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THE EFFECT OF ADRENALECTOMY ON THE SUBMAXILLARY AND GASTRIC IODIDE PUMP

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Evidence has been accumulated to indicate that the salivary glands, the stomach and the central part of the small intestine are digestive organs where iodide is concentrated (Brown-Grant, 1961). The concentration of ^{131}I by the salivary glands of man and several animals was compared by Cohen & Myant (1959). They observed a great variation in the iodine-concentrating power in different species and within a given species in different salivary glands. No special type of cells characterized by its capacity to concentrate iodine has been found in the salivary glands by these authors.

The main source of the ^{131}I found in the saliva of mouse is the submaxillary gland, this being the only salivary gland that concentrates iodine in this animal (Logothetopoulos & Myant, 1956*b*). A sex difference in the ^{131}I concentrating power of the submaxillary gland has been observed by Llach, Tramezzani & Cordero Funes (1960). It was found that the male concentrates more iodine than does the female.

Human gastric juice is well known to contain a higher concentration of iodine than does blood (Honour, Myant, Rowlands, 1952). Logothetopoulos & Myant (1956*a*) extended these observations to several species of animals and observed that a high gastric juice iodine/plasma iodine ratio exists in the hamster, mouse, rat and guinea-pig.

Concentration of ^{131}I by the submaxillary gland of the mouse is modified by gonadectomy (Llach & Tramezzani, 1962) and the administration of methylthiouracil (Brown-Grant & Taylor, 1963), but the effect of adrenalectomy has never been studied. However, it has been shown that adrenalectomy increases the structural changes induced by castration on the submaxillary gland of mice (Raynaud, 1947) and the administration of Rothane (DDD) (Osorio & Kraemer, 1959), a substance that inhibits corticoadrenal function, as well as removal of the adrenal glands in the cat (Kahlson & Renvall, 1956) are followed by atrophy of the submaxillary gland.

No information concerning endocrine influences upon the iodine-concentrating power of the stomach is available at present.

These facts drew our attention to the effect of adrenalectomy on the ability of the submaxillary glands and stomach to concentrate iodine.

These organs were chosen to determine whether the changes were due to some general action that influences the whole extrathyroidal iodine-concentrating mechanism or whether they were confined to one of these organs.

METHODS

The mice used in these experiments were of the C_3H, A_2G, CFW, Balb and DBA strains; their ages ranged between 70 and 90 days and their weights averaged 30 g. Animals were kept in metal cages, not more than ten per cage. In order to avoid the effect of changes in temperature on the iodine uptake by the thyroid and submaxillary glands, the animals were kept in a room at 22° C with artificial light for 16 hr a day. They had free access to water and 'Forramez' chow (^{127}I content 0·1–0·3 μg/500 mg). Adrenalectomy was performed through a dorsal incision and special care was taken to avoid incompleteness of the operation. All drinking water supplied to adrenalectomized animals contained 0·9 g NaCl/100 ml.

Castration was performed through the scrotum. The testes were removed together with the epididimus. When animals were submitted to both operations, castration was done as the first step and adrenalectomy was carried out 2–3 days later. The time between the operations and the autopsy varied in each experiment and are detailed later.

The radio-iodine used was supplied by the Radiochemical Centre, Amersham. The chromatographic study of samples obtained from this source (Lantos & Tramezzani, 1961) has shown that it does not possess the bands peculiar to stored ^{131}I from Oak Ridge. All the animals were injected subcutaneously with 5 μc of ^{131}I dissolved in 0·2 ml. of normal saline. To avoid the effect of anaesthetics (Llach & Tramezzani, 1961) on the concentration of iodine by the submaxillary glands the animals were killed by decapitation. The animals were killed 90 min after the injection of radio-iodine.

The submaxillary gland was dissected free from the retrolingual gland and a blood sample was taken from the severed neck vessels. The stomach was removed, opened along the greater curvature, its contents washed out and the rumen separated from the glandular portion. This part of the stomach was used for the measurements of radioactivity. The weights of the blood, of the submaxillary glands, and of the stomach, were determined to within 0·1 mg. Plasma protein-bound iodine was not determined because up to 4 hr after the injection of ^{131}I, 95 % of the activity is present as inorganic iodine (Taurog, Potter & Chaikoff, 1959).

The radioactivity of the samples was measured in a well counter by the usual technique. The number of counts/mg submaxillary gland and stomach were divided by the number of counts/mg blood and the resulting submaxillary/blood ratio or stomach/blood ratio was taken as an expression of the iodine-concentrating power of the submaxillary gland or the stomach.

All values given in the tables and figures are means ± standard error of the mean. The significance of differences between means was estimated by the t test of Fisher and probability values are quoted. A value for P of $> 0{\cdot}05$ is reported as not significant (N.S.).

A significant difference had been found in the submaxillary/blood ratio of control animals killed on different days, and so control and experimental results were obtained on the same day.

RESULTS

The results of the studies on the concentration of I^{131} by the submaxillary gland and the stomach in several pure strains of normal mice are summarized in Table 1. These results confirm that the concentration of ^{131}I in the submaxillary gland depends upon the strain used, the strain A_2G being the one that showed the highest power to concentrate radio-iodine. In three out of five strains, males showed a higher submaxillary/blood ratio than females. No sex difference in stomach/blood ratio was found in any of the strains studied. This sex difference appears to be a characteristic feature of the submaxillary gland and not of the stomach.

TABLE 1. Concentration of ^{131}I by the submaxillary gland and the stomach of different strains of mice. Values in this and other table are means ± standard error of the mean and P values refer to the t test.

	Males		Females			Males		Females		
Strain	No.	(submaxillary/blood ratio)	No.	(submaxillary/blood ratio)	P	No.	(stomach/blood ratio)	No.	(stomach/blood ratio)	P
C_3H	9	3·6 ± 0·2	9	2·3 ± 0·2	0·01	9	4·5 ± 0·4	9	4·0 ± 0·5	N.S.
A_2G	8	11·6 ± 1·4	9	5·4 ± 0·5	0·01	8	2·4 ± 0·3	9	2·9 ± 0·4	N.S.
CFW	10	4·1 ± 0·7	8	3·5 ± 0·6	N.S.	10	3·8 ± 0·3	9	6·0 ± 1·1	N.S.
Balb	7	7·0 ± 0·5	9	3·7 ± 0·6	0·01	7	3·2 ± 0·8	7	2·5 ± 0·4	N.S.
DBA	6	5·8 ± 0·9	8	5·8 ± 0·4	N.S.	6	3·6 ± 0·4	8	4·4 ± 0·5	N.S.

To study the effect of adrenalectomy on concentration of radio-iodine by the submaxillary gland and stomach, the submaxillary/blood and stomach/blood ratios were determined in mice adrenalectomized 5 or 12 days earlier. Male and female adrenalectomized mice showed an increased submaxillary/blood ratio (Fig. 1) compared with control animals, while the stomach/blood ratio was not modified by this operation (Fig. 2).

In order to verify the effect of adrenalectomy on the sex difference in the concentration of radio-iodine by the submaxillary gland, seven male mice and an equal number of females were adrenalectomized and submaxillary/blood ratios were measured 3 days after the operation. Male mice showed a submaxillary/blood ratio of 9·6 ± 1·6 while females gave 5·8 ± 0·2, the difference being significant ($P < 0·05$). This and other similar observations proved that while adrenalectomy increases the submaxillary/blood ratio in both sexes, the sex difference is maintained.

It is known that castration as well as adrenalectomy atrophies the granular ducts. When both operations are performed on the same animal a greater atrophy is obtained. Table 2 presents results showing the submaxillary/blood ratios in mice which underwent castration and adrenalectomy. The submaxillary/blood ratio was checked on animals killed at intervals from 3 days to 4 months after the adrenalectomy.

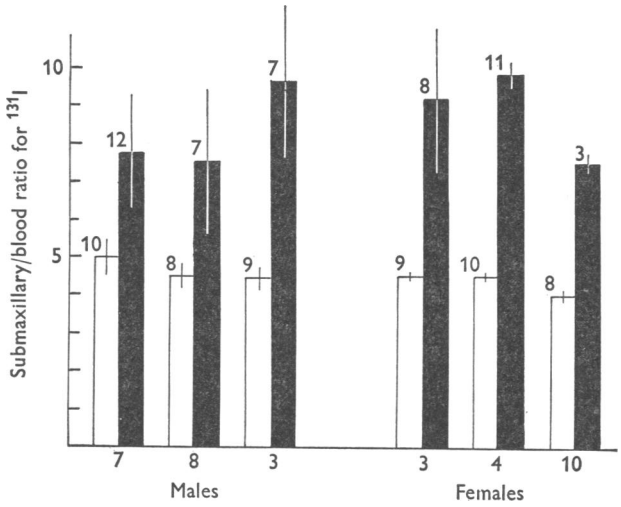

Fig. 1. The submaxillary/blood ratios for ^{131}I of normal (open columns) and adrenalectomized (filled columns) male and female C_3H mice. Figures above the columns give the number of animals in each group and figures below give the number of days between the adrenalectomy and autopsy. Standard errors of the means in all cases are indicated by the lines in the columns.

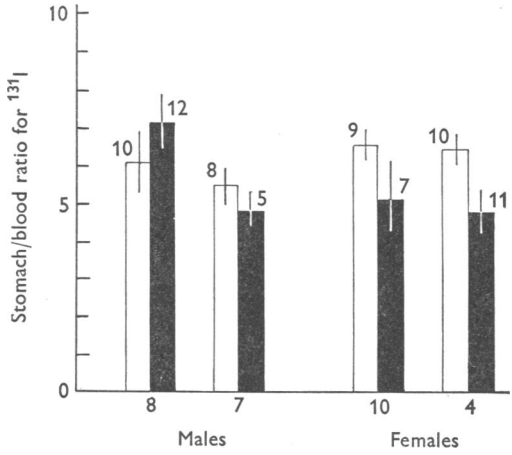

Fig. 2. The stomach/blood ratios for ^{131}I for normal (open columns) and adrenalectomized (filled columns) male and female C_3H mice. Figures above the columns give the number of animals in each group and figures below give the number of days between the adrenalectomy and autopsy. Standard errors of the mean in all cases are indicated by the lines in the columns.

Results were similar in all experiments. The submaxillary/blood ratio of adrenalectomized–castrated mice was higher than that of control animals. Higher submaxillary/blood ratios were observed in adrenalectomized-castrated mice compared with those of mice that underwent only castration or adrenalectomy.

TABLE 2. Concentration of ^{131}I by the submaxillary gland of normal, castrated, adrenalectomized and castrated-adrenalectomized male mice. D, Number of days between operation and measurement of ^{131}I concentration.

Control		Castrated		Adrenalectomized		Castrated-adrenalectomized		
No.	SM/B*	No.	SM/B	No.	SM/B	No.	D	SM/B
7	5·3 ± 0·2	6	10 ± 0·1	7	11·2 ± 0·8	8	3	15·1 ± 1·61
5	5·1 ± 0·5	—	—	—	—	4	6	18·5 ± 1·42
9	4·4 ± 0·3	—	—	—	—	6	120	11·4 ± 0·9

* Submaxillary/blood ratio.

DISCUSSION

The granular tubules of the submaxillary glands, the superficial epithelium, and the epithelium of the gastric pits of the fundus and pyloric portions of the stomach are the structures where radio-iodine is concentrated. These conclusions were reached by the radio-autographic studies of Logothetopoulos & Myant (1956*a*, *b*).

Our experiments showed that a similar concentration of radio-iodine in the stomach of male and female mice occurs and no sex difference could be found, while the submaxillary gland in three of the strains studied showed a sex difference. Lacassagne (1940) has shown that in the submaxillary gland of male mice granular tubules are more numerous than acini, whereas in female mice both elements are present in approximately equal number. Thus sexual dimorphism of the mouse's submaxillary gland is denoted by a different duct/acini ratio for each sex. It was also reported that there exists a sex difference in the enzyme content of the submaxillary gland (Raynaud & Rebeyrotte, 1949). At present, the sex difference in the concentration of radio-iodine by the submaxillary gland of mice appears to be related to this sexual dimorphism.

Since it is assumed that in the submaxillary gland there exists a close relation between the extent of development of the granular ducts and the concentration of iodine it was surprising to find that atrophy of the ducts, which occurs as a consequence of castration or administration of methylthiouracil, was followed by an increase in the iodide-concentrating power (Llach & Tramezzani, 1962; Brown-Grant & Taylor, 1963).

Our results raise the same problem because the presence of the adrenal is well known to be necessary for the preservation of the normal structure

of the submaxillary gland. It has been reported that adrenalectomy produces an atrophy of the submaxillary glands in cats (Kahlson & Renvall, 1956) and that the association of castration and adrenalectomy is followed in male mice by a greater atrophy of the granular ducts than that produced by castration alone (Raynaud, 1947).

It is clear that the quantity of iodine contained in the submaxillary gland at any one time is the result of two different processes: the uptake of iodine from the blood by the gland and the elimination of iodine from the gland into the saliva. An inverse relation between the volume of saliva secreted by the gland and the iodine content of the gland has been observed in dogs (Burgen & Terroux, 1962). Observations by Llach & Tramezzani (1961) permit one to suppose that a similar phenomenon takes place in mice. An alteration in the salivary secretion may be an important factor in the increased submaxillary blood/ratio observed in adrenalectomized mice. The fact that DDD is able to decrease the salivary flow in cats (Osorio & Kraemer, 1959) gives support to this hypothesis.

Morphological changes in the stomach (Baker & Bridgman, 1954) as well as a decrease in the gastric secretion (Tuerkischer & Wertheimer, 1945) were observed after adrenalectomy in the rat. Nevertheless, our results show that the removal of the adrenal gland does not cause any alteration in the power of the stomach to concentrate iodine.

SUMMARY

1. The concentration of ^{131}I by the submaxillary gland and stomach of normal, adrenalectomized, and castrated-adrenalectomized mice belonging to several strains was studied.

2. The power to concentrate iodine by the submaxillary gland and the stomach of mice varies with the strain of animals.

3. The sex difference in the power to concentrate iodine that has been described in the submaxillary gland does not exist in the stomach.

4. Adrenalectomy increases the power of the submaxillary gland to concentrate iodine but has no effect on that of the stomach.

5. Castrated-adrenalectomized mice showed an even greater power to concentrate iodine by the submaxillary gland than of animals that underwent castration or adrenalectomy as single operations.

6. It is suggested that a diminution in the salivary flow may be one of the factors that increases the submaxillary concentration of iodine observed in adrenalectomized and castrated-adrenalectomized animals.

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