

FUNCTIONAL ACTIVITY OF THE ADRENAL CORTEX
IN FETAL AND NEONATAL RABBITS UNDER NORMAL
CONDITIONS AND DURING INHIBITION
OF THE GESTATION DOMINANT

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The content of lipids, cholesterol, and ascorbic acid was investigated in fetuses developing during normal pregnancy and in physiologically mature newborn rabbits, and also in fetuses developing during inhibition of the gestation dominant and in physiologically immature newborn rabbits. The results showed that in the first group the functional state of the adrenal cortex was activated, as shown by a low content of lipids, cholesterol, and ascorbic acid. In a state of increased adaptive motor responses the content of these substances was reduced still further. In the second group (physiological immaturity) their content was considerably increased. It is concluded that normal antenatal development is possible during exposure to natural physiological stress.

KEY WORDS: adrenals; antenatal development; gestation dominant.

Special investigations by Arshavskii [1-4] have shown that normal growth and development of the organism during ontogeny are possible only if there is exposure to the action of natural physiological stress, specific for each age period. In the fetal period the physiological form of stress stimulation is created by the restricted area of the placental surface. As a result there is the episodic formation of a deficiency in the supply of nutrients and oxygen from the maternal blood into the fetal blood. The fetus responds to the resulting deficiency by an adaptive general motor reaction. This increases the rate of the fetal circulation and thus increases the quantity of blood flowing through the capillaries of the placenta in unit time, thus causing compensation of the deficiency. To what extent are the adaptive motor responses of the fetus just described, in normal pregnancy, a manifestation of the function of the hypothalamic-pituitary-adrenal system (HPAS)? A special investigation [9] has shown that this system begins to function in the beginning of the fetal period - in rabbit fetuses from the 18th-20th day of antenatal development. The importance of this system to the vital activity of the fetus under normal and abnormal intrauterine conditions of development has not been studied.

In the investigation described below the effect of inhibition of the gestation dominant on fetal adrenocortical function was investigated in pregnant rabbits.

EXPERIMENTAL METHOD

The state of adrenocortical function was judged from the content of chemical components participating in steroid production in them: lipids, cholesterol, and ascorbic acid. The determinations were carried out by histochemical methods: lipids were revealed by staining with Sudan Black B and Sudan IV, cholesterol by polarization microscopy, and ascorbic acid by Backhus' method. A histological investigation also was carried out. The newborn animals were studied during the first half of the day after birth. Fetuses on the

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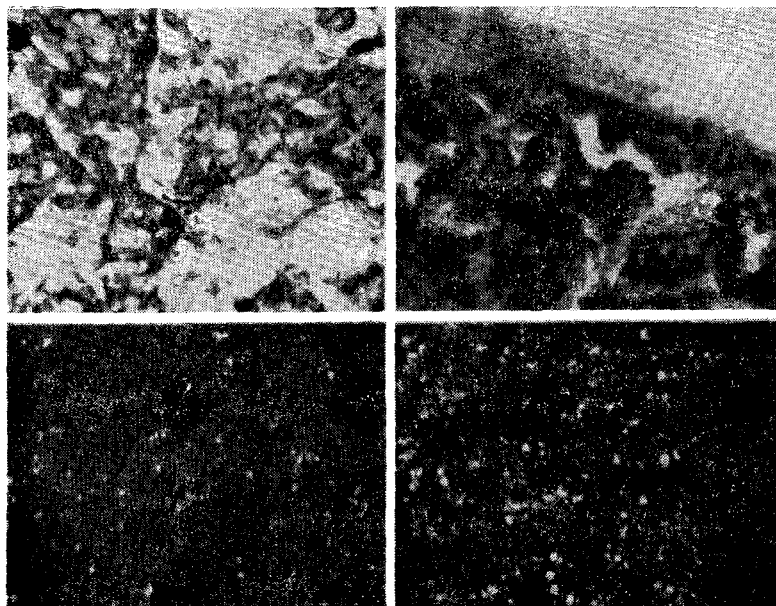


Fig. 1. Lipids (above) and cholesterol (below) in the adrenal cortex of fetuses on the 29th day of pregnancy under normal conditions (left) and physiological immaturity (right). Here and in Figs. 2 and 3, 160 \times .

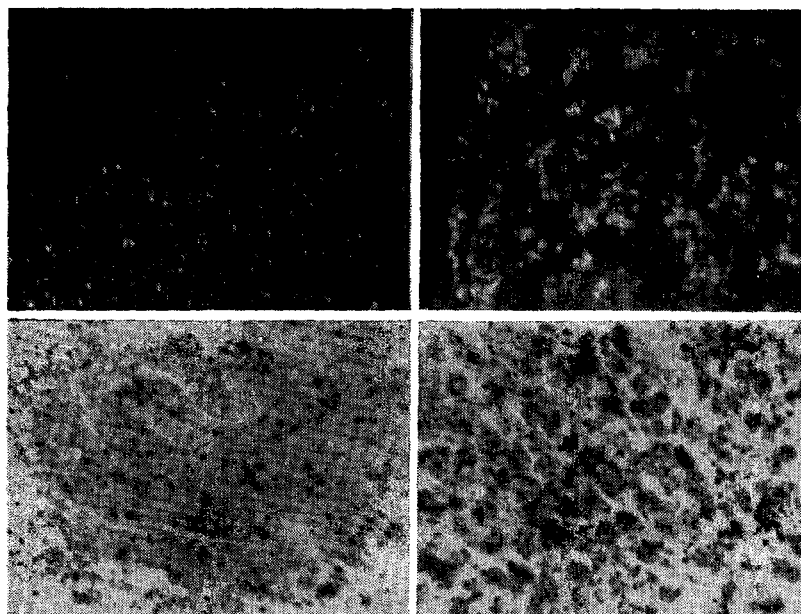


Fig. 2. Cholesterol (above) and cholesterol (below) in the adrenal cortex of newborn rabbits under normal conditions (left) and physiological immaturity (right).

19th, 21st, 23rd, 25th, 27th, and 29th days of normal pregnancy were studied. Inhibition of the gestation dominant was produced by the formation of an experimental neurosis in the pregnant females by the method usually adopted in the laboratory [1, 2, 5-8]. The pregnant rabbit was kept in a special chamber where she was exposed for 20 min to the alternate action (with intervals) of noise and weak electric stimulation (4-6 V) applied through the floor of the chamber. Altogether 458 fetuses and newborn rabbits from normal pregnancies and 183 from pregnancies accompanied by exposure to stress were investigated.

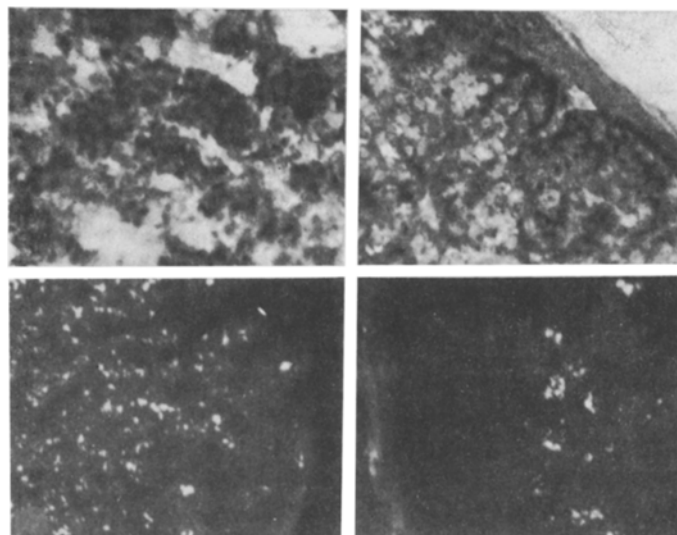


Fig. 3. Lipids (above) and cholesterol (below) in the adrenal cortex of fetuses on the 27th day of pregnancy under normal conditions (left) and with increased general motor adaptive reactions (right).

EXPERIMENTAL RESULTS

The histological analysis showed that under normal conditions the structural formation of the adrenal cortex takes place in the course of the fetal period. By the 19th-20th day the interrenal and suprarenal anlagen fuse to form the cortex and medulla. On the 21st-23rd day the cortex enlarges in size and differentiates into zones: on the 25th day the zona glomerulosa, zona fasciculata, and the primary zona reticularis are visible. After the 25th day the zonal differentiation of the cortex becomes clearer still, although no substantial changes take place before the end of pregnancy. Only very small quantities of lipids, cholesterol, and ascorbic acid are present in the adrenals of fetuses at the 21st day of pregnancy. With structural differentiation of the cortex its content of these substances increased, and this increase was particularly rapid before the 24th-25th day. When the secretion of hormones by the adrenal cortex is increased, as happens during exposure to stress, the lipids in its cells are quickly used up and the cholesterol and ascorbic acid content falls sharply. When the cortical cells revert to a state of relative rest, their lipid content is restored and the content of cholesterol and ascorbic acid rises.

As research in Arshavskii's laboratory has shown, a state of organized rest is absent in the antenatal period and in the early postnatal period until antigravity reactions begin to appear [2-4]. The question arises of how to assess the content of lipids, cholesterol, and ascorbic acid in the adrenal cortex found in the course of a normal pregnancy. Is it an expression of an activated state or of a state of rest of the fetus? What are the possible normal controls in this sense, and are they in fact possible? Answers to these questions could be obtained in fetuses from mothers in which the gestation dominant was inhibited. The living fetuses found at laparotomy on the mothers on the 27th or on the 29th day of pregnancy as well as living newborn rabbits in most cases had a body weight below the control. On the 27th day of pregnancy there were 50% of such fetuses, 62% on the 29th day, and 67% of the newborn animals weighed less than in the control. The weight of 17% of the fetuses on the 29th day of pregnancy and of 3% of the newborn rabbits was increased. In all fetuses and newborn rabbits with delayed development (physiologically immature) without exception the content of lipids, cholesterol, and ascorbic acid was sharply increased (Figs. 1 and 2). This increase was found if the comparison with the control fetuses was made by age or (in particular) by weight. In many fetuses and newborn animals with a normal and, in particular, with an increased body weight the content of these substances was lowered, but in some, just as in the fetuses and newborn rabbits with delayed development, it was increased to some degree.

Investigations in Arshavskii's laboratory have shown that the fetus responds to a disturbance of the conditions of its development (inhibition of the gestation dominant) by intensification of its adaptive general motor reactions, as a result of which its growth may be accelerated or may retain within normal limits. At the same time it has also been shown that, if the gestation dominant is inhibited, the mother develops an

acidotic shift of acid-base homeostasis. The acidotic changes thus arising in the fetal hypothalamus depress HPAS function. As a result, in physiologically immature fetuses and newborn rabbits the cholesterol, lipids, and ascorbic acid that accumulate in the adrenal cortex are not utilized, and corticosteroids are not formed or secreted. The high content of these substances found in the present experiments in the adrenal cortex of physiologically immature fetuses and newborn rabbits is evidence in support of this view. Consequently, inhibition of HPAS is closely linked with the cessation of the adaptive motor reactions of the fetus. The data given above reflecting a low content of cholesterol, lipids, and ascorbic acid in the adrenal cortex of fetuses during normal pregnancy thus indicate that the whole HPAS system in these fetuses is activated compared with its state in physiologically immature fetuses. The latter thus behave as a type of control for comparison with normally developing fetuses. During intensification of the adaptive reactions of the fetus the activation of the HPAS is increased still more, and this leads to a still further decrease in the level of cholesterol, lipids, and ascorbic acid in the adrenal cortex (Fig. 3). The content of lipids, cholesterol, and ascorbic acid in the adrenal cortex of physiologically mature newborn rabbits also was less than in the physiologically immature rabbits. The difference was even somewhat more marked than in the fetuses (compare Figs. 1 and 2). Investigations in Arshavskii's laboratory have shown that immediately after birth the ambient temperature, being lower than the intrauterine temperature, acts as a natural physiological stress stimulus [2-4]. The activated state of the adrenal cortex in newborn rabbits observed in the present experiments is the result of the influence of this physiological stress.

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