

EXPERIMENTAL BIOLOGY

EFFECT OF VITAMIN B₁₂ AND COMBINED ADMINISTRATION OF VITAMIN B₁₂ AND THYROID EXTRACT ON THE THYROID GLAND OF RATS DURING REPARATIVE REGENERATION AFTER SURGICAL TRAUMA

T. R. Dell'

UDC 616.441-089.168.64-085.3-577.164.16-059:615.361.441

The information concerning the effect of vitamin B₁₂ on function of the thyroid gland is very contradictory. Some authors [3, 9] describe the depressant action of cobalamin, attributing it to the presence of cobalt [4.5%] in the compound, prolonged administration of which depresses the function of the gland [8, 9, 12, 17]. Others [2, 13, 14, 17] deny that vitamin B₁₂ has any influence on the function of this gland and consider that it simply neutralizes the action of thyroxine. However, the administration of cobalt salts or vitamin B₁₂ does not always give positive results [1].

The study of the effect of massive doses of vitamin B₁₂ on the processes of reparative regeneration of the skeletal muscles in rats [7] motivated an investigation of the changes in the microstructure of the thyroid gland of the same animals.

Taking into consideration results showing the positive effect of vitamin B₁₂ in hyperthyroidism [3, 8, 9], it was interesting to study the result of its action on the gland in conjunction with thyroid extracts in the same experimental conditions.

EXPERIMENTAL METHOD

A study was made of the thyroid gland of 65 male rats weighing 200-250 g, on which a standard injury was inflicted to the tibialis anterior muscle, 5 mm in diameter, in aseptic conditions and under ether anesthesia, and of the thyroid of 6 intact rats. The experiments were performed in the autumn. The glands were investigated 7, 10, 15, 20, 25, 30, and 45 days after the operation. Altogether four series of experiments were carried out on the rats undergoing the operation. In series I the animals received vitamin B₁₂ in a daily dose of 30 µg for 20 days after the operation, and thereafter until 45 days after the operation they received 20 µg on alternate days. In series II the rats received, besides the vitamin, thyroid extracts by mouth in a dose of 25 mg on alternate days. Series III was the control. The rats of series IV received thyroid extracts.

The material was fixed in Zenker-formol, and stained with Carazzi's hematoxylin with eosin and with iron hematoxylin by Heidenhain's method. The maximal and minimal diameters of the follicles were measured and the mean values of each 100 measurements were calculated. The height of the follicular epithelium and the degree of vacuolation of the colloid were also studied.

EXPERIMENTAL RESULTS

In series III in the early postoperative periods (7 days) some degree of stimulation of thyroid gland function was observed, as shown by the small size of the follicles (mean diameter 18 µ), the higher than normal follicular epithelium (normal 7.5-9 µ), and the considerable vacuolation of the acidophilic colloid (see figure, b and c). With an increase in the postoperative period, the diameters of the follicles also increased (see table). Consequently, the rate of elimination of intrafollicular secretion into the blood stream gradually fell in the postoperative period.

Hyperfunction of the thyroid gland during regeneration has been observed by other investigators [4, 6]. It has been shown [6] that operations carried out under local anesthesia inhibit the functions of the gland for various periods of time (stress). Under general anesthesia, because of the blocking of pain sensation, stimulation of the gland is often observed.

Department of General Biology, I. P. Pavlov First Leningrad Medical Institute (Presented by Active Member of the Academy of Medical Sciences of the USSR N. N. Zhukov-Verezhnikov). Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 62, No. 11, pp. 91-94, November, 1966. Original article submitted March 11, 1965.

Variations in Diameter of Follicles and Height of Follicular Epithelium of Thyroid Glands of Rats Undergoing Operation and Receiving Vitamin B₁₂, Vitamin B₁₂ Together with Thyroid Extracts, and Thyroid Extracts Alone (in μ)

Days after operation	Control				Treated with vitamin B ₁₂				Treated with vitamin B ₁₂ and thyroid extracts				Treated with thyroid extracts			
	diameter of follicles			Height of epithelium	diameter of follicles			Height of epithelium	diameter of follicles			Height of epithelium	diameter of follicles			Height of epithelium
	mean	maxi-mal	mini-mal		mean	maxi-mal	mini-mal		mean	maxi-mal	mini-mal		mean	maximal	mini-mal	
7	18	54	3,6	10,8±0,06	62	166	16	7,2±0,06	45	110	22	7,5±0,05	45	108	20	5,0±0,07
10	36	90	10,8	7,2±0,06	65	180	14,5	3,6±0,05	45	130	30	5,0±0,09	41	112	20	4,4±0,05
15	36	90	10,8	12,6±0,06	72	108	18	5,4±0,07	79	154	44	4,6±0,06	44	104	23	4,5±0,05
20									66	142	22	4,7±0,05	44	88	22	4,5±0,08
25									66	154	31	5,5±0,08	35	88	22	4,0±0,06
30	43	144	18	9 ±0,06	57	252	18	5,4±0,05	—	—	—	—	—	—	—	—
45	55	192	10,8	9 ±0,05	90	288	28,8	5,4±0,08	—	—	—	—	—	—	—	—

Hyperfunction of the gland in the early postoperative periods in the present experiment was associated with the process of reparative regeneration after trauma and attributed to an increase in the body's requirements of thyroid hormone [5]. However, the present author's conclusions, like those of other workers [4, 6], differ from conclusions expressed after certain other investigations [10, 11]. Under the influence of vitamin B₁₂ (experiments of series I) the follicles increased considerably in size (see table); vacuolation was absent in the basophilic colloid, which was firmly packed and contained a number of fissures. The height of the follicular epithelium came close to normal (7.2 μ) only on the 7th day after the operation, and at other times the epithelial cells were low, with dark, dense nuclei. Similar results have been obtained by other workers [8, 9].

The polymorphism of the follicles under the influence of vitamin B₁₂ was much more marked than normal (see table), and the peripheral follicles with their low epithelium reached a diameter of 288 μ , indicating delay in the phase of elimination of intrafollicular colloid. The positive action of vitamin B₁₂ sometimes observed in hyperthyroidism may possibly be due to the fact that it prevents the secretion of colloid into the blood stream.

The dose of vitamin B₁₂ used in the present experiment was evidently a "shock" dose [8, 15] and it depressed the thyroid function to such an extent that no postoperative changes, in the direction of an increase in function, were observed.

For convenience in the subsequent account the experiments of series II (vitamin B₁₂ and thyroid extracts) will be compared separately with series IV (thyroid extracts) and series I (vitamin B₁₂).

Initially in the experiments of series II (see figure, c and table), while the process of wound healing took place intensively the mean diameters of the follicles were almost identical with those in series IV; the difference between the maximal and minimal diameters also was very small. However, starting with the 15th day of combined treatment these indices were higher than the corresponding values in the experiments of series IV (see figure, c). The height of the epithelium on the 10th day (series II) corresponded to the lower limit of normal (7.5 μ). By the 15th day it had fallen and was close to the values in series IV (see table), but did not reach them and in the later periods remained slightly higher than them. On the 10th day in series IV the epithelium was low, inactive and contained dense nuclei, but with an increase in the postoperative period the epithelium showed a tendency to diminish in size. This indicates depression mainly of the phase of colloid synthesis under the influence of thyroid extracts.

During combined treatment with vitamin B₁₂ and thyroid extract, the diameter (especially the maximal diameter) of the follicles did not reach such high values as during treatment with vitamin B₁₂ alone. The height of the epithelium in the rats of series I and II was small. Evidently during combined treatment the stage of secretion of colloid into the blood stream was depressed by vitamin B₁₂ and the stage of its synthesis was depressed by thyroid extract.

LITERATURE CITED

1. M. I. Balakhovskaya, *Probl. Éndokrinol.*, No. 6, 100 (1958).
2. V. N. Bukin, L. Ya. Areshkina, and L. S. Kutseva, In the book: Vitamin B₁₂ and Its Clinical Application [in Russian], Moscow (1956), p. 5.
3. A. O. Voinar, Effect of Operation Trauma on the Functional State of the Thyroid Gland. The Biological Role of Trace Elements in the Animal and Human Body [in Russian], Moscow (1953).
4. A. A. Voitkevich, *Vestn. Éndokrinol.*, No. 1-3, 498 (1935).
5. S. G. Genes, In the book: Current Problems in Endocrinology [in Russian], Moscow, No. 2 (1963), p. 163.
6. V. P. Dyskin, Effect of Operation Trauma on the Functional State of the Thyroid Gland. Author's abstract of candidate dissertation. Donetsk (1957).
7. T. M. Kovalenko, *Arkh. Anat., Gistol. Émbriol.*, No. 6, 30 (1960).
8. S. M. Maksimov and I. N. Sharkevich, *Vrach. Delo*, No. 11, 1133 (1959).
9. I. N. Sharkevich, *Probl. Éndokrinol.*, No. 3, 69 (1956).
10. I. A. Éskin, Yu. B. Skebel'skaya, and A. E. Rabkin, *Doklady Akad. Nauk SSSR*, 68, No. 5, 981 (1949).
11. I. A. Éskin and Yu. B. Skebel'skaya, *Doklady Akad. Nauk SSSR*, 68, No. 4, 801 (1949).
12. V. Antila et al., *Acta endocr. (Kbh.)*, Vol. 20 (1955), p. 351.
13. P. Fatterpaker, U. Marfatia, and A. Sreenivasan, *Nature*, Vol. 176 (1955), p. 165.
14. W. Lavate and A. Sreenivasan, *Ibid.*, Vol. 178 (1956), p. 804.
15. D. Leroy and S. Robin., *Sem. Hop. (Paris)*, Vol. 31 (1955), p. 1097.
16. M. Roche and M. Layrisse, *J. clin. Endocr.*, Vol. 16 (1956), p. 831.
17. B. A. Sure and L. Easterling, *J. Nutr.*, Vol. 42 (1950), p. 221.

Note

The figure referred to throughout this article was omitted in the original.