ACTION OF BLOOD SERUM OF ADULT RATS ON FETAL ORGANS

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Injection of blood serum of normal rats into pregnant rats leads to an increase in the weight of the lungs, heart, and liver of the fetuses and also stimulates thyroid and adrenal metabolism. Blood serum of pregnant rats does not possess this action.

Injection of blood serum of rats from which a lung had been removed leads to an increase in the weight of the lungs and to stimulation of adrenal metabolism in the fetuses.

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It has been shown experimentally [7, 11, 13] during the study of regeneration of organs that the blood serum (plasma) of animals from which part of an organ has been removed stimulates proliferation in the homonymous organ of intact animals. Similar results have been obtained in experiments on parabionts [8, 9, 14].

It has been postulated on the basis of these observations that in animals with an intrauterine type of development, in which an intimate humoral connection exists between the developing embryo and the maternal organism, a humoral mechanism of control of growth of the fetal tissues and organs is also established in the process of embryogenesis. Clinical and experimental observations show [2-4, 6, 12] that injury to any maternal organ disturbs the development of the same fetal organ. However, the mechanism responsible for this linked reaction of the organs is not yet known.

The object of the present investigation was to study the action of blood serum of adult rats on growth of fetuses and their organs under different experimental conditions.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats injected with blood serum of other rats on the 10th day of pregnancy. Blood was taken from the heart under sterile conditions. A mixture of serum from several rats, diluted with physiological saline in the ratio 1:2 was injected in a volume of 0.8 ml. Injections were given intraperitoneally twice daily: the first at 10:30-11:30 A.M., and the second at 3-4 P.M., for three days. On the 16th day of pregnancy the recipient rats were decapitated, and the fetuses were extracted and fixed in "Susa" solution for 20 h and kept in 70% alcohol with iodine.

Growth of the fetuses and their organs was assessed by weight and by volume in fixed preparations. The fetuses and their large organs (lungs, heat, liver) were weighed on torsion scales (with an accuracy of up to 0.1 mg), while the volume of smaller organs (thyroid and adrenal glands) was measured from the formula for an ellipsoid of rotation ($^4/_3$ lab^2, where a represents the large and b the small diameter of the lobes of the glands measured by an ocular micrometer and expressed in scale divisions).

Altogether five series of experiments were carried out. In series I the action of serum of normal rats was studied on growth of the organs of fetuses of pregnant animals. Blood serum from normal rats was injected into pregnant rats on the 10th, 11th, and 12th days of pregnancy. In series II the action of serum of normal rats from which a lung had been removed on growth of organs in the fetuses of pregnant rats was studied. The left lung was removed from normal animals and 48 h after the operation blood was taken from the rats and the serum obtained from it was injected into pregnant animals of the 10th, 11th, and 12th days of pregnancy. In series III the action of serum of pregnant rats on growth of the organs of fetuses of other pregnant rats was investigated. In this series, blood serum from rats 10 days pregnant

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TABLE 1. Action of Blood Serum of Pregnant and Normal Rats on Growth of Fetal Organs

Procedure	No. of fetuses	Size of organ relative to size of fetus											
		lungs		heart		liver		thyroid		adrenal			
		%	% of control	%	% of control	%	% of control	%	% of control	%	% of control
Injections of serum of normal rats	33	1,8±0,06	112	1,0±0,03	125	8,9±0,18	109	22,0±0,91	106	81,5±3,03	108
Injections of serum of normal rats after removal of one lung	31	1,8±0,07	112	0,9±0,05	113	8,1±0,18	98	18,7±1,61	90	82,2±3,14	109
Injection of serum of pregnant rats	45	1,6±0,04	100	0,8±0,03	100	8,0±0,19	98	19,7±0,95	95	77,4±3,27	102
Injections of serum of pregnant rats after removal of one lung	53	1,9±0,04	119	0,9±0,03	113	8,5±0,15	104	21,5±0,77	103	72,0±3,15	95
Control	50	1,6±0,03	100	0,8±0,03	100	8,2±0,18	100	20,8±0,72	100	75,7±2,68	100

Note. A line is drawn around figures showing statistically significant difference from controls ($P < 0.03$).

was injected into other pregnant rats on the 10th, 11th, and 12th days of pregnancy. In series IV the action of serum of pregnant rats with one lung removed on growth of organs of fetuses from other pregnant rats was studied. For this purpose the left lung was removed from pregnant rats on the 8th day of pregnancy (the time when lung anlagen appear in fetuses). In control series V, the dimensions of the rat fetuses and their organs were measured on the 16th day of normal intrauterine development.

EXPERIMENTAL RESULTS

Determination of the absolute weight and volume of the organs showed that injections of blood serum of normal rats led to a very slight increase in the total weight of the fetus (by 4%) and also to an increase in the weight of the lungs (by 13%), the heart (by 23%), and the liver (by 13%), and to an increase in the metabolism of the thyroid gland (by 10%) and adrenals (by 12%) compared with the corresponding values for the fetuses of control pregnant rats. Statistical analysis showed that the increase in size of all the fetal organs was significant.

Blood serum from normal rats undergoing an operation also caused some increase in the weight of the fetal organs. The increase in weight of the fetus itself (by 7%) and of the lungs (by 14%) and the increase in adrenal metabolism (by 17%) were significant.

Injections of the serum of pregnant rats caused no increase in the weight or volume of the fetal organs of other pregnant rats. On the other hand, injections of serum of pregnant rats after removal of one lung caused a statistically significant increase in the weight of the fetal lungs (by 14%).

Comparison of the results obtained with results of our previous investigations [5], demonstrating that operations on the lungs of pregnant rats accelerate growth and tissue differentiation of the fetal lungs, shows that the increase in size of the fetal lungs in the experiment when serum of pregnant rats with one lung removed was injected likewise was not caused by edema, hemorrhage, or by proliferation of interstitial tissue, but was due to accelerated growth of the organ itself.

Analysis of the relative sizes of the fetal organs showed (see Table 1) that injections of serum of normal rats accelerated growth of the heart (by 25%) and liver (by 9%) of the fetuses. The stimulation of growth of these organs was evidently due to the nonspecific action of normal rat serum [1]. Injections of the serum of normal rats undergoing the operation and also of pregnant rats, not undergoing operation, into other pregnant rats showed that the preliminary removal of the lung from non-pregnant rats, and also from pregnant rats, caused loss of the properties, present in normal serum, of stimulating growth of the fetal organs. At the same time removal of the lung from pregnant rats caused the serum to acquire the ability to accelerate growth of the lungs specifically in fetuses (by 19%).

It may be considered from these results, and also from data in the literature, that the blood serum of normal rats contains factors which, when injected into pregnant rats, caused nonspecific stimulation of growth of the fetal organs. Pregnancy in rats causes disappearance of these factors from the blood serum. Removal of a lung from pregnant rats at the moment of appearance of fetal lung anlagen leads to the appearance, within 48 h after the operation, of certain other factors in the blood of these rats, stimulating growth only of the fetal lungs. These blood factors can be transmitted by injections of the blood serum into other pregnant rats not undergoing operation.

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