# CONTENT OF CATECHOLAMINES IN THE KIDNEYS, MYOCARDIUM, AND ADRENALS IN EARLY HUMAN DEVELOPMENT

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UDC 612.46+612.173.1+612.45]: 612.452.018:612.64

The content of adrenalin, noradrenalin and dopamine was studied in the kidneys, heart, and adrenals of human fetuses and adults. The catecholamine level changes substantially from the 12th to the 40th week of fetal development. It reaches its highest level at 13-16 weeks and its lowest 33-36 weeks of antenatal development. Dopamine accounts for between 82 and 92% of the total content of catecholamines throughout development. The total content of catecholamines in the organs is highest by the end of the antenatal period. The content of catecholamines in the fetal heart and kidneys at the 13th-16th week is close to its level in the adult.

One of the principal factors reflecting the function of the sympathico-adrenal system is the content of mediators of this system in the tissues. In the modern view catecholamines, before they perform the role of mediators, function as special hormones playing an active role in the regulation of embryogenesis [1-3]. In this connection, an interesting aspect of the study of the biochemical basis of human antenatal development is the examination of the quantitative catecholamine dynamics in the tissues of the developing fetus.

Data in the literature on the tissue catecholamine levels in human fetuses are scarce and highly contradictory. In some reports it is stated that noradrenalin is present and adrenalin absent in human fetal tissues [15, 17]. According to West et al. [18] noradrenalin accounts for approximately 90% of the

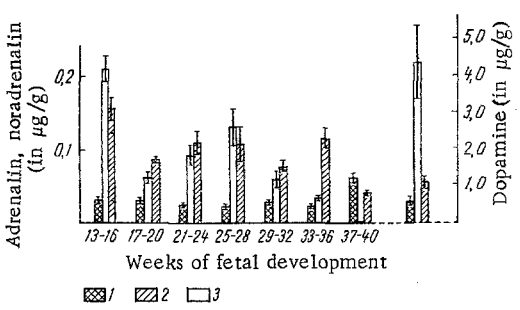


Fig. 1

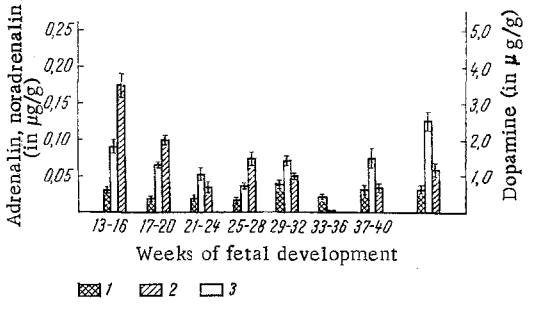


Fig. 2

Fig. 1. Content of catecholamines in myocardium of human fetuses and adults. Here and in Fig. 2: 1) adrenalin; 2) dopamine; 3) noradrenalin.

Fig. 2. Content of catecholamines in kidneys of human fetuses and adults.

Department of Biochemistry, A. M. Gor'kii Donetsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR, V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 73, No. 6, pp. 27-30, June, 1972. Original article submitted November 16, 1971.

TABLE 1. Content of Catecholamines (in μg/g fresh tissue) in Adrenals of Human Fetuses

| Age of fetuses (in weeks) | Number of experiments | Adrenalin | | Noradrenalin | | Dopamine | |
|---|---|---|---|---|---|---|---|
| | | M±m | P | M±m | P | M±m | P |
| 13—16 | 8 | 5,62±0,49 | >0,05 | 4,73±0,31 | >0,1 | 65,75±4,90 | <0,02 |
| 17—20 | 8 | 4,39±0,37 | <0,001 | 3,89±0,39 | <0,001 | 45,42±5,49 | <0,02 |
| 21—24 | 9 | 1,53±0,24 | <0,001 | 2,18±0,10 | <0,001 | 29,48±2,31 | <0,001 |
| 25—28 | 9 | 5,55±0,43 | >0,5 | 4,30±0,16 | >0,2 | 71,45±8,68 | <0,01 |
| 29—32 | 9 | 5,54±1,04 | <0,001 | 3,54±0,75 | <0,05 | 40,09±5,08 | <0,001 |
| 33—36 | 8 | 1,80±0,15 | <0,001 | 1,71±0,13 | >0,05 | 15,65±0,87 | <0,001 |
| 37—40 | 8 | 3,59±0,26 | | 2,15±0,17 | | 53,11±5,90 | |
| Adult | 6 | 463,37±82,56 | | 208,78±41,60 | | 238,57±34,22 | |

adrenal catecholamines. Most workers state that during the development of mammals and birds the content of adrenergic substances is constantly changing [7, 10, 11].

To fill in the gaps in our knowledge of the catecholamine dynamics in the tissues of the developing organism, in the investigation described below the content of adrenalin, noradrenalin, and dopamine was determined in the kidneys, heart, and adrenals of human fetuses in the course of development.

## EXPERIMENTAL METHOD

The tissues of human adults and fetuses from the 12th to the 40th week of development were investigated; the fetuses were divided into seven age groups, with not less than eight in each group. A weighed sample of tissue was homogenized in the cold with 10 mg EDTA and 20 ml 0.4 N perchloric acid. The excess of perchloric acid was neutralized with 5 N potassium carbonate solution and the precipitate was separated by centrifugation. The supernatant was rendered alkaline with 1 N ammonia solution to pH 8.5 and transferred quantitatively to a chromatographic column. Elution was carried out with 0.25 N acetic acid. For determination of noradrenalin and adrenalin the samples were oxidized with 0.1 ml 0.25% potassium ferricyanide solution, and for determination of dopamine, they were oxidized with 0.2 ml 0.02 N iodine solution [8]. Fluorescence was measured with the ÉF-ÉM fluorometer with the improvements suggested by Esikov [4].

## EXPERIMENTAL RESULTS

The Myocardium. Between the 13th and 36th weeks of development the adrenalin content was virtually unchanged and lay between 0.02 and 0.03 μg/g fresh tissue, while during the last 4 weeks it rose to 0.06 μg. The noradrenalin content in the 13th-16th weeks of development was 0.21 μg, falling to 0.06 μg in the 17th-20th week, and then rising again to 0.13 μg between the 20th and 28th weeks. This was followed by a gradual decrease in the noradrenalin level (Fig. 1), and by the end of the intrauterine period it was too low to be determined by the instrument used in the investigation. The dopamine level in the 13th-16th weeks of development was 3.10 μg/g fresh tissue, and by the 40th week it had fallen to 0.8 μg. More than 90% of the total quantity of catecholamines in the myocardium throughout the antenatal period of development was accounted for by dopamine. Positive correlation (r = +0.83) was established between the concentrations of dopamine and noradrenalin. This means that the increase in the dopamine content in the myocardium determines the increase in the noradrenalin content.

The Kidneys. The adrenalin level in the kidneys was virtually unchanged from the 12th until the 40th weeks of development, and its mean value was 0.03 μg/g fresh tissue. The noradrenalin content in the 13th-16th weeks was 0.09 μg, falling to 0.04 μg by the 29th week. During the last 12 weeks of development sharp fluctuations were observed in the noradrenalin content: from 0.07 μg in the 29th-32nd weeks it fell to 0 in the 33rd-36th week and then rose again to 0.07 μg in the 37th-40th week (Fig. 2). The dopamine content was highest in the 13th-16th weeks of development (3.48 μg), after which it fell to reach 0.7 μg by the 40th week.

Positive correlation ($r = +0.66$) was found between the dopamine and noradrenalin levels, but it was below the limits of significance.

The Adrenals. The adrenals in human fetuses are large and their relative weight is 10-20 times more than in the adult. The change in the content of adrenalin, noradrenalin, and dopamine in the adrenals during development takes place stepwise with maxima at the 13th-16th, 25th-28th, and 37th-40th weeks (Table 1). The adrenalin content in the adrenals is slightly higher than in the noradrenalin content. This ratio between the catecholamines is characteristic of the adrenals only. Dopamine accounted for between 82 and 92% of the total catecholamine content. Positive correlation was found between the noradrenalin and adrenalin content ($r = +0.89$). Significant correlation also was found between dopamine and noradrenalin ($r = +0.79$). The increase in the level of the precursor in the mechanism of amine synthesis thus determines an increase in the concentration of the product.

The results confirm those obtained by Greenberg and Lind [14], who found that adrenalin and noradrenalin are present in human fetal tissues during the first 3 months of development, but who were unable to demonstrate the presence of dopamine.

The highest content of catacholamines in the myocardium and kidneys was thus observed in the 13th-16th weeks of antenatal development of the fetus and it fell toward the end of pregnancy. A similar decrease in the catecholamine concentration during development has been observed in the myocardium, spleen, and other tissues of the chick embryo [7]. The dynamics of hormonal activity of the fetal adrenals revealed by the present investigation is in agreement with results obtained by other workers who have studied thyroid function in the guinea pig and sheep [9] and pituitary function in rat fetuses [12, 13]. They show that the endocrine glands of fetuses in the early stages of development pass through a stage of increased activity, which is replaced by reduced function by the time of birth. The results may also be explained by some degree of mismatching between the rates of accumulation of catecholamines in the organ and the rate of growth of the organ: in the period studied, from the 12th to the 40th weeks of development, the weight of the human fetal heart increases by about 40 times, the kidneys by 45 times and the adrenals by 22 times. This view is confirmed in the literature [6, 16]. The total content of catecholamines in the organs is highest at birth. Comparison of the catecholamine content in the heart and kidneys of human fetuses and adults shows that in the fetus at 13-16 weeks the noradrenalin and adrenalin contents are close to their levels in the adult, while the dopamine level is about three times higher than in the adult (Figs. 1 and 2). The content of catecholamines in the adrenals is much lower in the fetus than in the adult (Table 1).

It can be concluded from these results that the human sympathico-adrenal system is functioning in the early stages of development. The concentration of catecholamines in the fetal tissues is constantly changing during antenatal development. The levels of these substances in the fetal tissues and organs evidently depend not only on the degree of maturity of the fetus, but also on the demands of the developing organism for these substances at the different periods of development. For example, the human fetal testis, which produces the hormones necessary for morphogenesis of the genital tract along male lines, loses all trace of secretory activity by the 20th-21st week of development and thereafter remains in that state until the period of sexual maturity [5]. It may be that the developing organism also has different requirements of catecholamines, which depend on the degree to which these substances participate in morphological and functional differentiation of the tissues.

## LITERATURE CITED


1. G. A. Buznikov, in: The Formation of Endocrine Functions in Embryonic Development [in Russian], Moscow (1966), p. 40.
2. G. A. Buznikov, Zh. Évolyuts. Biokhim. i Fiziol., 2, 23 (1966).
3. G. A. Buznikov and B. N. Manukhin, Zh. Obshch. Biol., 22, 223 (1961).
4. A. D. Esikov and V. V. Men'shikov, Lab. Delo, No. 4, 22 (1961).
5. S. E. Levina, in: The Formation of Endocrine Functions in Embryonic Development [in Russian], Moscow (1966), p. 141.
6. T. I. Mazina, in: The Formation of Endocrine Functions in Embryonic Development [in Russian], Moscow (1966), p. 97.
7. B. N. Manukhin, Z. E. Pustovoitova, and N. M. Vyaz'mina, Zh. Évolyuts. Biokhim. i Fiziol., 5, 42 (1969).
8. É. Sh. Matlina and T. B. Rakhmanova, in: Methods of Clinical Biochemistry of Hormones and Mediators [in Russian], Moscow (1969), p. 95.

9. M. S. Mitskevich, The Glands of Internal Secretion in the Embryonic Development of Birds and Mammals [in Russian], Moscow (1957).
10. N. A. Smitten, Dokl. Akad. Nauk SSSR, 135, 728 (1960).
11. E. M. Stabrovskii, Fiziol. Zh. SSSR, 51, 1261 (1965).
12. A. Cohen, Arch. Anat. Micr. Morph. Exp., No. 3, 265 (1955).
13. A. Cohen, C. R. Soc. Biol (Paris), 153, 1956 (1959).
14. R. E. Greenberg and G. Lind, Pediatrics, 27, 904 (1961).
15. B. Hökfelt, Acta Physiol. Scand., 25, 92 (1951).
16. L. M. Rinaldini, J. Embroyol. Exp. Morph., 8, 527 (1960).
17. G. B. West, Quart. Rev. Biol., 30, 116 (1955).
18. G. P. West, D. M. Shepherd, and R. B. Hunter, Lancet, 2, 966 (1951).