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CHANGES IN MASS OF THE RIGHT VENTRICLE AND ITS RNA CONTENT DURING REGRESSION OF HYPERTROPHY

E. G. Kolokol'chikova and V. I. Korol'kov

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Noninbred male rats weighing 250-300 g were used. Adaptation to high-altitude hypoxia was produced by keeping the animals once a week for 5 h in a pressure chamber at an "altitude" of 6000 m. The degree of hypertrophy of the right ventricle and its RNA content were studied after 20 days of adaptation and also 2, 10, 20, and 40 days after the end of exposure to hypoxia. The mass of the right ventricle and its RNA concentration and content were significantly increased 20 days after the beginning of adaptation. After the end of exposure to hypoxia half of the increase in mass of the right ventricle was lost during the next 10 days and half of the increase in RNA during the next 2 days. Forty days after the end of exposure to hypoxia the mass of the right ventricle and its RNA content in the adapted animals were indistinguishable from those in the controls.

KEY WORDS: adaptation; hypoxia; hypertrophy of the right ventricle; regression of hypertrophy; RNA.

With an increase in the load on the heart the synthesis of nucleic acids and protein in the myocardial cells is activated and hypertrophy develops. A reduction in the load on the heart leads to a decrease in the intensity of nucleic acid and protein synthesis and in the mass of the organ [2, 3, 7]. Correspondingly, it has been shown that hypertrophy of the heart is a reversible process: After removal of aortic stenosis, creating a load on the heart, the mass of the myocardium decreases fairly rapidly [8, 10]. However, the extent to which the dynamics of regression of hypertrophy depends on the decrease in myocardial function is not quite clear, for aortic stenosis and its removal necessitated a surgical operation, and repeated operations, like changes in the region of the aorta to which the stenosing ring was applied, could affect the state of the heart and the regression of its hypertrophy.

To rule out the action of these factors, in the investigation described below hypertrophy of the right ventricles was produced by adaptation to high-altitude hypoxia; the mass of the right ventricle and its RNA content were measured during regression of the hypertrophy.

Laboratory of Pathophysiology of the Heart, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 12, pp. 1421-1422, December, 1976. Original article submitted May 24, 1976.

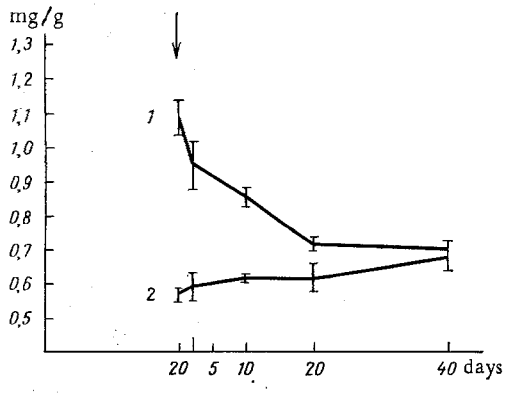

Fig. 1

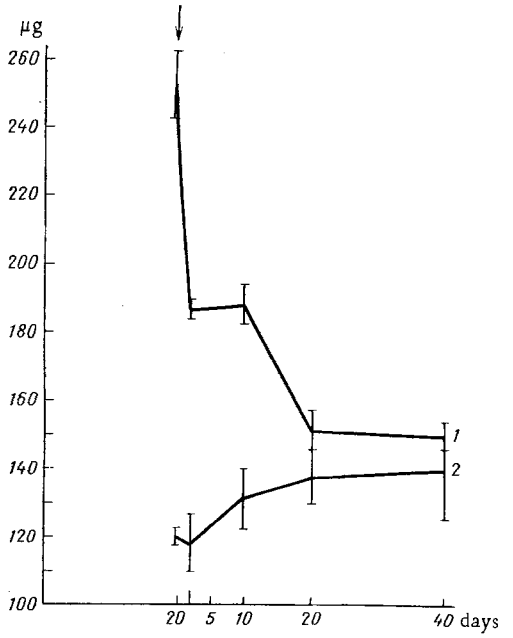

Fig. 2

Fig. 1. Changes in relative weight of right ventricle during regression of hypertrophy. 1) Adapted animals; 2) control. Arrow indicates time of termination of adaptation to high-altitude hypoxia (20 days). Ordinate, relative weight of right ventricle (in mg/g); abscissa, time (in days).

Fig. 2. Changes in RNA content (RNA concentration × relative weight of ventricle) in right ventricle during regression of hypertrophy. Ordinate, RNA content (in μg). Remainder of legend as in Fig. 1.

EXPERIMENTAL METHOD

Noninbred male rats weighing 250-300 g were used. For 5 h daily the animals were kept in a pressure chamber at an "altitude" of 6000 m. The degree of hypertrophy of the heart and its RNA content were determined after 20 days of adaptation, and again 2, 10, 20, and 40 days after the end of exposure to hypoxia. At each of these times the hearts of 11 to 15 animals were studied. The degree of hypertrophy of the hearts was judged from the relative weight of the right ventricle (the ratio between the absolute weight of the ventricle with the septum and the body weight). RNA was isolated from a heart muscle homogenate from the right ventricle [11] and was determined spectrophotometrically [9].

EXPERIMENTAL RESULTS AND DISCUSSION

The curves in Figs. 1 and 2 reflect the effect of adaptation to high-altitude hypoxia and subsequent determination of exposure to hypoxia on the weight of the right ventricle and its RNA content. Twenty days after the beginning of adaptation the mass of the right ventricle of the animals was considerably increased. This increase in mass was due to a sharp increase in the concentration and absolute content of RNA which, as we know [5], plays a decisive role in the activation of protein synthesis. After the end of exposure to hypoxia the RNA content and mass of the right ventricle fell quite rapidly. If the increase in mass of the right ventricle and in its RNA content is taken as 100%, simple calculations show that this increase became progressively smaller, as follows: After 2 days 48% of the RNA and 31% of the mass of the ventricle were lost, after 10 days the figures were 57 and 54%, and after 20 days 90 and 81%, respectively; after 40 days the mass of the right ventricle and its RNA content did not differ significantly from those in unadapted animals.

The results show that after removal of the load from the right ventricle its mass decreased so that half of the increase then present disappeared during the next 10 days.

This rate of disappearance of the structures of the organ after a sudden reduction in its function can most usefully be compared with the rate of increase in the mass of the heart structures after a sudden increase in the load placed upon it. Such an increase in load caused by aortic or pulmonary stenosis leads to a

very rapid increase in mass of the corresponding ventricle, and as a result, half of the eventual increase in mass is achieved during the next 3-4 days [1]. The more rapid rate of increase in the mass of the organ in response to loading than its decrease after removal of the load fits in with Meerson's views regarding the rapid onset and slow disappearance of the structural changes that constitute the basis of adaptation. This concept implies that structural changes arising as the result of a single exposure to a certain factor may persist for a long time and undergo summation with the structural changes in response to the repeated action of the same factor on the body. As a result, adaptive cumulation of structures and adaptation of the organism to a periodically operating environmental factor take place [4].

The total RNA of the myocardium determined in the present experiments was accounted for to the extent of 90% by ribosomal RNA; consequently, the sharp decrease in its content in the early stage of regression of hypertrophy is evidence of destruction of many ribosomes. This activation of the destruction of ribosomes, which under ordinary conditions have a long half life, together with the activation of ribonuclease and other factors, may be attributable to a decrease in the synthesis and content of messenger RNA. Such a decrease would lead to an increase in the number of unprogrammed, nontranslating ribosomes, which break up more rapidly than programmed ribosomes under the influence of various factors [6].

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