

SECRETION OF INTESTINAL ENZYMES BY ISOLATED INTESTINAL SEGMENTS AT DIFFERENT INTERVALS AFTER "DENERVATION"

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Much work has been done on the effect on intestinal secretion of severing various nerve trunks [1, 5, 6, 8, 16, 18]. There are indications [15] that the paralytic secretion found after severing nervous connections with the intestine takes place during their degeneration. Paralytic secretion ceases between the 3rd and the 4th week after section of the nerves, and this coincides with the time required for the growth of new nerves, together with the blood vessels.

Most of the authors who have studied paralytic secretion have taken into consideration only the fluid part of the intestinal secretion, with its dissolved enzymes, but have not paid sufficient attention to the solid fraction of the secretion. Very few papers have appeared dealing with the intestinal secretion as a whole.

The papers published from the Institute of Nutrition of the Academy of Medical Sciences, USSR, of recent years [9, 10, 13] have shown the necessity, in studying the enzyme-secreting function of the intestine, of including in the survey the solid fraction of the secretion, with its contained enzymes.

Observation of "denervated" intestinal segments has usually been conducted over a relatively short period of time after "denervation," and the effect of new ingrowth of nerves has not been considered.

There are indications [4, 2] of partial restoration of function of "denervated" organs during ingrowth into them of nerves derived from other systems. It may hence be expected that the ingrowth of nerves into "denervated" intestinal segments should have some effect on their functioning.

We have in this research attempted to ascertain the effect of "denervation" of isolated intestinal segments on the secretion of enzymes, in both the fluid and the solid fractions of the secretion, and to follow the changes in secretory function of the isolated segment over greater periods of time after "denervation." The term "denervation" is written in quotation marks because the intramural nervous system of the isolated intestinal segment remains intact.

EXPERIMENTAL METHODS

The experiments were performed on 12 dogs, each of which had two isolated intestinal segments, formed from neighboring parts of the intestine. One of these was isolated by the Thiry procedure, and the other was "denervated" in two ways: in 6 dogs the segment of intestine was implanted under the skin of the abdomen, and 1-5 months later we severed its neurovascular bundle intraabdominally. The other way, practiced on 6 dogs, consisted of cutting all visible branches of the mesenteric nerves, and painting the vessels with 5% phenol solution, leaving the isolated segment within the peritoneal cavity, with the blind end, similarly to the Thiry preparation, fixed to the lesser omentum, so as to put them in a convenient position for the collection of secretion. In 8 dogs the isolated segments were from the upper regions of the intestine, and in 4 dogs from the lower ones. The secretion from the isolated segments was collected over 5-hour periods from dogs which had been fasted for 18 hours. During the first 2 months after "denervation" the experiments were performed 2-3 times a week, after which they were repeated in series of 6-8 every 3-6 months.

We recorded the amount of the solid and fluid fractions of the secretion, after which it was homogenized, and, using the quantitative methods applied in our other researches, we determined its content of enterokinase [14, 7], alkaline phosphatase [12], invertase, peptidase, and lipase [10]; The enzyme contents were calculated per g of solid content of the juice, and the amount of enzymes secreted per hour was also calculated.

We observed an abrupt change in the secretory function immediately after transection of the neurovascular bundle supplying the transplanted segment of intestine; paralytic secretion began. The amount of secretion produced in unit time (Figure 1) rose markedly, reaching a maximum on the 5-7th day, and there was a considerable admixture of blood. The amount of secretion then fell abruptly, to a value lower than the initial one, and it was no longer tinged with blood. The amount of solid fraction of the secretion also rose during the phase of paralytic secretion, and then fell abruptly, in the same way as the liquid phase.

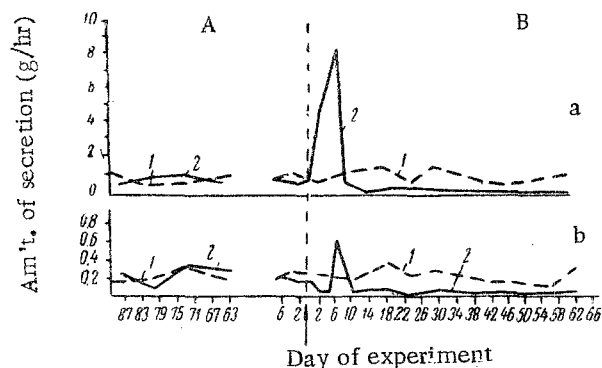


Fig. 1. Amount of secretion produced by isolated intestinal segments. A) Before severing the neurovascular bundle; B) after severing it; a) total amount of secretion; b) amount of solid fraction of secretion; 1) Thiry preparation; 2) transplanted segment. The arrow indicates when the neurovascular bundle supplying the abdominal transplant was cut.

Secretion of all the enzymes fell very considerably during the phase of paralytic secretion (Figure 2). The content of some of the enzymes fell almost to zero immediately after "denervation;" thus, enterokinase could not be detected on the 2nd and 3rd days, either in the homogenate or in the solid secretion. The content of

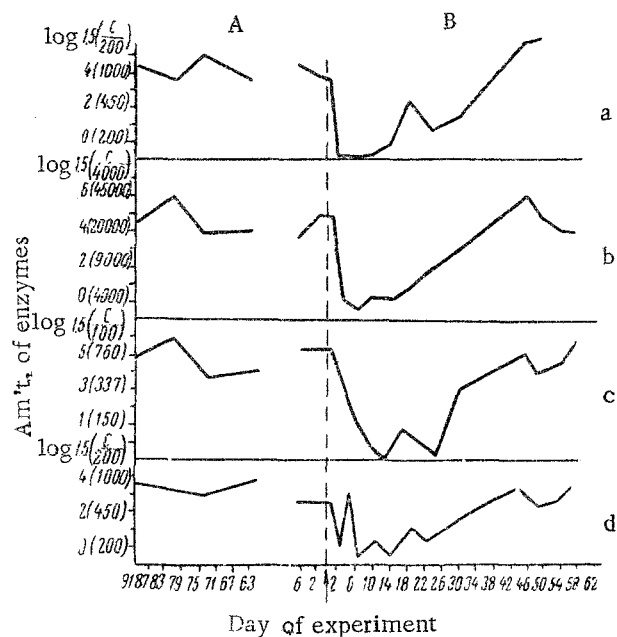


Fig. 2. Content of enzymes in the solid fraction of the secretion from a transplanted segment of intestine. A) Before severing the neurovascular bundle; B) after severing it; a) enterokinase; b) phosphatase; c) invertase; d) peptidase. The arrow indicates when the neurovascular bundle supplying the abdominal transplant was cut. The graduations on the ordinate axis refer to logarithmic values; the enzyme concentrations are given in parentheses (C), i.e., as the number of arbitrary units of activity in 1 g of the solid content of the secretion.

other enzymes (peptidase, invertase, lipase) began to fall 2-3 days after "denervation," and their total absence from the secretion was not observed for all the dogs. The enzyme content of the secretion began to rise again after 8-10 days, and had attained the initial levels after 1-2 months.

Transection of the neurovascular bundle of a transplanted segment had no perceptible effect on the amount and enzyme content of the secretion from the Thiry preparation. Nor was there any appreciable difference in the general condition of the animal.

Similar effects were found for intestinal segments "denervated" by the second method.

With either of the "denervation" techniques, paralytic secretion was associated with an abrupt fall in the concentration of the enzymes, as well as in the absolute amount secreted in unit time, notwithstanding the marked increase in the volume of secretion. The amount of enzymes secreted rose gradually with time, but remained considerably lower than from the Thiry preparation [11].

The differences between the secretion from isolated intestinal segments "denervated" in different ways persisted as time went on. The subcutaneous transplant secreted considerably less liquid and solid secretion a month after transection of the neurovascular bundle than before this operation. At still greater intervals of time (observations were continued on 4 dogs for over 3 years), the amount of secretion produced fluctuated slightly, but remained at a general low level, with even a certain tendency to fall still lower (Table 1).

TABLE 1

Amount of Secretion Produced from a Thiry Isolated Intestinal Segment and from a Transplanted Segment of the Upper Part of the Jejunum of Dog No. 1.
Mean Values in g for 5 Hours

When experiments performed	Thiry intestinal segment		Transplanted segment	
	fluid part	solid part	fluid part	solid part
Before "denervation"	5.50	1.32	1.32	0.81
Time after "denervation"				
1 month	5.03	1.16	0.18	0.21
1 year	1.90	1.90	0.22	0.22
1 1/2 years	2.68	1.02	0.17	0.36
2 years 5 months	1.28	1.08	0.11	0.24
2 years 8 months	2.59	0.91	0.09	0.19
2 years 11 months	1.31	0.89	—	—
3 years 3 months	1.64	1.36	0.11	0.16

The more long-term changes in secretion from segments "denervated" by transection of mesenteric nerves, followed by painting the vessels with phenol, proceeded rather differently, at 1-2 months after "denervation" (Table 2). Paralytic secretion had disappeared by the end of the month, but the amount of secretion continued to diminish, falling to a minimum at the end of the second month. It then began to rise slightly, both for the fluid and the solid fractions, but did not reach the same levels as for the Thiry segments, and continued at a low level.

The enzyme content of the secretion from intestinal segments "denervated" by both methods remained about the same, for 1-2 months, as before "denervation," or as from Thiry segments. The concentration of the enzymes remained at the same level over the remainder of the period of observation (Table 3).

The lower enterokinase content of the secretion from "denervated" segments is due to these having been formed from lower levels of the jejunum than were the Thiry segments.

Enzyme secretion over 1½-2 months varied parallel with the variations in the amount of secretion produced, or, more closely, with the amount of the solid fraction. It was very low after "denervation," particularly from the transplanted segment, over the whole of the period of observation.

TABLE 2

Amount of Secretion Produced by a Thiry Segment and by a Segment of the Upper Jejunum Denervated by Transection of the Mesenteric Nerves, in Dog No. 2.

Mean values in g for 5 hours

Time after operation	Thiry segment		"Denervated" segment	
	fluid part	solid part	fluid part	solid part
1 month	2.38	0.86	0.29	0.80
2 months	1.52	1.12	0.02	0.13
1 year	1.33	0.84	0.24	0.39
1 year 4 months	1.32	0.71	0.15	0.40
1 year 11 months	1.54	0.73	0.18	0.46

The secretion of the solid part of the juice produced by Thiry segments (Tables 1, 2, and 3), and of the enzymes contained therein, settled down to a steady level over the whole of the period of observation, after recovery from the operational trauma (10-14 days). Secretion of fluid juice was fairly high for some time (up to 6 months for some dogs), then fell by 1½ to 2 times this level, and varied very little thereafter, over a few years.

TABLE 3

Secretion of Enzymes by Isolated Thiry Transplanted Segments of the Upper Jejunum of Dog No. 3.

Mean values in arbitrary units

When experiments performed	Entero-kinase	Phos-phatase	In-vertase	Pepti-dase	Lipase
	Thiry segment				

Content of enzymes in one g of solid fraction of secretion

Before "denervation" of the trans-planted segment	4 280	38 000	700	637	173
3 weeks "after denervation"	4 500	29 900	590	572	170
After 7 months	2 940	30 450	451	457	114
After 2 years 7 months	—	41 000	796	386	161

Amount of enzymes secreted per hour

Before "denervation" of the trans-planted segment	855	7 770	161	131	34
3 weeks "after denervation"	620	5 640	111	103	32
After 7 months	1 060	7 700	108	117	28
After 2 years 7 months	—	6 800	143	69	30

TABLE 3 (continued)

When experiments performed	Entero- kinase	Phos- phatase	In- vertase	Pepti- dase	Lipase
Content of enzymes in one g of solid fraction of secretion					
Before "denervation"	1 100	24 960	723	604	162
3 weeks "after denervation"	1 000	22 900	375	435	73
After 7 months	2 000	27 600	674	752	292
After 2 years 7 months	1 680	—	375	590	166
Amount of enzymes secreted per hour					
Before "denervation"	301	6 080	181	185	33
After "denervation"	20	463	3	10	2
After 3 weeks*					
After 7 months	60	805	16	26	8
After 2 years 7 months	39	—	18	24	10

* Numbers omitted on original page.

Five dogs were killed 1-1½ years after formation of "denervated" segments, and the mucous membrane was examined histologically, and for the presence of enzymes.*

We could find no differences between the contents of intestinal enzymes of the mucous membranes of the Thiry preparations and of the "denervated" segments (by both methods), and of those of sections of intestine anatomically resembling the segments (Table 4).

TABLE 4

Enzyme Content of 1 g of Mucous Membrane from the Intestine and from Isolated Intestinal Segments (Arbitrary Units) Dog. No. 4

Part of intestine studied	Entero- kinase	Phos- phatase	Invertase
Above the level from which isolated segments formed	450	15 000	470
Thiry segment	500	23 000	620
Segment "denervated" by transection of the mesenteric nerves and painting the vessels with phenol	500	30 000	500
Below the level from which isolated segments formed	300	30 000	570

The transplanted segment was macroscopically markedly atrophied, its length and diameter having been reduced to about half the initial sizes. Microscopic examination showed well-marked degenerative changes in the mucous membranes and in the intramural nervous plexi.

In contrast to this, the segments "denervated" by transection of the mesenteric nerves, and left in the abdominal cavity, were macroscopically unchanged, and the histological signs of degeneration were much less pronounced. We found nerve fibers in the mesentery, distal to the transection, which were histologically of normal structure, and which were apparently functional. This indicates that nervous connections with the central nervous system were reestablished in the "denervated" segment of intestine.

* The morphological studies were conducted by N. A. Nilova, S. I. Matveeva, and E. A. Rudik.

Our results show that the enzyme-secreting function of the intestine is profoundly affected by severing connections with the central nervous system. Production of enzymes is greatly depressed during the phase of paralytic secretion. It seems probable that termination of paralytic secretion is connected with ingrowth of new nerves into the intestinal segment. This is in complete accord with the known rate of growth of regenerating nerves, of about $1\frac{1}{2}$ mm per diem [3], and with the time taken for the enzyme content of the secretion to revert to its initial level (1-1 $\frac{1}{2}$ months).

The degree of restoration of the secretory function of the intestine, and the extent of the degenerative processes observed in "denervated" segments are connected with the nature of the newly ingrowing nerve fibers.

At considerable times after "denervation," when the ingrowing nerves come from the subcutaneous tissues, the mucous membranes of the intestinal segment regain the ability of secreting enzymes in concentrations usual for the intestine, but in only very small amount. A somewhat fuller degree of recovery of the secretory function of "denervated" segments is seen when the ingrowing nerve fibers come from the abdominal organs. The secretion produced by such segments has approximately the same concentration of enzymes as that from segments newly innervated from subcutaneous tissue, although the amount secreted is somewhat greater, but is still much less than from segments with intact nervous connections.

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* In Russian.