

# THE EFFECT OF ADMINISTRATION OF THYROID SUBSTANCE, OF POTASSIUM IODIDE, AND OF EXTIRPATION OF THE GREATER PORTION OF THE THYROID GLAND ON THE EPIDERMIS OF THE GUINEA-PIG

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## INTRODUCTION

In a previous investigation(1) we found a very marked effect of the functional states of the female generative organs and of the internal secretions of the ovary on the proliferative activity and structure (number of cells) of the guinea-pig epidermis. We now continue these studies, investigating the effect of another important gland with internal secretions, namely, the thyroid. The influence of a surplus of, as well as of a deficiency in, thyroid hormones on the epidermis was tested. In particular, the effect of a single dose of thyroid substance, and also of daily doses given over definite periods of time, was studied.

In addition, we tested the effect of partial thyroidectomy on the epidermis and then the result of multiple doses of thyroid substance in guinea-pigs in which the greater part of the thyroid gland had previously been extirpated. Lastly, we compared the action of the thyroid hormone with that of a substance intimately connected with the function of the thyroid gland, namely, iodine, in the form of potassium iodide, on the proliferative activity and structure of the epidermis.

One reason for selecting thyroid substance and potassium iodide for these experiments was that in former studies(2, 3)

we found that these two substances produced opposite effects on the cell proliferation and structure of the acini of the thyroid gland of the guinea-pig. We also selected the hormone substance of the thyroid gland for this study, because it is known that this gland affects differentiation of tissues, accelerating metamorphosis in the tadpole; furthermore, according to some authors, it promotes the regenerative growth of peripheral nerves and of bone.

A number of years ago, we showed that the internal secretions of the ovary, in association with hereditary factors, exert a definite effect on the development of mammary cancer in mice, and that this effect can be determined in a quantitative manner(4). In our previous publications concerning the influence of ovarian secretion, we suggested that perhaps other internal secretions may play a similar rôle in the development of certain types of cancer similar to that established in the case of the ovary(4). With this thought in mind, we undertook the present quantitative study of the effect of the thyroid gland and its hormone and also of potassium iodide on the growth processes of the epidermis of the guinea-pig ear. As in the preceding paper dealing with the effects of underfeeding, older experiments of series A and more recent ones of series B are distinguished.

THE EFFECT OF REPEATED DOSES OF THYROID SUBSTANCE ON  
THE CELL PROLIFERATION IN THE EPIDERMIS OF  
NORMAL MALE GUINEA-PIGS

*Series A*

One or two tablets, each containing 0.1 gram of thyroid substance (Armour & Co.) and, in several cases, one-half of a tablet, were fed daily. The feeding extended over periods varying between five and forty days. In general, no definite relation between the number of mitoses and length of the period, during which the substance was given, could be demonstrated. However, in two animals, in which the period of feeding was longest (thirty to forty days), the counts were above those found in the averages of normal guinea-pigs. As

a rule, the cell number was highest in those animals in which the feeding took place over the longer periods of time.

Table 1 presents the average figures for a group weighing between 400 and 600 grams, treated as described above.

TABLE 1					
<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
517 grams	16	2.01	4.51	165	286
		(Var., 0.64 to 3.65)			(Var., 218 to 388)

<sup>1</sup> The Roman figures have the same significance as in the preceding paper.

The average of results obtained with heavier guinea-pigs, those weighing above 600 grams, is shown in table 2. The thyroid feeding extended over periods varying between six and sixty days. Again, no definite relation could be observed between the length of these periods and the mitotic proliferation. For example, in an animal fed for sixty days, the number of mitoses was 1.92 per 1 mm. skin; another, fed the same amount, gave a figure of 1.69 after only six days.

TABLE 2					
<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
643 grams	8	1.27	2.90	162	254
		(Var., 0.44 to 1.92)			(Var., 259 to 325)

The results of the total average of twenty-four guinea-pigs considered above and of five additional ones which were treated for periods of eighteen and twenty days, but the weights of which were lost, are presented in table 3.

TABLE 3					
<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>	
29	1.72	3.85	165	285	
	(Var., 0.50 to 4.31)			(Var., 196 to 388)	

Comparing these data with those of the controls, given in the preceding paper, we may conclude that daily administration of thyroid substance extending over periods varying between five and sixty days does not lead to an increase in proliferative activity of the epidermis in the guinea-pig. The averages of mitoses are actually somewhat lower than those

of the controls, but it is doubtful how much significance can be attached to these differences. They may be due to the loss of weight, which a number of animals showed under the influence of thyroid administration, or to some other accidental factors. Only by excluding these possibilities could we attribute to thyroid feeding a specific lowering effect on the proliferative activity of epidermis.

As to the number of cells found in the lower layer of the epidermis, the average was about the same as in the controls, while for the upper layers the average number was slightly below that of the normal animals, but well within the range of variations there observed. Therefore, we are justified in drawing the above conclusion, that prolonged feeding of thyroid substance does not increase the number of cells in the epidermis.

EFFECT OF THYROID FEEDING ON THE EPIDERMIS IN PREVIOUSLY THYROIDECTOMIZED GUINEA-PIGS

*Series A*

In six animals, two weighing below 400 grams (average, 329 grams), three weighing between 400 and 600 grams (average, 549 grams), and one weighing 660 grams, all but a small part of one lobe of the thyroid gland was extirpated. Following this operation, 0.1 to 0.2 gram thyroid substance was administered orally, over periods ranging between five and twenty days.

The average figures obtained in this group are seen in table 4.

TABLE 4				
<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
6	2.76	5.55	153	321
	(Var., 0.51 to 6.28)		(Var., 270 to 408)	

It will be seen that a slight increase was found in the number of mitoses and also in the number of cells. At the present time, we do not wish to discuss the significance of this increase, but shall limit ourselves to the conclusion that feeding thyroid substance after an incomplete thyroidectomy does not diminish either the proliferative activity or the number of cells in the epidermis.

## THE EFFECT OF A SINGLE DOSE OF THYROID SUBSTANCE ON THE EPIDERMIS OF THE GUINEA-PIG

*Series A*

One dose, consisting of four tablets of thyroid substance (Armour & Co.) was administered orally to six guinea-pigs, some of which had been starved for two days previous to the feeding, so that absorption of the material ingested would be hastened. The fasting animals weighed slightly below 400 grams. In five guinea-pigs examination took place five to seven hours following feeding of the thyroid substance, and in one animal it occurred twenty-four hours later. The results are shown in table 5.

TABLE 5

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
381 grams	6	1.79	3.63	162	323
		(Var., 1.02 to 3.07)			(Var., 293 to 381)

We see in this group a reduction in the number of mitoses. However, undernourishment may play a part in this result. The number of cells, on the other hand, is normal or slightly above the average.

TABLE 6

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
451 grams	7	2.27	5.04	160	281
		(Var., 0.32 to 4.74)			(Var., 272 to 325)

Table 6 gives the results for the heavier guinea-pigs, those weighing between 400 and 600 grams.

Here, the average number of mitoses is even slightly above the average of the controls. Examination took place in three cases five to seven hours, in three cases ten to twenty-four hours, and in one case forty-eight hours after administration of thyroid substance. In the three guinea-pigs examined after five to seven hours, the average number of mitoses per 1 mm. skin was 2.71; after fifteen to twenty-four hours, it was 2.49, and in one examined after forty-eight hours it was 0.32.

*Series B*

Seventeen guinea-pigs ranging in weight between 215 and 425 grams were examined. Each animal was fed 0.1 gram thyroid substance (Armour & Co.). Examination took place six, eight, twelve, twenty-four, and forty-eight hours afterward. The results are presented in table 7.

TABLE 7

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
333 grams	17	1.27	2.87	155	287
	(Var., 0.35 to 2.32)			(Var., 262 to 319)	

In table 8, which follows, figures showing the variations with the time of examination are tabulated.

TABLE 8

<i>Time of examination,</i> <i>hours</i>	<i>Average weight,</i> <i>grams</i>	<i>Number of</i> <i>guinea-pigs</i>	<i>Average number of mitoses</i> <i>per 1 mm. skin</i>
6	410	2	1.52 (Var., 0.97 to 2.08)
8	396	3	1.61 (Var., 1.11 to 2.00)
12	412	2	1.80 (Both 1.80)
24	288	7	0.76 (Var., 0.35 to 1.10)
48	365	3	1.61 (Var., 1.13 to 2.32)

The average in this group is below that of the control animals of series B, being 1.27 in the thyroid-fed guinea-pigs, as compared with 1.97 in the control animals. The most marked reduction was observed in the animals examined twenty-four hours after feeding thyroid substance; in these guinea-pigs the weight was also lower than in the others. In evaluating the differences in the results of single-dose feeding in the corresponding animals of series A and series B we must take into consideration the fact that in this series (B) the average weight of the animals was somewhat lower than in the corresponding guinea-pigs of series A.

We may conclude that single doses of thyroid substance do not increase the cell proliferation in the epidermis, nor do they noticeably change the number of cells; on the other hand, they may produce a relatively slight diminution in proliferative activity, especially in the animals weighing less than 350 grams.

## THE EFFECT OF THYROIDECTOMY ON THE EPIDERMIS OF THE GUINEA-PIG

*Series B*

In twenty-five guinea-pigs one lobe and three-fourths of the second of the thyroid gland were extirpated. The isthmus connecting the lobes in guinea-pigs was left intact.

Definite compensatory hypertrophy of the remaining portion of the gland began to set in, in many cases, within ten days following the operation. However, in some cases the hypertrophy was very slight or even lacking. In our experiments examination of the epidermis took place at periods varying between six and thirty-two days following thyroidectomy. We found no definite relation between the length of these periods and the counts obtained. The total averages of this group will be found in table 9.

TABLE 9

<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
25	2.74	5.57	159	331
	(Var., 1.02 to 6.79)			(Var., 230 to 418)

We have a record of the weight in only eleven of these animals.

The averages for the small group weighing less than 400 grams are given in table 10 and for those between 400 and 600 grams, in table 11.

TABLE 10

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
353 grams	3	3.15	6.43	161	366
		(Var., 3.02 to 3.38)			(Var., 331 to 386)

TABLE 11

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
478 grams	8	2.69	5.44	166	337
		(Var., 1.84 to 5.00)			(Var., 286 to 382)
Total, 444 grams	11	2.81	5.71	164	345

We may conclude from these results that in guinea-pigs with the greater part of the thyroid extirpated, the proliferative activity and the number of cells in the epidermis remain

normal or possibly become slightly increased. A diminution in either mitoses or cell numbers cannot be demonstrated in this group.

EFFECT OF MULTIPLE DOSES OF POTASSIUM IODIDE ON THE EPIDERMIS OF NORMAL MALE GUINEA-PIGS

*Series A*

Doses of either 0.01, 0.05, or 0.1 gram potassium iodide were given daily by mouth. There was no definite difference between the effects of these various doses. The periods during which the potassium iodide was administered varied between five and sixty days, and in one case it extended over 108 days. In several animals the proliferative activity was found to be very low, after eight to ten days' feeding with potassium iodide, but in other cases it was still normal after ten days; in some cases it was low even after thirty days. In two guinea-pigs which had received daily doses of potassium iodide over periods of sixty days, the number of mitoses per 1 mm. of skin was 1.85 and 1.43, respectively, figures which were only slightly below the normal average. In the one case, which extended over 108 days in an animal weighing 735 grams, the number of mitoses per 1 mm. skin was 2.24. Thus there was no reduction in the activity in this instance. Also, the number of cells was within the normal range in those animals examined after sixty and 108 days of feeding. The total number of thirty-five guinea-pigs has been divided into three groups according to their weights, namely, those weighing below 400 grams, those between 400 and 600 grams, and those above 600 grams. The average figures for these different groups are given in tables 12, 13, and 14, respectively. Table 15 gives the total averages for the whole series, that is, a combination of the above three groups.

TABLE 12

	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
360 grams	4	0.47	2.89	172	273
		(Var., 0.19 to 1.02)			(Var., 259 to 286)



TABLE 13

	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
492 grams	20	1.37	2.93	158	304
		(Var., 0.12 to 3.58)			(Var., 225 to 353)

TABLE 14

	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
672 grams	11	1.54	3.49	160	282
		(Var., 0.32 to 2.62)			(Var., 230 to 359)

TABLE 15

<i>Average end weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
505 grams	35	1.32	2.89	161	294
		(Var., 0.12 to 3.58)			(Var., 225 to 359)

We may conclude from these results that the daily administration of potassium iodide to guinea-pigs, during certain variable periods of time, does not increase either the proliferative activity of the epidermis or the number of cells of which it is composed. Actually, the proliferative activity in this series was below that of normal guinea-pigs and even slightly below that of guinea-pigs fed with thyroid substance. The number of cells in the upper layers of the epidermis was also slightly below the average found in normal guinea-pigs, but was still well within the range of normal variations. The changes in proliferative activity took place in these guinea-pigs, notwithstanding the gain in weight, which these animals usually showed, during the progress of the experiment.

THE EFFECT OF MULTIPLE DOSES OF POTASSIUM IODIDE ON THE EPIDERMIS OF GUINEA-PIGS, FOLLOWING EXTIRPATION OF THE GREATER PORTION OF THE THYROID GLAND

In a group of male guinea-pigs one lobe and the greater part of the second lobe were extirpated, and subsequently potassium iodide, in daily doses which in different guinea-pigs varied between 0.01 and 0.1 gram, was administered orally, during periods of time varying between four and thirty-two days. No definite relation was found between the epidermal proliferation and the length of the period during which the potassium iodide was administered or the amount of potassium iodide given.

As was recorded in the preceding series, the total number of animals have been similarly divided into three groups, according to their weights.

In table 16 are recorded the average figures for those weighing below 400 grams; in table 17, for those weighing 400 and 600 grams, and table 18, for those above 600 grams. Table 19 gives averages for all the groups combined.

TABLE 16

	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
365 grams	1	2.10	4.69	158	288

TABLE 17

	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
504 grams	17	2.38	5.63	162	322
		(Var., 1.45 to 4.29)		(Var., 262 to 380)	

TABLE 18

	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
614 grams	2	1.48	3.12	162	312
		(Var., 1.37 to 1.60)		(Var., 278 to 347)	

TABLE 19

<i>Average weights</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
Total, 508 grams	20	2.27	5.33	162	320
		(Var., 1.37 to 4.29)		(Var., 262 to 380)	

As we have seen above, administration of thyroid substance to not quite completely thyroidectomized guinea-pigs is not followed by a lowering of the proliferative activity of the epidermis.

Similarly, we find in this series that after previous removal of the greater part of the thyroid gland, the lowering of epidermal proliferation which we observed in normal guinea-pigs fed either with thyroid substance or with potassium iodide was lacking. In both cases the counts of mitoses became either normal or even slightly above normal in the thyroidectomized animals. We may, therefore, draw the conclusion that in such guinea-pigs a definite deviation from the normal intensity of proliferative activity is not found. As far as the number of cells composing the epidermis is concerned, it is approximately normal, although it is possible

that the number of cells in the upper layers is very slightly increased. We find, therefore, complete parallelism in the conditions found in the thyroid-fed and in the potassium-iodide-fed animals, after a preceding incomplete thyroidectomy.

Our counts suggest that thyroidectomy, even if it is not quite complete, prevents the lowering of proliferative activity, which we observed in animals not thyroidectomized, and that the effects of this operation and those of administration of thyroid substance or of potassium iodide, to a certain extent, balance each other as far as the epidermis is concerned. However that may be, we can be certain that the epidermis of the thyroidectomized guinea-pigs fed with thyroid substance or with potassium iodide remains approximately normal.

THE EFFECT OF THE ADMINISTRATION OF SINGLE DOSES OF  
POTASSIUM IODIDE ON THE EPIDERMIS OF THE GUINEA-PIG

*Series A*

Four guinea-pigs, the weights of which varied between 360 and 500 grams, were used in this experiment. To three animals 0.1 gram potassium iodide was given orally and to the fourth, twice this amount. In the first three guinea-pigs, which were examined eight to nine hours after giving the potassium iodide, the number of mitoses and of upper cells was found to be diminished. In the animal which received 0.2 gram potassium iodide, the mitoses count after forty-eight hours was almost normal, while the number of cells (348) in the upper layer was above the average. In table 20 will be seen the average figures for the entire group.

TABLE 20

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
442 grams	4	0.98	2.10	158	281
		(Var., 0.80 to 2.11)		(Var., 251 to 348)	

*Series B*

A single dose of 0.1 gram potassium iodide was administered to each of twelve male guinea-pigs, the weight of which ranged between 300 and 410 grams. Examination took place six, eight, twelve, and twenty-four hours following the feeding.

<i>Average weight</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>
370 grams	12	1.23	2.78	157	289
		(Var., 0.62 to 1.94)			(Var., 241 to 319)

In table 21 are tabulated the average results for the guinea-pigs, arranged according to the number of hours which were allowed to elapse between the time of feeding and the time of examination.

TABLE 21  
*Mitoses and number of cells at different time periods*

<i>Period, hours</i>	<i>Average weight, grams</i>	<i>I</i>	<i>II</i>	<i>V</i>
6	392	3	1.68	317
			(Var., 1.31 to 1.94)	(Var., 315 to 319)
8	398	3	1.34	291
			(Var., 1.11 to 1.66)	(Var., 249 to 328)
12	370	3	0.94	289
			(Var., 0.62 to 1.52)	(Var., 272 to 311)
24	323	3	1.08	259
			(Var., 0.90 to 1.25)	(Var., 241 to 291)

From the table it will be seen that the decrease in number of mitoses is most marked after twelve and twenty-four hours. If potassium iodide should actually diminish the proliferative activity in guinea-pigs, it might reasonably be expected that the effect would become noticeable between eight and twenty-four hours, and this appeared to be the case in both series A and B. The time values in this series were similar to those obtained after feeding a single dose of thyroid substance, only in the latter the effect appeared somewhat more slowly, which might be expected, considering the difference in the character of potassium iodide and thyroid. However, our results only suggest such a conclusion; a larger number of experiments would be necessary to establish this time

relation definitely. At present, we may state that, in our experiments, a single dose of potassium iodide administered to fairly young guinea-pigs diminished the number of mitoses within twenty-four hours; the number of cells remained about the same as in the controls of series B.

#### DISCUSSION

In evaluating our results we can consider them, as we have to do in the case of all statistical data, merely as more or less close approximations. As far as the effect of administration of thyroid substance is concerned, we may be certain that it neither increases the proliferative activity of the epidermis nor the number of epidermal cells. This is true of the administration of multiple doses extending over various periods of time, as well as of single doses. On the other hand, it is possible that it leads, in both cases, to a slight, or, occasionally, even to a more marked, lowering of proliferative activity and perhaps of the number of epidermal cells as well. After single doses such a lowering effect was observed, especially twenty-four hours after administration of thyroid substance. However, complicating factors, such as the loss of weight, effected by thyroid feeding, and the age of the animals, are to be dealt with. The youngest were the most affected. We must be content, at present, to state that our results prove that the feeding of thyroid substance to normal guinea-pigs does not increase the proliferative activity of the epidermis nor the number of cells in the epidermis; on the other hand, they suggest a depressing effect due to this substance.

Such a depressing effect, however, was absent when multiple doses of thyroid substance were administered to animals in which the greater part of the thyroid had previously been removed. Under these conditions there was even a suggestion of a slight rise in proliferative activity and in the number of cells in the epidermis.

As we should expect from the results obtained by us in thyroidectomized guinea-pigs in which we administered at the

same time thyroid substance, we found that thyroidectomy, even when not complete, does not lower the proliferative activity or the number of cells in the epidermis, but on the contrary, may raise both in experiments in which thyroid substance has not been fed.

As far as the relation of the thyroid gland to the epidermis is concerned, we have obtained no indication that this gland may function as an agent in increasing the proliferating power of the epidermis; and there is therefore no probability that it may play a part in initiating carcinomatous proliferation of the skin or in aiding it, in the sense in which we found that the ovary, through its internal secretion, influences the development of carcinoma of the mammary gland.

How far these findings are applicable to other species we cannot be certain at the present time. In human and animal cretinism, secondary changes, in the connective-tissue constituent of the skin, enter as complicating factors, so that the results which we obtained in the guinea-pig and conditions as cretinism in man and in certain other mammals are not directly comparable.

As to the effects of administration of potassium iodide on the epidermis, we find a certain parallelism between its action and that of thyroid substance.

Multiple doses of potassium iodide, as of thyroid substance, administered by mouth do not increase cell proliferation in the epidermis of the guinea-pig, neither do they cause a rise in the number of epidermal cells. On the contrary, we found a lowering of the proliferative activity and possibly also the number of cells in the epidermis. Furthermore, there is no doubt that the effect produced by administration of potassium iodide cannot be attributed to a loss in weight of the animals during the experiment.

As in the case of administration of thyroid, so also in the case of feeding of potassium iodide, a previous removal of the greater part of the thyroid gland prevented the lowering in epidermal proliferation otherwise effected by the administration of the latter substance.

Furthermore, as after administration of single doses of thyroid substance, similarly, single doses of potassium iodide did not increase the proliferation or the number of cells in the epidermis, but on the contrary, decreased both. Therefore, again there is a very strong suggestion that not only in our experiments, but as a general rule, the potassium iodide in single doses may lower the proliferation and possibly also the number of epidermal cells. This effect seems to be pronounced especially twelve to twenty-four hours after administration of this substance. However, as stated above, we consider the latter conclusion, at present, as merely tentative. On the other hand, we can be certain that single doses of potassium iodide do not raise the epidermal proliferation within the ranges of time used in our experiments.

We see, then, that in contrast to the effects of potassium iodide on the thyroid gland of the guinea-pig, where this substance increases the proliferative activity of the acinus cells in a remarkable manner, it has no such effect on the epidermis, and, on the contrary, it may possibly even lower the multiplication of cells in the latter tissue. Whereas administration of thyroid substance and potassium iodide have opposite effects on the thyroid gland, these two substances have similar effects on the epidermis. This is presumably due to the fact that potassium iodide exerts a direct stimulating effect on the thyroid gland and possibly leads to an increased production of the hormone, whereas administration of thyroid substance removes the incentive to activity on the part of the gland. In the case of the epidermis, the effect of potassium iodide may be an indirect one, perhaps due to excess production and mobilization of thyroid hormone. In tissues other than the thyroid gland, potassium iodide does not, therefore, need to exert a stimulating effect; on the contrary, there is a suggestion that it may lower their activity, as we have seen in the case of the epidermis of the guinea-pig.

## SUMMARY

Administration of thyroid substance as well as of potassium iodide to guinea-pigs does not lead to a rise in proliferative activity of the epidermis or to an increase in the number of epidermal cells. On the contrary, there is a suggestion that both multiple as well as single doses of these two substances may cause a lowering in both proliferative activity and number of cells.

After a not quite complete thyroidectomy, no lowering of the proliferative activity in the epidermis nor of the number of epidermal cells in the guinea-pig takes place; there is even a suggestion that it may increase the number of cells. In accordance with these findings, we observed that after a previous (incomplete) thyroidectomy, administration of thyroid substance and of potassium iodide did not lead to a lowering of cell proliferation or of the number of epidermal cells.

The effects of these substances on the epidermis are compared with their effects on the thyroid gland, and furthermore the bearing of our findings on the problem of the significance of internal secretions in the origin of cancer is discussed.

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