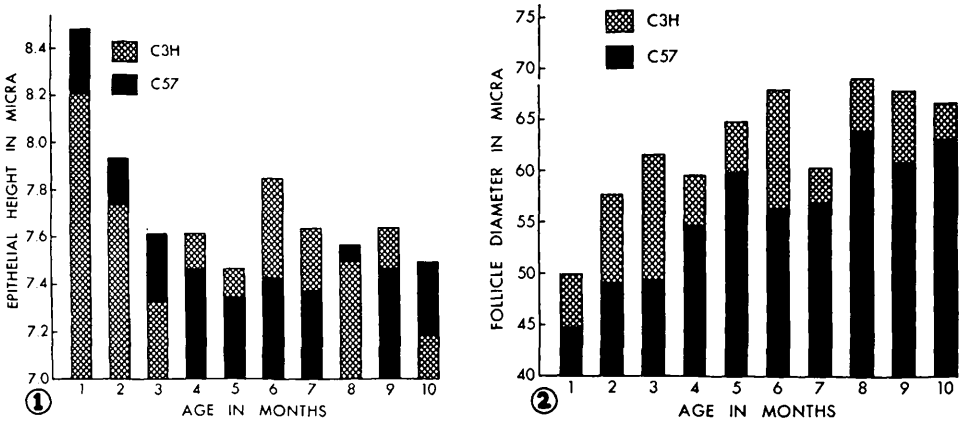

FIG. 1. Mean thyroid epithelial heights of non-parous C3H and C57 mice.
FIG. 2. Mean diameters of thyroid follicles of non-parous C3H and C57 mice.

differences are significant at the 1% level of confidence. Follicle diameter measurements from thyroids of non-parous mice exhibited an inverse relationship. That is, there was a marked increase in these values through the first 3 months in the C3H strain and through the first 5 months in the C57 strain, Fig. 2. In both strains there was a tendency for a continued, although less consistent increase in the follicle diameter size throughout the remainder of the 10 months of observation. A similar trend was also evident in the non-tumorous parous females, Fig. 3 & 4. These differences in follicular diameter measurements are also significant at the 1% level of confidence.

Parity. When data for epithelial height of tumor-free parous and non-parous C3H mice of corresponding ages were compared statistically, the observed differences were not significant, Fig. 5. However, in the C57 strain the thyroids of the parous females had a lower epithelial height than did those of the non-parous group at all ages except at the 5 month level, Fig. 6. Analysis of variance of the data in relation to parity indicates that the tendency for lower epithelial height in parous females in the latter strain is significant ($P = .01$). The differences in the mean follicular diameters of the parous versus the non-parous mice were not consistent, Fig. 3 & 4, but they did show a tendency for larger thyroid follicles to be present in the parous than in the non-parous mice ($P = .01$). The exceptions were at the 3 and 6 month intervals in the C3H and at the 5 and 8 month intervals in the C57 strain. Measurements from 211 parous mice were employed for these analyses.

Strain. There was not a statistically significant difference in epithelial heights when C3H and C57 mice of corresponding ages were compared, Fig. 1. However, the mean follicular diameters of the C3H thyroids were significantly greater than were those of the C57 ($P = .01$), Fig. 2. The functional significance of these anatomical differences between the two strains is, however, questionable.

Presence of tumor. Data obtained from 21 tumor-bearing parous C3H mice 8-11 months of age were compared with those from 33 non-tumor parous C3H mice of the same age. The height of the follicular epithelium of the tumorous animals was found to be significantly lower ($P = .05$) than that of the non-tumor-

TABLE I. Thyroid Measurement of Tumor and Non-Tumor-Bearing C3H Mice.*

Age in mo	Presence of tumor	No. mice	Mean diameter	Mean epithelial ht
8	—	8	70.35	7.69
	+	6	77.47	6.63
9	—	12	70.80	7.30
	+	9	79.05	6.74
10	—	12	74.50	7.39
	+	3	75.74	7.23
11	—	1	73.59	7.84
	+	3	78.54	7.44

* In micra.

ous animals. The follicular diameters were also correspondingly greater but these differences were not of statistical significance.

Discussion. Observations of a tendency for decreased epithelial height and increased diameter of thyroid follicles in both strains with increasing age, suggest that there is a decrease in thyroid activity with increasing age. These results are in agreement with other findings. Legait *et al.*(5) found increasing colloid accumulation in thyroids of rats as they matured. Hurst and Turner(6), using the assay method of Dempsey and Astwood, concluded that mature albino mice of both sexes secrete less "thyroxine" than do younger mice. Grad and Hoffman(7) came to similar conclusions, employing rats.

The results of this study indicate that although there are no consistent differences between the thyroid morphology of males and of virgin females within either strain, the thyroids of the parous females of both strains show morphological evidence suggesting that they have a lower activity than do those in the non-parous group.

Tumor-bearing parous C3H mice also show

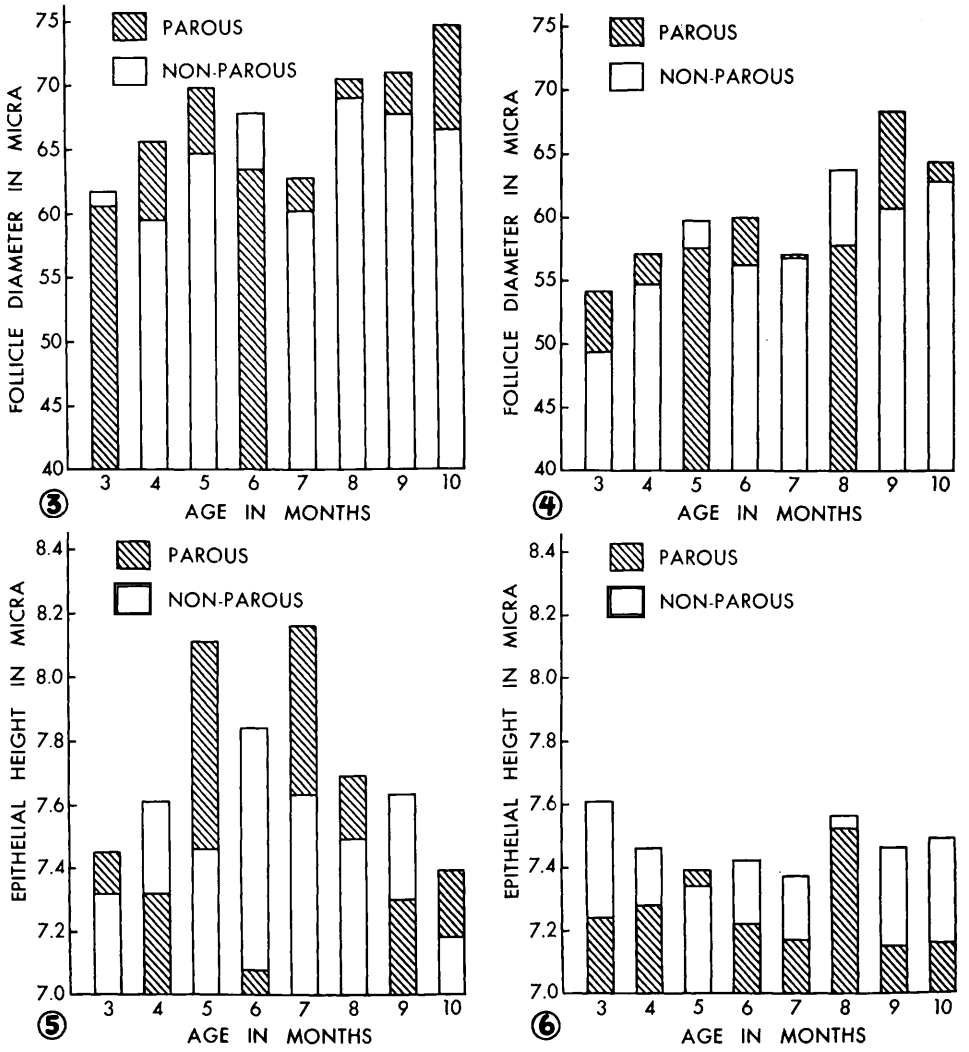

FIG. 3. Mean diameters of thyroid follicles of parous and non-parous C3H mice.
FIG. 4. Mean diameters of thyroid follicles of parous and non-parous C57 mice.
FIG. 5. Mean thyroid epithelial heights of parous and non-parous C3H mice.
FIG. 6. Mean thyroid epithelial heights of parous and non-parous C57 mice.

morphological evidence of decreased thyroid secretion when compared to tumor-free parous mice of corresponding ages. This is in agreement with the report of Larinow(8) that rabbits with tar-induced papillomata and mice with spontaneous and transplanted mammary adenocarcinoma show a depression in the height of the follicular epithelium. In these latter studies, the epithelium became increasingly lower as the tumors became larger. A lowered thyroid activity in tumor-bearing mice might well reflect metabolic changes within the host associated with the presence of tumor.

Summary. Observations of thyroid follicle epithelial heights and diameters were analyzed with respect to age and parity in C3H and C57 mice. Epithelial heights decreased and follicle diameters increased with aging and breeding. The presence of tumors in the C3H parous females was associated with decreased epithelial height and increased diameter of the thyroid follicles as compared to non-tumor-bearing mice of corresponding ages. These changes suggest that aging, breeding and the presence of tumor are associated with decreased thyroid function.

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Increase in Heidenhain Pouch Secretion after Portacaval Transposition in the Dog.* (23663)

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Several studies have indicated that peptic ulcers occur with greater frequency in patients with cirrhosis of the liver than in patients without cirrhosis(1,2,3). Malnutrition, deficient amounts of biliary elements, central nervous system damage, and inflammation and congestion of the stomach mucosa have been cited as possible causes(4). Baronofsky and Wangensteen(11) showed that partial obstruction to the venous outflow of the stomach in rabbits and dogs increases the speed and incidence of ulcer formation in response to injection of histamine in beeswax. In their animals a well-developed collateral circulation developed around the liver. Excess gastric secretion of acid or pepsin has not been demonstrated in patients with cirrhosis(4), although studies on this point are few. Out of 29 patients who underwent portacaval shunt at the Veterans Administration Center, Los Angeles, since 1948 two, who had no previous ulcer history, developed peptic ulcers within 9 months after shunt. Four other cases have been reported of peptic ulcers which originated or underwent exacerbation after portacaval or splenorenal shunt(5,6). These observations throw some doubt on the importance of portal hypertension *per se* in the etiology of ulcers associated with cirrhosis. The presence of a well-developed collateral circulation through which portal blood bypasses the liver is a striking feature of many patients with cirrhosis and of all with func-

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