

EXPERIMENTAL BIOLOGY

MORPHOLOGICAL CHANGES IN THE JEJUNUM AND ILEUM OF RATS AFTER WIDE RESECTION OF THE SMALL INTESTINE

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Information in the literature on the subject of the character of the morphological changes taking place in the mucous membrane of the area of the intestine left behind after resection, is controversial. Albu [5], Trzebicky [12], Diliberti-Herbin [7] and Schlatter [10], for instance, completely deny the development of any essential morphological changes in the intestine after resection. Other authors [1, 4, 9, 11] believe that thickening of the mucous membrane, dilatation of the lumen of the bowel and hypertrophy of the villi take place in the portion of the intestine remaining after resection. A third group of workers [6, 8] asserts that in addition to processes of hypertrophy, there is an increase in the number of structural units in the intestine (crypts, villi, lymphoid follicles).

All these investigations suffer from an essential technical fault: the changes in the mucous membrane were not compared with the changes in the length and diameter of the intestine. Nevertheless, without at the same time allowing for the length of the intestine, its diameter and the number of villi per unit area, it is impossible to assess correctly either the degree or the character of the morphological changes, since the thickness of the mucous membrane, the dimensions of the villi and their number per unit area depend on the degree of contraction of the muscular coats.

EXPERIMENTAL METHOD

As experimental animals white rats were used. In this way experiments could be carried out on a large number of animals. Furthermore, the relief of the mucous membrane of the intestine is not so complicated in rats as in other mammals. The experiment was performed on 48 animals with an initial weight of 100-140 g (each group consisted of 8-12 animals). At the end of the experiment the rats weighed 200-300 g. From $\frac{1}{3}$ to $\frac{1}{2}$ of the middle portion of the small intestine was resected from the experimental rats (Table 1).

Animals were killed at various times: 10 days, 1 and 2 months after resection of the intestine. In the first days after operation the weight of the majority of rats fell by 10%. Its restoration was observed by the 7th-10th day. Control rats were killed at the beginning and end of the experiment. The rats underwent operation and were killed at the same time of day, always after starvation for 24 hrs. The following conditions were observed during removal of the intestine for examination. Under ether anesthesia the duodenum was divided from the stomach and the ileum from the large intestine. A cannula was inserted in the proximal end of the intestine, and through it the intestine was perfused with warm physiological saline at a pressure of 25-30 mm of mercury for 2 minutes. At this pressure the intestine is distended to roughly the same extent as by the passage of chyme. The fluid emerges from the ileum in drops. The intestine is washed completely free from food particles. The washing with physiological saline was replaced by perfusion for 5 minutes with Bouin's fluid. At this time the intestine was completely cut away from the mesentery and immersed in fixing solution. After 24 hours the

TABLE 1

Mean Values of the Length, Diameter and Area of the Intestinal Mucosa Before and After Resection of the Intestine

Measurements \ Nature of experiment	Initial control	Final control	Time of operation					
			10 days		1 month		2 months	
			resected portion	residual portion	resected portion	residual portion	resected portion	residual portion
Length of intestine (in cm)	102	129	46	75	35	76	38	83
Circumference of mucous membrane (in cm)	0,85	0,85	0,87	1,31	0,98	1,19	1,02	1,19
Area of mucous membrane (in cm ²)	87	110	40	98	34	90	39	99
Diameter of intestine (in mm)	4,3	4,6	—	5,4	—	5,3	—	5,1

TABLE 2

Average Number of Villi in an Area of 9 mm²

Part of intestine \ Character of the experiment	Initial control	Final control	Time after operation		
			10 days	1 month	2 months
Duodenum	71	38	36	42	48
Middle of the jejunum	103	84	48	71	61
Middle of the ileum	148	133	117	127	97
Distal end of the ileum	212	147	139	153	135

TABLE 3

Mean Thickness of the Crypt-Bearing Layer of the Mucous Membrane in μ , Before and After Resection of the Intestine

Portion of intestine \ Nature of experiment	Initial control	Final control	Time after operation		
			10 days	1 month	2 months
Jejunum	83	81	144	134	109
Ileum	99	83	142	129	132

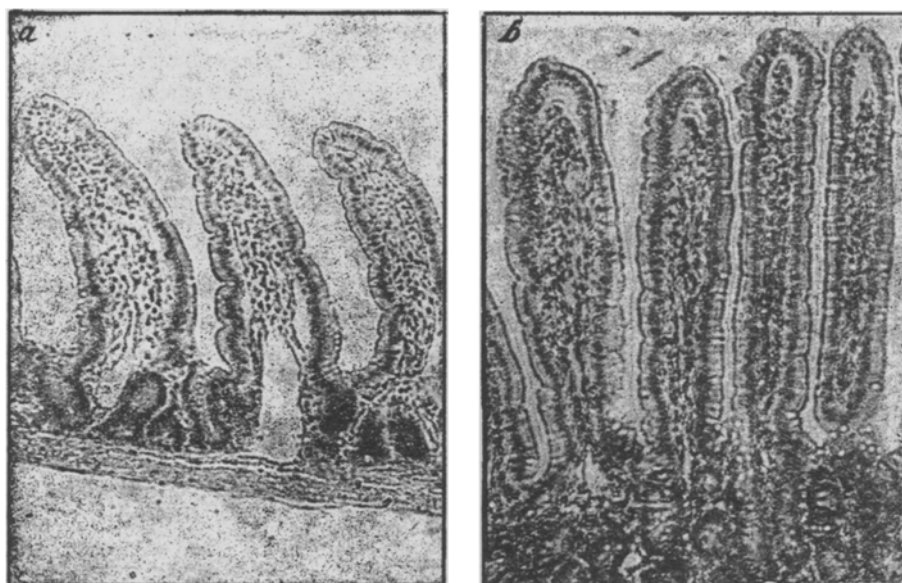
length of the intestine was measured, together with its diameter in 30-40 places (by means of a ruler and millimeter squared paper), the number of lymphoid follicles was counted, and sections were cut for histological examination. The resected area was subjected to the same treatment. Specimens of tissue were taken in the control rats from the middle of the jejunum and ileum, and in experimental animals 5-7 cm proximally and distally to the point of anastomosis. Transverse and longitudinal histological sections were cut to a thickness of 7 μ , and stained with hematoxylin-eosin. The circumference of the mucous membrane was measured at its junction with the submucosal layer in the jejunum and ileum, and the average deduced.

The length and width of the villi were measured (in their middle part), and the number of cells counted in the epithelial layer of the middle part of the villi throughout the diameter of one field of vision with magnification of $10 \times 60 \times 1,5$. By means of a binocular loupe the number of villi was counted in an area of 9 mm² of the

TABLE 4

Mean Length and Width of the Villi in μ Before and After Resection of the Intestine

Portion of the intestine \ Nature of the experiment	Measure-ment	Initial control	Final control	Time after operation		
				10 days	1 month	2 months
Jejunum	Length	250	250	340	350	300
Ileum		190	200	320	300	280
Jejunum	Width	90	90	100	80	100
Ileum		90	90	90	100	100



The mucous membrane of the intestine in the same rat.

a) From the resected portion at the moment of operation; b) From the residual portion of the intestine 1 month after operation. Hypertrophy of the villi can be seen. Stained with hematoxylin-eosin. Magnification: ocular 5 \times , objective 12 \times .

TABLE 5

Mean Number of Cells per Unit Length of the Epithelial Layer of the Middle Portion of the Villi Before and After Resection of the Intestine

Portion of the intestine \ Nature of the experiment	Initial control	Final control	Time after operation		
			10 days	1 month	2 months
Jejunum	34,3	33,6	31,2	31,5	31,2
Ileum	32,5	33,0	32,7	32,1	30,5

duodenum, the middle portion of the jejunum, the middle portion and end of the ileum in the fixed intestine.

EXPERIMENTAL RESULTS

The mean values of the length and area of the intestinal mucous membrane given in Table 1 show that in control (unoperated) rats the length of the intestine was increased by 27 cm in 2 months, whereas its diameter and the circumference of the mucous membrane was hardly changed. The degree of lengthening was 26%. The area of the mucous membrane of the intestine, relating to the crypt-bearing layer, was increased during this period by 23 cm².

After resection the length of the residual portion of intestine altered a little. The degree of its increase was 29%, i.e. the same as in the control rats. The area of the mucous membrane of the residual portion of the intestine almost reached that of the mucous membrane of the control rats only 10 days after operation, and remained for 2 months at roughly the same size as in the control rats of the same age. This was mainly due to an increase in the circumference of the mucosa of the residual portion of intestine: both jejunum and ileum. As may be seen from Table 1, after resection the diameter of the intestine also increased considerably. Many authors [4, 6, 8, 11] have pointed out an increase in the diameter of the residual part of the intestine, when describing the morphological changes after resection. We did not, however, confirm the findings of Monari [8] that there was a shortening of the residual intestine after resection.

Counting of the number of villi (Table 2) in total preparations of the fixed intestine showed that their number in a certain area of the duodenum and the terminal ileum at all stages after operation differed only slightly from their number in the final control rats.

There was a small increase in the number of villi per unit area in the middle portion of the jejunum and ileum. This took place due to the fact that there was either an increase in the number of foliaceous villi or an increase in the degree of their extensibility in a transverse direction. The same change was observed in the final control rats compared with the initial control.

The area of the intestinal mucosa had increased by 28 cm² 10 days after the operation (this group was compared with the final control rats at the moment of operation and after being killed), and by 51 cm² 2 months afterwards. At the same time the number of villi per unit area was only very slightly altered. From this it could be assumed that after resection of the intestine the total number of villi was increased.

Further analysis of the experimental results showed that the structural reorganization took the form not only of an increase in the area of the intestinal mucosa and the number of villi, but also of changes in the thickness of the crypt-bearing layer and in the length of the villi. In Table 3 are given the mean values of the thickness of the crypt-bearing layer of the mucous membrane, and in Table 4 — the length and width of the villi.

As is evident from Table 3, the thickness of the crypt-bearing layer of the mucous membrane in the initial and final control rats was roughly equal. By the 10th day after operation it had increased almost twofold. Two months after operation the thickness of the crypt-bearing layer in the jejunum diminished, although its value was higher than that of the control animals. Thickening of the crypt-bearing layer was noted in both the jejunum and ileum.

It can be seen from Table 4 that the dimensions of the villi in the initial and final control rats were the same; the length of the villi in the jejunum was 25% greater than in the ileum. After resection of the intestine the length of the villi increased considerably, whereas their width did not perceptibly alter. The villi of different portions of the intestine were close to each other in size.

By way of illustration we show microphotographs of sections through the intestine of one of the rats (see Figure).

Counting the number of cells per uniform area of the epithelial layer of the villi showed that their number was unchanged after resection of the intestine, i.e. the hypertrophy of the villi and the increase in their number takes place at the expense of hyperplasia of the cells (Table 5).

In this investigation we were unable to confirm Monari's findings of an increase in the number of lymphatic follicles after resection of the intestine. The number of lymphatic follicles in the experimental rats was less than in the controls. If in the experimental groups, the number of lymphatic follicles in the resected portion of

the intestine was added to the number of lymphatic follicles in the residual area, then the values observed in the experimental and control rats differed little from each other (variation between 16 and 19).

It has been demonstrated by much experimental and clinical data that the removal of considerable areas of the small intestine is possible without harmful consequences for the body. This shows that "processes of regulation" (M. A. Vorontsova and L. D. Liozner [2]) take place in the intestine after resection, dispelling the consequences of the operation.

Until the present time the processes taking place in the intestine after resection have been regarded by all authors, including Monari [8] and Bornstein [6], as compensatory. The abundant experimental evidence of regeneration of the internal organs, together with modern theoretical considerations, compel us to re-examine this problem. It is now accepted that phenomena of regeneration may be displayed not only on the wounded surface, but in the residual portion of an organ. Under these circumstances we are concerned not only with hypertrophy, but also with the formation of new structural units within the organ. L. D. Liozner [3] suggested the name endomorphosis for this type of regenerative process, which is particularly observed in regenerative hypertrophy. These new ideas and the experimental findings of ours, in rats, suggest that the proliferative processes developing in the residual portion of the intestine after resection may be reparative processes of the endomorphosis type, taking the form of hypertrophy of the villi and an increase in their number. The investigation of the processes of repair in the intestine are even more interesting because after resection of a portion of the intestine there is no wounded surface.

SUMMARY

One third to one half of the medial portion of the small intestine was resected in white rats. The length of the remaining intestinal portion remained unchanged, but its diameter increased. The area of the intestinal mucous membrane of the operated rats in 10 days after the resection reached that of control rats. The structural reconstruction after the resection consisted in the hypertrophy of the villi and their increased number. These changes occurred in the jejunum and ileum and were retained for 2 months after the operation.

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