

POSTNATAL DEVELOPMENT OF THE PANCREAS IN ALBINO RATS

V. F. Sidorova and A. G. Babaeva

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The duration of that period of postnatal ontogenesis of rats was determined during which the pancreas remains capable of morphogenetic processes. The pancreas was investigated 3, 5, 14, 22, 40, and 75 days after birth. New acini are formed in large numbers during the first 3-4 weeks after birth. Later during growth of the animal the acini increased in size. Mitotic activity of the acinar cells falls sharply with age.

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Few studies have been made of the postnatal development of internal organs of vertebrates. This is particularly true of the mammalian pancreas [4-8, 12-15]. Nevertheless, as we [10] and other investigators [9] have pointed out previously, the character of postnatal ontogenesis of organs plays an important role in the outcome of regenerative processes observed in the internal organ after surgical operation. The length of the period in postnatal ontogenesis during which the organ remains capable of processes of internal morphogenesis, i.e., of the development of new anatomical and physiological units (acini, etc.), is particularly important. Maintenance of morphogenetic ability for a long period in postnatal ontogenesis facilitates the manifestation of such processes during regeneration of organs after extensive resections [1, 11]. From what has been said above, the need for detailed investigations to study the character of postnatal development of vertebrate internal organs will be apparent.

In the present investigation changes taking place in the pancreas of albino rats during postnatal development were studied. Attention was concentrated on changes in weight of the organ, mitotic activity of its cells, and the degree of manifestation of morphogenetic processes in the gland (the formation of new acini and of islets of Langerhans).

EXPERIMENTAL METHOD

The pancreas was investigated in rats 3, 7, 14, 22, 40, and 75 days after birth. At each period of investigation 4 or 5 animals were sacrificed by decapitation (always at 10-11 a.m.). The body weight was determined. After autopsy on the animals, the group of organs in contact with the pancreas (spleen, stomach, loops of duodenum) was removed and fixed along with the pancreas in Carnoy's fluid. After fixation the topography of the gland becomes clearer, and it can then be dissected more easily from the other organs and tissues. The fixed glands were weighed on torsion scales and embedded in paraffin wax, and sections were cut to a thickness of 7μ . Some sections were stained with hematoxylin-eosin for general survey purposes and counting mitoses, while others were impregnated by Gomori's method to determine the boundaries of the islets of Langerhans and individual acini. Mitotic activity was determined by counting mitoses in 3000 acinar cells from rats aged 3 and 7 days, and in 16,000 cells from rats of the other age groups. The mitotic index was expressed in promille.

The dimensions of the acini and islets were determined from drawings made under the microscope using a drawing apparatus. For each animal 100 acini were drawn from one section passing through the middle of the gland (magnification $350\times$). Next, all the islets of Langerhans in the same section were then drawn (magnification $130\times$). The area occupied by individual acini or islets was determined by the method described previously [2] and expressed in square microns.

Laboratory of Growth and Development, Institute of Experimental Biology, Academy of Medical Sciences of the USSR, Moscow (Presented by Active Member of the Academy of Medical Sciences of the USSR A. P. Avtsyn). Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 65, No. 5, pp. 105-109, May, 1968. Original article submitted September 3, 1966.



Fig. 1. Changes in structure of the pancreas during postnatal ontogenesis of rats. Structure of gland in animals aged 7 (a) and 21 (b) days. Acini small, cells in them compactly arranged. Abundant connective tissue in organ. In rats aged 40 (c) and 75 (d) days, islets and acini visibly enlarged; dimensions of cells also increased. Impregnated by Gomori's method. 200 x.

TABLE 1. Changes in Certain Indices Characterizing Postnatal Growth of Pancreas in Albino Rats

Age (in days)	No. of animals	Mean data			
		body weight (in mg)	weight of gland (in mg)	mitotic index (in %)	dimensions of one acinus (in μ^2)
3	4	5 310 \pm 300	18 \pm 1.2	13.4 \pm 2.5	420 \pm 23.0
7	5	7 640 \pm 420	35 \pm 2.8	5.3 \pm 2.7	418 \pm 10.9
14	5	18 640 \pm 3 700	63 \pm 8.1	6.9 \pm 3.0	500 \pm 52.2
22	5	27 250 \pm 1 350	153 \pm 8.6	1.5 \pm 0.35	522 \pm 35.1
40	5	100 000 \pm 6 535	500 \pm 53.1	0.23 \pm 0.07	999 \pm 37.5
75	5	179 000 \pm 12 272	812 \pm 61.8	0.11 \pm 0.04	938 \pm 123.5

EXPERIMENTAL RESULTS

Soon after birth (3-7 days) the rat pancreas consists of individual small and relatively compact clusters of acinar and islet tissue scattered among the well developed connective-tissue of the organ. As growth of the islet and acinar portions of the gland proceeds, the connective-tissue spaces between the clusters becomes smaller. The epithelial cells in individual acini and islets are more loosely arranged than on the first days after birth, they become juicy and they gradually accumulate secretion (Fig. 1).

The weight of the gland increases fairly rapidly from the first days after birth. For example, its weight increases by more than 8 times between the 3rd and 22nd days after birth (Table 1). Later, after the 40th day, the rate of increase in weight of the organ slows down a little. The rapid increase in weight of the pancreas in the first 3 weeks of postnatal ontogenesis is due to the high level of proliferative activity of its cells (Table 1). The level of mitotic activity of the acinar cells is highest on the 3rd day after birth. It stays constant for the next 10-12 days, and then falls sharply until the 3rd week after birth of the animal, so that 40 days after birth the mitotic activity is low. Mitoses are found in cells of the islets of Langerhans also.

TABLE 2. Change in Content of Islet Tissue Relative to Acini in Pancreas of Albino Rats at Various Stages of Postnatal Ontogenesis

Age (in days)	Mean area of section of gland (in μ^2 ; 13 \times)	Mean area of islet tissue per section (in μ^2 ; 130 \times)	Ratio between islet and acinar tissue (in percent)
7	5, 261, 862	86, 506	1.71
14	7, 190, 418	81, 326	1.18
22	6, 976, 184	45, 326	0.73
40	17, 214, 148	68, 376	0.39
75	19, 476, 034	52, 059	0.26

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It may be concluded from the results described above that the period of high mitotic activity of acinar cells in the rat pancreas occupies the first 3-4 weeks after birth. By the 5th-6th week after birth mitotic activity falls sharply. According to data in the literature, subsequent postnatal growth of the pancreas is due to a combination of proliferation and enlargement of the cells. Enlargement is accompanied by an increase in ploidy of the nuclei [3].

The intensity of morphogenetic processes in the pancreas at various stages of postnatal ontogenesis was judged from changes in the ratio between the increase in weight of the organs and the dimensions of its anatomo-physiological units (acini and islets). As Table 1 shows, despite the fact that the weight of the pancreas increased by more than 8 times from the 3rd to the 22nd day after birth of the rats, there was little change in the size of individual acini. In rats aged 3 days, for instance, the mean area of one acinus was $420 \mu^2$, compared with $522 \mu^2$ in rats aged 22 days ($P = 0.07$).

The results show that during this time interval considerable morphogenetic activity was present, i.e., new acini were formed in the gland. The increase in size of the acini was slight.

Still more demonstrative evidence of the formation of new acini in the gland is given by the fact that the relative content of islet tissue falls significantly from the 7th to the 22nd day after birth (Table 2).

Further increase in weight of the pancreas (40th and 75th days after birth) is accompanied by considerable enlargement of individual acini. The mean area of one acinus in rats aged 40 days is almost twice its area in animals aged 22 days (999 and $522 \mu^2$, respectively; Table 1). Between the 40th and 75th days after birth the possibility is not ruled out that a second wave of formation of new acini in the gland may occur, because their dimensions change only a little during this period. Nevertheless, the weight of the organ increases significantly—from 500 to 812 mg.

The relative content of islet tissue continues to fall progressively with an increase in age of the animals (Table 2). It should be remembered, however, that this decrease relative to the content of islet tissue in the organs during growth does not mean that its absolute amount becomes smaller. On the contrary, with age the individual islets of Langerhans grow larger, and at the same time there is the possibility that new islets are formed [15].

The results described above show that postnatal development of the pancreas in albino rats is accompanied by an increase in weight of the organ, considerable mitotic activity of its cells (reaching a maximum in the first 5-6 weeks after birth), and by morphogenetic processes. These morphogenetic processes in the gland (the formation of new acini) are most marked in the first three weeks after birth. The possibility of morphogenetic reactions at later stages of postnatal growth of the organ also is not ruled out, al-

though their intensity is much lower. An increase in size of individual acini is a more characteristic feature of the later stages of postnatal ontogenesis of the rat pancreas (40-75 days after birth).

The ratio of the quantity of islet tissue to the quantity of acinar tissue falls with age.

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