# CHANGES IN SIZE OF RAT LIVER CELLS AND THEIR NUCLEI DURING PREGNANCY

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During pregnancy no significant changes take place in the mean diameter of the nuclei in the liver cells of Wistar rats, but with an increase in the length of pregnancy the predominant dimensional class of the nuclei is shifted in the direction of an increase. The mass of cytoplasm of the cells increases particularly sharply on the 8th and 16th days of pregnancy, when cells of the larger dimensional classes appear.

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Investigations have shown that the mean size of nuclei can be used as criterion of cell function during life [8].

The additional physiological load arising during pregnancy brings about an intensification of metabolism, an increase in the volume of certain organs including the liver [12, 15], and an increase in mitotic activity [4, 9]. In the reports of some investigations mention is made of an increase in size of the cells during pregnancy, although no precise details are given of the character of these changes, the time when they appear, and their duration.

In this paper the results of measurements of liver cells and their nuclei in rats at different periods of pregnancy are described.

## EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats initially weighing 160-180 g. Five animals were used at each period of pregnancy (8, 9, 10, 13, 16, and 19 days). The rats were always sacrificed at the same time of day, at 8 A.M. Material was fixed with Carnoy's fluid, and paraffin sections 7 $\mu$ in thickness were stained by the Feulgen method and counterstained with light green. One diameter of the nucleus and two diameters of the cell were measured by means of a screw-adjusted ocular micrometer (objective, immersion 90×, ocular 7×). Only mononuclear cells were measured. Altogether 100 nuclei and 100 cells were measured in the liver of each animal. Nonpregnant animals of the same group acted as controls.

## EXPERIMENTAL RESULTS

No significant changes took place in the mean dimensions of the nuclei at the times of pregnancy studied. The mean diameter of the nuclei varied between the 8th and 19th days of pregnancy from 25.5 to 26.8 $\mu$. In the control (nonpregnant rats of the same group) the mean diameter of the nuclei was 25.1 $\mu$ (Table 1). Examination of the relative percentages of nuclei of different dimensional classes shows, however, that with an increase in the duration of pregnancy there is an increase in the precentage of larger nuclei and a shift of the predominant dimensional class of nuclei toward an increase (Table 2). Starting from the 9th day of pregnancy, classes of nuclei of larger size became predominant.

This increase in size was evidently not connected with an increase in ploidy of the nuclei, because large numbers of cases of an increase in size of the nuclei by a whole number of times were never observed, although the final answer to this question must await the use of more precise methods of investigation.

The changes in the mean dimensions of the liver cells are given in Table 1, where two increases on the 8th and 16th days of pregnancy can be clearly discerned.

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TABLE 1. Mean Dimensions of Liver Cells and Nuclei of Rats at Different Times of Pregnancy (M±m)

| Index studied | Control | 8 days | 9 days | 10 days | 13 days | 16 days | 19 days |
|---|---|---|---|---|---|---|---|
| Diameter of nucleus (in $\mu$) | 25,1± 0,08 | 25,6± 0,05 | 26,2± 0,5 | 25,5± 0,05 | 26,2± 0,08 | 26,8± 0,7 | 26,8± 0,05 |
| Area of cell (in $\mu^2$) | 148,4± 0,12 | 201 0± 0,12 | 173,0± 0,08 | 178,2± 0,1 | 173,0± 0,1 | 217,0± 0,14 | 191,0± 0,1 |

TABLE 2. Relative Percentages of Nuclei in Different Dimensional Classes

| Time of pregnancy (in days) | Dimensional classes | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Control | 12,5 | 31.0 | 38.5 | 15,0 | 2.5 | 0,5 | — | — | — | — |
| 8 | 7,4 | 20.8 | 42.8 | 21,6 | 6.0 | 1,2 | 0,2 | — | — | — |
| 9 | 2.6 | 9,0 | 30.4 | 45.2 | 9.8 | 1.0 | 1,6 | 0.4 | — | — |
| 10 | 6,8 | 14,2 | 33.2 | 38.4 | 4,6 | 1,6 | 1.0 | 0,2 | — | — |
| 13 | 5.4 | 12,4 | 22,8 | 39.0 | 14.4 | 4.8 | 0.8 | 0,4 | — | — |
| 16 | 3,6 | 7.4 | 22,4 | 32.6 | 16.4 | 9,4 | 6.0 | 1,4 | 0.6 | 0,2 |
| 19 | 0,6 | 7,2 | 18.6 | 43.0 | 24.8 | 2,8 | 2,2 | 0,4 | 0,4 | — |

TABLE 3. Relative Percentages of Cells of Different Dimensional Classes

| Time of pregnancy (in days) | Dimensional classes | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Control | 44.5 | 30.0 | 22.0 | 3.5 | — | — | — | — | — | — |
| 8 | 7,0 | 23.8 | 27,4 | 23.8 | 11.6 | 3.2 | 2.2 | 0.2 | 0,4 | 0,4 |
| 9 | 10.8 | 39,0 | 33.0 | 13.8 | 3.0 | 0,2 | 0,2 | — | — | — |
| 10 | 14.0 | 29,6 | 34.2 | 16,4 | 4,2 | 1,0 | 0,6 | — | — | — |
| 13 | 20.0 | 33.0 | 26.8 | 12.6 | 5.8 | 1,2 | 0,6 | — | — | — |
| 16 | 7,2 | 19.2 | 25,4 | 21,2 | 13,4 | 5,8 | 4,8 | 1,2 | 1,0 | 0,8 |
| 19 | 4.2 | 25,6 | 36.0 | 23.0 | 8,6 | 1.4 | 1,0 | — | — | 0.2 |

Hence, in the course of pregnancy there is an increase in the mass of cytoplasm (148-191 $\mu^2$), which is particularly marked on the 8th and 16th day of pregnancy.

Examination of the relative precentages of cells in the various dimensional classes (Table 3) shows that in the control group 44.5% of cells were small, with a mean area of 110 $\mu^2$, and all the liver cells of the nonpregnant rats were distributed among 4 dimensional classes (i.e., large cells were completely absent). During pregnancy (at the different periods) the highest percentage of cells had a mean area of 150-190 $\mu^2$, and classes of larger cells appeared, especially on the 8th and 16th days.

In the course of pregnancy, an increase in the size of the cells thus takes place in the liver of rats, while the size of their nucleus remains more or less unchanged. These morphological findings are in full agreement with biochemical data indicating an increase in the intensity of metabolic processes in the liver during pregnancy [10, 11, 14], and they are the result of increased physiological activity of the cells.

An increase in the physiological load continuing for a substantial length of time must inevitably cause the more rapid wear and tear of the cells. Reports of increased mitotic activity of cells during pregnancy in the literature are not fortuitous [4, 13]. However, mitotic division is not the only method of making good a loss of functioning structural units. Among the other mechanisms of this type can be mentioned the division of binuclear cells [2, 3, 5], and the polyploidization [1] and hypertrophy of cells [6, 7]. In the case of pregnancy, hypertrophy of the cells evidently plays this compensatory role.

Changes in the dimensions of the liver cells and nuclei observed during pregnancy are an adaptive response to increased physiological demands, and they are evidently temporary in character, because they do not involve mechanisms connected with changes in the DNA content in the cell.

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