GROWTH PATTERN OF RABBIT FETUSES DURING NORMAL PREGNANCY AND WITH INHIBITION OF THE "GESTATION DOMINANT"

T. A. Bal'magiya and Z. F. Surovtseva

UDC 618.33-092.9-02:616.85

Growth of fetuses was studied under normal conditions and with inhibition of the "gestation dominant." Exposure of the pregnant rabbit to stress in the form of simultaneous electrical stimulation and acoustic stimulation by means of an automobile horn, if carried out in the embryonic (4th-16th days) or partly in the embryonic (16th-22nd days) periods of development leads to death of the fetus. Exposure in the early periods of fetal development (22nd-23rd days of pregnancy) causes delay of growth of the fetuses and their organs, but in the middle of the fetal period (24th-25th days) it does not change the weight of the fetuses compared with the control although the normal weight ratios of the organs are disturbed. Stress applied at the end of the fetal period (25th-27th days of pregnancy) leads to an increase in weight of the fetuses and to acceleration of growth of the organs.

Investigations in the Laboratory of Age Physiology and Pathology have shown that normal antenatal development takes place as the culmination of a physiologically normal gestation dominant. If the pregnant animal is exposed to various forms of stress the gestation dominant is inhibited with resulting delay or even cessation of antinatal development [1-6, 9].

In the investigation described below growth of fetuses and their individual organs (heart, lungs, brain) was studied during normal pregnancy and when the gestation dominant was inhibited.

EXPERIMENTAL METHOD

Growth during normal pregnancy was studied in 295 fetuses obtained by caesarian section from rabbits undergoing the operation daily from the 19th to the 30th days of pregnancy. The weight of the whole body, heart, lungs, and brain was measured. The following parameters were determined for the fetus as a whole and for the individual organs: 1) absolute growth, 2) absolute rate of growth, i.e., daily increase in weight, by the equation

$$C = \frac{V_2 - V_1}{t},$$

where V_1 and V_2 are the weight of the fetus or corresponding organs, and t the time (in days) between two weighings, and 3) Shmal'gauzen's growth constant [11]:

$$K = \frac{\lg V_2 - \lg V_1}{\lg T_2 - \lg T_1},$$

where T_1 and T_2 are the age (in days).

Laboratory of Age Physiology and Pathology, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 77, No. 4, pp. 44-47, April, 1974. Original article submitted February 6, 1973.

Inhibition of the gestation dominant was caused by the formation of an experimental neurosis by the method used in authors' laboratory [1, 4]. Stress (electrical stimulation combined with sounding an automobile horn) was applied for 30 min on two consecutive days.

The experimental neurosis was produced at certain times in accordance with the classification of the periods of antenatal ontogeny adopted in the laboratory: in the embryonic period – from the 4th to the 9th day of pregnancy (group 1 – 12 rabbits) and from the 10th to the 16th day (group 2 – 19 rabbits); in the embryonic period – from the 16th to the 22nd day (group 3 – 21 rabbits), and in the fetal period – from the 23rd to the 27th day of pregnancy (group 4 – 32 rabbits). Fetuses were obtained from the experimental rabbits by caesarian section on the 27th and 30th days of development. The weights of the experimental fetuses and of the organs mentioned were compared with the corresponding figures for the control groups.

EXPERIMENTAL RESULTS

As Figs. 1 and 2 show normal growth of the fetuses is irregular. The absolute rate of growth reached a maximum on the 23rd day, when it started to fall and reached a minimum by the 25th day of intrauterine development. This pattern corresponds to changes in the growth constant and some delay in the curve of absolute growth during this period. From the 25th-26th day the growth constant and, in particular, the absolute rate of growth again increased. This increase applied to the fetus as a whole, to the brain, and to the heart. The initial increase in the case of the lungs was followed by a decrease in the absolute rate of growth and in the growth constant. A similar periodicity of growth has been found in postnatal ontogeny [7, 8, 10]. At laparotomy on the rabbits of group 1 (exposed to stress in the period of implantation and the beginning of placentation) at the end of prenancy no fetuses or placenta were found in the uterus. However, the uterine mucosa was thickened and hyperemic and the corpora lutea in the ovaries were involuted (histological investigation), showing that pregnancy had taken place but had been interrupted soon after exposure to stress.

In the rabbits of group 2 (stress during the period of placentation and intensive organogenesis) either maceration of the fetuses or their complete absorption was found on the 27th-30th day of pregnancy. Dead, unmacerated fetuses were found in only two rabbits. The histological tests revealed involution of the corpora lutea in the ovaries.

In the rabbits of group 3 (stress in the period of completion of placentation and organogenesis) living or, in a few cases, dead but unmascerated fetuses were found. The weight of the experimental fetuses and the absolute weight of their brain, heart, and lungs were lower than in the control fetuses. In addition, the ratio between the relative weights of the organs differed in the experimental and control fetuses (Table 1).

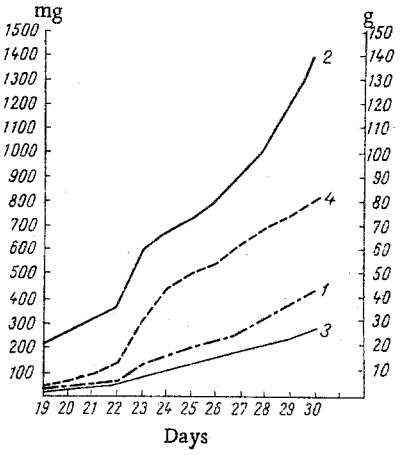

Fig. 1

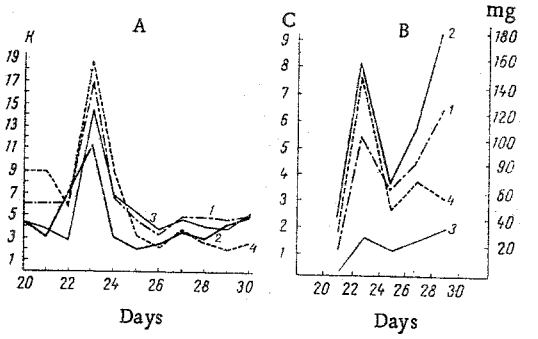

Fig. 2

Fig. 1. Changes in weight of whole body (1) and brain (2), heart (3), and lungs (4) of fetus from 19th to 30th days of intrauterine development during normal course of pregnancy. Abscissa, age (in days); ordinate: on left) weight of organs (in mg); on right) weight of fetuses (in g).

Fig. 2. Growth of fetuses and organs from 19th to 30th days of intrauterine development during normal course of pregnancy: A) growth constants; B) absolute rate of growth. Remainder of legend as in Fig. 1.

TABLE 1. Weight Characteristics of Rabbit Fetuses (absolute and relative weight of brain, heart, lungs) after Experimental Neurosis Produced in Mother Rabbits on 16th-22nd Day of Pregnancy (0) Compared with Control by Weight (K_1) and by Age (K_2)

Group of animals	Days of intrauterine development	Weight of fetus (in g)	Weight of brain: absolute (in g)	Weight of brain: relative (in g)	Weight of heart: absolute (in g)	Weight of heart: relative (in g)	Weight of lungs: absolute (in g)	Weight of lungs: relative (in g)
K_1	24	16,00±0,36*	0,678±0,018*	4,291±0,060*	0,103±0,002	0,646±0,005	0,433±0,007	2,719±0,037
0	27	16,43±0,46	0,667±0,017	4,157±0,082	0,076±0,001	0,465±0,013	0,374±0,014	2,324±0,046
K_2	27	26,59±0,38	0,929±0,008	3,503±0,030	0,173±0,002	0,650±0,008	0,621±0,007	2,336±0,089*
K_1	25	19,36±0,35*	0,737±0,007*	3,809±0,040*	0,125±0,002	0,647±0,002	0,495±0,006*	2,561±0,021
0	28	19,92±0,86	0,758±0,021	3,888±0,086	0,096±0,003	0,482±0,014	0,442±0,020	2,182±0,065
K_2	28	31,61±0,36	1,035±0,011	3,277±0,032	0,200±0,002	0,633±0,030	0,685±0,004	2,170±0,016*
K_1	27	26,59±0,38*	0,929±0,008*	3,503±0,030	0,173±0,002*	0,650±0,006*	0,621±0,007	2,336±0,018
0	29	25,58±0,73	0,947±0,028	3,719±0,057	0,174±0,003	0,679±0,016	0,768±0,016	3,035±0,043
K_2	29	37,19±0,37	1,195±0,006	3,217±0,029	0,230±0,002	0,623±0,011	0,737±0,006*	1,978±0,014
K_1	27	26,59±0,40*	0,929±0,008	3,503±0,030*	0,173±0,002*	0,650±0,006*	0,621±0,007*	2,336±0,018*
0	30	28,64±0,78	0,992±0,020	3,500±0,045	0,170±0,007	0,619±0,016	0,654±0,018	2,310±0,052
K_2	30	43,73±0,86	1,409±0,017	3,230±0,037	0,272±0,005	0,625±0,013*	0,804±0,013	1,815±0,020

Note: Differences of K_1 and K_2 relative to 0 are examined; in all cases except those marked by an asterisk ($P > .05$) differences are significant ($P < 0.005$).

In the rabbits of group 4 (stress on the 23rd-27th day) the weight of the fetuses was lower or higher than or equal to that of the age control. If exposure to stress was given at the beginning of the fetal period (22nd-23rd days of pregnancy) the weight of the fetuses was reduced. The ratios between the relative weights of the organs in the experimental and control fetuses, just as in the preceding group, differed. Exposure to stress in the middle of the fetal period (24th-25th day) did not change the weight of the fetuses relative to the control but the ratio between the relative weights of the organs in the experimental and control fetuses differed. Exposure to stress at the end of the fetal period (25th-27th day of pregnancy) led to an increase in weight of the fetuses if the tests were carried out on the 30th day, namely 58.2 ± 1.0 g (normal 43.7 ± 0.9 g; $P < 0.001$) and the relative weight of the brain (3.60 ± 0.03%), the heart (0.9 ± 0.02%), and the lungs (2.31 ± 0.04%) compared with the controls (3.23 ± 0.04, 0.62 ± 0.01, and 1.81 ± 0.02% respectively; $P < 0.001$ in all cases). It is interesting to note that with an increase in weight of the fetuses there was a corresponding increase in the size of the placenta (5.68 ± 0.11 g in the experimental and 3.00 ± 0.02 g in the control series; $P < 0.001$).

Exposure to stress in the embryonic period and also to some extent in the embryonic-fetal periods thus gives rise to death of the fetuses, whereas exposure in the early stages of the fetal period leads to their delayed growth. Exposure to stress on the 25th-27th day of pregnancy evidently leads to strengthening of the gestation dominant, as is reflected, in particular, in the increased size of the placenta. In addition, the fetuses respond in this period with an adaptive reaction of their own to stress, resulting in an increase in their rate of growth.

LITERATURE CITED

1. I. A. Arshavskii, Physiology of the Circulation in the Intrauterine Period [in Russian], Moscow (1960).
2. I. A. Arshavskii, Outlines of Age Physiology [in Russian], Moscow (1967).
3. I. A. Arshavskii, Z. F. Surovtseva, and M. G. Nemets, in: Tissue-Blood Barriers [in Russian], Moscow (1961), p. 293.
4. I. A. Arshavskii, V. I. Verulashvili, and Z. F. Surovtseva, in: Problems with Tissue-Blood Barriers [in Russian], Moscow (1965), p. 251.
5. I. A. Arshavskii, M. G. Nemets, Z. A. Bibileishvili, et al., in: Structure and Function of Tissue-Blood Barriers [in Russian], Moscow (1971), p. 20.
6. M. G. Nemets and Z. F. Surovtseva, in: Perinatal Pathology and Coli-Enteritis [in Russian], Minsk (1964), p. 305.
7. V. D. Rozanova and T. A. Bal'magiya, Byull. Eksperim. Biol. i Med., No. 10, 100 (1972).
8. S. G. Sipachev, The Rhythmic Nature of Animal Growth [in Russian], Tyumen' (1970).

9. Z. F. Surovtseva, Characteristics of Growth and Development of Rabbit Fetuses in Connection with the Experimental Disturbance of Pregnancy. Author's Abstract of Candidate's Dissertation [in Russian], Moscow (1969).
10. V. I. Fedorov, in: Conference on the Problem of Individual Development of Livestock and the Formation of Their Fertility [in Russian], Kiev (1966), p. 20.
11. I. I. Shmal'gauzen, in: Growth of Animals [in Russian], Moscow–Leningrad (1935), p. 134.