# DYNAMICS OF CHANGES IN NUCLEIC ACID CONTENT IN THE ENDOCRINE GLANDS OF RABBITS WITH EXPERIMENTAL ATHEROSCLEROSIS

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Nucleic acids play a direct part in protein synthesis and have an important role in secretory processes in the endocrine glands in connection with hormone formation [5, 14]. It has been reported that the content of nucleic acids in the endocrine glands is closely connected with the functional activity of the endocrine apparatus [4, 11, 15].

In the pathogenesis of atherosclerosis great importance is attached to changes in the functional state of the endocrine glands and, in particular, of the thyroid [2, 8, 10, 12, 16] and the adrenals [1, 3, 7]. It is therefore important to study the content of nucleic acids in the tissues of the endocrine glands in experimental atherosclerosis.

The object of the present investigation was to study the content of nucleic acids in the thyroid and adrenal glands of rabbits with experimental atherosclerosis.

## EXPERIMENTAL METHOD

Experiments were carried out on 29 male chinchilla rabbits weighing 2.5-3 kg. Experimental atherosclerosis was reproduced in 19 animals by Anichkov's method, by feeding them with cholesterol daily in a dose of 0.2 g/kg body weight for 20-25 days (experiments of series I) and 120-130 days (experiments of series II). Ten healthy rabbits were used as controls. The animals were decapitated, the thyroid and adrenals were rapidly removed and kept in the cold, and the content of nucleic acids in the glands was determined by the Schmidt–Thannhauser method as modified by Tsanev and Markov, using the SF-4 quartz spectrophotometer [13]. The content of nucleic acids was calculated in mg% P/dry weight of tissue. The experimental data were subjected to statistical analysis.

The content of cholesterol and phosphatides in the blood serum of the rabbits was determined by the usual methods. The degree to which the aorta was affected by atherosclerosis was assessed macroscopically at necropsy in accordance with a four-point system.

## EXPERIMENTAL RESULTS

A significant increase in the serum cholesterol concentration (mean 532.5 mg%, normal level 51.6 mg%) and in the phosphatides (mean 361.2 mg%, normal 103.5 mg%), with a decrease in the phosphatide-cholesterol ratio by 2.8 times compared with its normal value, were found in the rabbits receiving an atherogenic diet for 20-25 days. Macroscopic investigation of the aorta of the rabbits of series I revealed traces of isolated atherosclerotic plaques only in individual cases (in 2 of 9 animals).

The content of R-RNA in the thyroid and adrenal tissues of the rabbits of series I was only slightly altered, with only a tendency for it to fall. The content of R-DNA in the adrenals of the animals remained practically unchanged during the short period of development of experimental atherosclerosis (Table 1).

After a period of 120-130 days on the atherogenic diet the cholesterol concentration in the blood of the experimental animals rose to a mean value of 707.3 mg%, the phosphatides rose to 307.7 mg%, and the phosphatide-cholesterol ratio fell by 3.5 times compared with normal. Extensive atherosclerotic lesions were found in the aorta of the animals in the experiments of series II.

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TABLE 1. Content of Nucleic Acids (in mg% P/Dry Weight of Tissue) in Thyroid and Adrenals of Rabbits at Various Times during Development of Atherosclerosis, M±m

| Period of development of atherosclerosis | No. of animals | R-RNA | R-DNA | R-RNA/R-DNA |
|---|---|---|---|---|
| | | Thyroid | | |
| Control | 10 | 368,86±28,14 | 134,81±16,56 | 3,56±0,57 |
| 20—25 days | 9 | 385,64±14,86 $P>0,5$ | 173,97±15,00 $P=0,05$ | 2,42±0,21 $P>0,05$ |
| 120—130 days | 10 | 294,36±17,80 $P<0,05$ | 136,90±14,14 $P>0,5$ | 2,36±0,85 $P=0,25$ |
| | | Adrenals | | |
| Control | 10 | 402,09±17,09 | 132,18±7,31 | 3,12±0,20 |
| 20—25 days | 9 | 380,10±15,79 $P>0,25$ | 120,02±10,66 $P>0,25$ | 3,54±0,25 $P>0,1$ |
| 120—130 days | 10 | 287,66±18,52 $P<0,001$ | 58,66±7,67 $P<0,01$ | 5,56±0,74 $P<0,01$ |

TABLE 2. Changes in Weight of Adrenals of Rabbits with Atherosclerosis, M±m (n = 10)

| Series of experiments | Weight of organ | | Dry wt. of tissue (in % of fresh wt.) |
|---|---|---|---|
| | in g | in % of body wt. | |
| Control | 0,360±0,032 | 0,011±0,0026 | 45,00±0,24 |
| Atherosclerosis | 1,280±0,093 $P<0,001$ | 0,039±0,0084 $P<0,01$ | 61,50±0,62 $P<0,001$ |

The content of R-RNA in the thyroid and adrenal tissues of the rabbits in which experimental atherosclerosis was induced for a longer period showed a considerable decrease (Table 1). The content of R-DNA content in the thyroid of the rabbits in this series of experiments was almost unchanged.

In the course of development of the pathological state in the endocrine glands the ratio between between the nucleic acids changed. Whereas in the healthy rabbits the RNA/DNA ratio in the thyroid was 3.56, while that in the adrenals was 3.12, in the experimental animals of series I the ratio was 2.42 and 3.54 respectively, and in the animals of series II, 2.36 and 5.56 respectively.

Comparison of the changes in the content of nucleic acids in the endocrine gland tissues of the experimental rabbits of series I and II shows that in the adrenals the trend of the changes was the same after both long and short periods of development of experimental atherosclerosis. A tendency for the nucleic acid content to diminish was observed 20-25 days after the beginning of cholesterol feeding by the animals. In the adrenals of the rabbits receiving an atherogenic diet for long periods, in which the course of the pathological process was severe, as reflected by the extensive atherosclerotic lesions in the aorta, the decrease in the nucleic acid content was very clear. Perhaps the relative decrease in the R-DNA content in the adrenals is connected with an increase in the lipid content of the cells of these glands as a result of infiltration of lipids. Marked hypertrophy of the adrenals was observed in the animals with atherosclerosis. Whereas the adrenals of the healthy rabbits weighed on the average 0.36 g, in the animals kept for a long period on an atherogenic diet the weight of the adrenals increased to 1.28 g ($P < 0.001$). The relative weight of the adrenals (as a percentage of the body weight) showed a statistically significant increase. These results are given in Table 2.

Subsequent investigations showed that the increase in weight of the adrenals took place on account of an increase in weight of the dry residue of the tissue (see Table 2). There are reports in the literature of a considerable increase in the content of cholesterol and phosphatides in the adrenals of rabbits with atherosclerosis [9]. Probably these substances may also account for the observed increase in the weight of the dry residue of the adrenal tissue.

The decrease in the R-DNA content in the adrenals observed in the present investigation during development of atherosclerosis, irrespective of whether absolute or relative, was the result of development of the pathological process and could have an adverse effect on protein metabolism in these glands.

So far as the thyroid is concerned, its weight in the different series of experimental animals showed only very slight changes.

In a series of experimental investigations and clinical studies [1, 6, 7] it was found that in the process of development of experimental atherosclerosis the thyroid and adrenal function was substantially modified. Very probably the changes in the functional levels of these glands in experimental atherosclerosis are closely connected with a disturbance of nuclear metabolism therein, which the present investigation revealed.

The increase in the R-DNA content,while the R-RNA content in the thyroid remained almost unchanged in the early periods of reproduction of atherosclerosis,evidently reflects a compensatory increase in functional activity of this gland in response to the action of the pathogenic factor. The results obtained are in agreement with data in the literature indicating an increase in function of the endocrine glands of rabbits in the early stages of development of experimental atherosclerosis [1]. However, with further progressive development of the atherosclerosis the content of nucleic acids in the thyroid and adrenals fell. These results are in good agreement with the lowering of functional activity of the thyroid and adrenals in severe atherosclerosis reported in the literature [1, 6, 7, etc.].

It may be postulated that the change in the content of the nucleic acids and in their relative proportions, from the normal values, observed in the present investigation in the thyroid and adrenal tissues,may be the cause of the disturbance of protein synthesis, and hence, of the change in functional activity, in the endocrine glands in atherosclerosis.

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