MECHANISM OF PREMATURE DEVELOPMENT OF EMBRYONIC RAT LUNG AFTER UNILATERAL PNEUMONECTOMY ON THE MOTHER DURING PREGNANCY

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The relationship between proliferative (mitosis) and destructive (karyolysis and karyopyknosis) processes during development of the lung was investigated in rat embryos after unilateral pneumonectomy on the mother during pregnancy. A lowering of the level of destructive processes and a sharp increase in the number of mitoses in the experimental animals compared with the controls (normal development) were found.

KEY WORDS: karyolysis; karyopyknosis; mitosis; unilateral pneumonectomy.

In the last decade much clinical and experimental evidence of the specific effect of the maternal organs on the development of the homonymous fetal organs during pregnancy has been collected [1, 2, 6-12, 17, 18, 20, 21]. Investigations in the writer's laboratory [3, 13, 14] have shown that experimental unilateral pneumonectomy on the mother rat during the stage of laying down of the embryonic lung leads to premature development of the lungs in the fetus. The mechanism of this phenomenon is not clear. All that is known is that the growth-stimulating factor may be transferred from mother to fetus by the humoral route [13, 14].

To study the morphological changes arising in the lungs of fetuses developing after pneumonectomy on the mother and leading to premature maturation of the organ, the levels of proliferative and destructive processes in the epithelium of the rat fetal lung were investigated.

Physiological death of the cells during normal embryonic development is known [16] to be just as essential a part of embryogenesis as cell proliferation. Physiological degeneration of epithelial cells in the rat embryonic lung has been shown [24] to take place by means of karyolysis and karyopyknosis. The total number of dying cells increases as development proceeds, but mitotic activity remains at about the same level. Processes of destruction are correlated with mitosis and the degree of its severity varies with the stage of embryogenesis.

There is thus reason to suppose that this correlation may lie at the basis of one possible mechanism whereby growth and maturation of organs are regulated in embryogenesis. From this point of view, the results obtained in experiments involving pneumonectomy on the pregnant rat are of considerable interest, for one result of such an operation is to accelerate the development of the lungs in the fetuses, in which it is easy to study the changes in the course of physiological destruction.

EXPERIMENTAL METHOD

Wistar rats were used. The left lung was removed from the females on the 8th day of pregnancy. Fetuses of intact rats were used as the control. On the 13th, 16th, and 19th days of pregnancy 5 experimental and 5 control animals were killed. The 13-day embryos were fixed in Carnoy's fluid and embedded whole in paraffin wax but only the left lung was used from the 16- and 19-day fetuses. Serial sections 5 μ

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TABLE 1. Level (in percent) of Destructive and Proliferative Processes in Epithelium of Developing Lung of Rat Embryos under Normal Conditions (I) and after Unilateral Pneumonectomy on the Mother (II)

Age of fetuses (in days)	Dying cells			Dividing cells		
	I	II	P	I	II	P
13	15,89	10,92	0,017	2,32	33,53	0,000
16	23,31	14,66	0,013	7,51	9,30	0,770
19	35,72	20,48	0,000	2,24	5,27	0,020

in thickness, stained with Mayer's hematoxylin and counterstained with eosin, and also by Feulgen's method. Only one section from each embryo was used for counting. In the 13-day embryos all epithelial cells cut through in all the tubules were counted, but in the 16- and 19-day embryos only 1000 cells from each embryo were counted. Of the total number of epithelial cells at each time the number dividing and the number degenerating were determined; only cells with evidence of karyolysis and karyopyknosis of the IInd and IIIrd degrees were counted [15]. The numerical results were subjected to statistical analysis in order to determine the significance of the differences.

EXPERIMENTAL RESULTS

The level of the destructive and proliferative processes during the development of the lung when exposed to the action of specific humoral factors arising in the mother after pneumonectomy differed sharply from that in the normally developing lung (Table 1). The first feature noticed was a decrease in the general level of destruction in the epithelium of the fetal lungs of the experimental group at all times of development studied, together with an increase in mitotic activity, especially on the 13th day. Whereas no difference compared with the lungs of intact embryos was found as regards the course and appearance of destruction, mitosis showed two distinguishing features: first, an increase in the number of early phases (early prophases were particularly numerous on the 13th day of development); second, at all times many dying mitoses were found in the epithelium of the fetal lungs of the experimental group, mainly in the early stages of division. In the control group only solitary dying mitoses were found.

These observations indicate that pneumonectomy on the pregnant rats gives rise to some factor that stimulates mitotic activity sharply and, in the fetal period, probably leads to the earlier formation of the lungs than normally [13, 14, 19]. However, another effect of this factor is evidently that these "early" lungs are less resistant to unfavorable environmental conditions in the postnatal period [4, 5].

During the decrease in the general level of destruction in the pulmonary epithelium of the experimental group of embryos, however, the same tendency remained as in the control group: during development the number of dying cells increased, i.e., the principle of normal development was maintained, but the process continued on a lower level. By the end of the period of observation (the 19th day) the number of dying cells increased but was still below the control level.

Comparison of the course of destruction and proliferation (Table 1) also reveals that the decrease in the level of destruction was accompanied by an increase in mitotic activity. In the control (development of intact fetuses), in which the mitotic activity was much lower than in the experimental group, the level of destructive processes was much higher than in the experimental series. Conversely, the higher mitotic activity in the experimental group was matched by a low level of destruction. The idea of the correlation between these processes was thus justified, for the results of this experiment did not contradict it.

The data on destruction given in this paper are aggregated: cells in a state of karyolysis and karyorrhexis were considered together, for both these processes led to death of the cell. However, in their character, their mechanisms, the rate of their course and, evidently, their significance these phenomena are by no means equivalent. Investigations to study these processes during normal embryogenesis of the rat lung have confirmed this view; consequently, the comparison of individual types of physiological destruction with mitotic activity can be expected to yield further evidence in support of the validity of the idea of the mutually regulatory role of the processes of physiological destruction and of mitotic activity in embryogenesis.

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