KARYOLYSIS, KARYOPYCNOSIS, AND MITOSIS IN EPITHELIAL CELLS OF THE LUNG IN THE DEVELOPING RAT FETUS

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Processes of physiological cell destruction, manifested as karyolysis and karyopycnosis, in the epithelium of the developing rat embryonic lung correlate not only with each other but also with mitotic activity. There is reason to suppose that the increase in the number of cells showing signs of karyolysis is connected with the increase in mass of the lung parenchyma and that karyopycnosis is connected with the commencement of differentiation of the pulmonary epithelium.

Key words: karyolysis; karyopycnosis; mitosis; pneumonectomy.

Physiological death of cells, a phenomenon constantly observed during the embryonic development of anlage and organs of both vertebrates and invertebrates, is nowadays regarded as just as essential a part of embryogenesis as cell division, although its role has been established in far from every case [11].

The part played by products of cell disintegration in the mechanism of growth regulation is accepted by many [15, 16]. However, for embryos the problem is not yet clear.

Clinical and experimental observations show that damage to an organ in the pregnant female leads to abnormality in the embryonic development of the homonymous fetal organ [1-3, 5-7, 12]. Unilateral pneumonectomy, performed on the pregnant rat during formation of the lung anlage in the embryo, accelerates the development of the lungs in the fetus [8, 9, 13].

By studying changes in the number of cells destroyed and the number of mitoses, their possible role in growth and differentiation of the organ may perhaps be revealed.

EXPERIMENTAL METHOD

Wistar rats were used. In some animals the left lung was removed on the 8th day of pregnancy and the others were left intact. Five females of each group were killed on the 13th, 16th, and 19th days of pregnancy. The 13-day fetuses were fixed in Carnoy's fluid and embedded in toto, whereas only the left lung was similarly dealt with from the 16- and 19-day fetuses. Serial sections 5 μ in thickness were stained with Mayer's hematoxylin (counterstained with eosin) and by Feulgen's method. All the epithelial cells cut through transversely in all the tubules were counted in the lung anlage of the 13-day fetuses, and an average of 1000 cells in each 16- and 19-day fetus. No fewer than five fetuses were taken from different females at each time. In every case the counts were carried out on only one section from each fetus. The number of mitoses and the number of cells in states of karyolysis and karyopycnosis of the IInd and IIIrd degrees were determined per 1000 cells [10]. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

As was shown previously, during normal embryonic development of the rat lung physiological death of the epithelial cells takes place by karyolysis and karyopycnosis, which vary in intensity and occur in

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TABLE 1. Changes in Number of Dying and Dividing Cells in Epithelium of Developing Lung of Rat Fetus under Normal Conditions and after Pneumonectomy on the Pregnant Female (in ‰)

Age of fetus (in days)	Destructive processes						Mitosis		
	karyolysis			karyopycnosis					
	control	*P*	experiment	control	*P*	experiment	control	*P*	experiment
13	110,6	0,014	70,1	69,3	0,094	39,1	25,8	0,000	335,3
P	196,7	0,000	72,5	36,4	0,447	74,1	75,1	0,770	93,0
16	0,005		0,392	0,128		0,700	0,004		0,000
P	136,4	0,023	98,3	214,9	0,000	106,5	22,1	0,020	52,7
19	0,009		0,922	0,000		0,005	0,003		0,017

TABLE 2. Level of Proliferative and Destructive Processes When Development of Fetal Lung Accelerated by Pneumonectomy on Female (in % of normal)

Age of fetus (in days)	karyolysis	karyopicnosis	Mitosis
13	63,4	56,4	1445,3
16	36,9	203,6	123,8
19	72,1	49,6	235,3

different combinations at different periods of intrauterine development. When maturation of the embryonic lung was accelerated by pneumonectomy on the pregnant rat (Table 1), the levels of both karyolysis and karyopycnosis were lowered at all times of development studied (except karyopycnosis on the 16th day). Whereas under normal conditions in the course of both destructive processes a critical moment was observed on the 16th day of embryogenesis (the maximum for karyolysis and the minimum for karyopycnosis), this did not happen under experimental conditions: the two processes followed a parallel course and increased quantitatively during development of the lung, although they never reached values characteristic of normal. Mitotic activity under the experimental conditions was considerably intensified. Normally the number of mitoses reaches a maximum on the 16th day of development, but in the experimental series this maximum occurred earlier, on the 13th day.

To estimate the degree of the changes in proliferative and destructive processes under experimental conditions the values obtained for normal development were taken as 100% (Table 2). As Table 2 shows, a decrease in the intensity of destructive processes in the experimental series occurred at all times of development, on the average by 50%, except for karyopycnosis on the 16th day when the process, instead of being reduced, was more than doubled in intensity. Mitotic activity in the experimental series at all times exceeded 100%, this excess being minimal on the 16th day.

If each type of physiological destruction is compared with the mitotic activity it will be clear that on the 16th day, when the changes in the proliferative and destructive processes were most marked, the changes in the level of karyolysis and mitotic activity were parallel: the maximum for karyolysis in the control (normal development) coincided with the maximum of mitotic activity (Table 1), whereas the maximal decline in karyolysis in the experimental series (when development of the lung was accelerated by pneumonectomy on the pregnant rat) took place parallel with the minimal increase in mitotic activity (Table 2). The karyopycnotic changes during the same period were opposite to those affecting karyolysis and mitosis. The different types of destructive processes thus showed different tendencies in this case also: karyolysis was minimal (about 37% of normal) and the intensity of karyopycnosis was doubled.

According to data in the literature [4, 14] a series of morpho-functional transformations takes place on the 16th day of normal development in the rat fetal lung and an increase in the mass of the parenchyma on the organ is observed. In the present experiment, on the 16th day, because of the earlier development, the intensity of the increase in mass of the organ was reduced (this is shown by the lowest increase in mitotic activity) and the period of differentiation began [9]. Consequently, the sharp increase in karyopycnosis can be regarded as connected with the commencing differentiation of the epithelium, whereas the minimal level of karyolysis is somehow connected with the decrease in mitotic activity. In other words, the impression is obtained that karyolysis is related to the increase in mass of the parenchyma of the embryonic lung whereas karyopycnosis is connected with differentiation. However, the cause-effect relationship between these phenomena is not yet clear. One thing is certain: karyolysis and karyopycnosis perform different roles in embryogenesis; this is perfectly understandable because the processes taking place in the cell in the two types of degeneration differ sharply from each other and, consequently, the products of destruction formed under these circumstances may also differ.

It can be concluded from the present investigation, at this stage, that the processes of karyolysis, karyopycnosis, and mitosis are closely interdependent in the course of embryonic development of an organ.

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