PROLIFERATION AND MIGRATION OF EPITHELIAL CELLS OF THE SMALL INTESTINE IN RATS INFECTED WITH *Salmonella typhimurium*

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Injection of thymidine-H^3 into male albino rats showed that after infection of the animals with *Salmonella typhimurium* the proliferative activity of the crypt epithelium was increased in both the jejunum and ileum, in the latter mainly on account of an absolute increase in the number of crypt cells. The rate of migration of enterocytes both from the zones of proliferation in the crypts to the villi and in the villi themselves also was increased.

Histological investigations of biopsy material from patients with enterocolitis of varied etiology have revealed an increase in the depth of the crypts of the small intestine and an increase in the mitotic index in these structures [9]. The increased mitotic index is not always evidence only of an increase in the number of proliferating cells, but it may be connected with changes in the duration of mitosis itself [1, 7]; in addition, a single determination of the number of mitoses gives no idea of the migration of the epithelial cells of the small intestine.

Bearing in mind that the infectious factor [2, 8] plays an important role in the etiology of enteritis and colitis, it is interesting to study the effect of infection on the proliferation and migration of the intestinal epithelium, and the investigation described below was carried out for this purpose.

EXPERIMENTAL METHOD

Experiments were carried out on 42 male rats weighing 120-140 g. Infection was produced by Val'dman's method [3]: a suspension of a 24-hour culture of *S. typhimurium* was introduced into the duodenum of 22 of the animals. On the 5th day after infection thydimide-H^3 was injected intraperitoneally into the infected and control animals at between 9 and 9.10 a.m. in a dose of 0.5 μCi/g body weight (Soviet thymidine with specific activity of 9.3 μCi/ml). The experimental and control animals were sacrificed at the same times between 30 min and 96 h after injection of the isotope. Pieces of the jejunum and ileum were fixed in Carnoy's fluid. Paraffin sections (4-5 μ) were coated with type M (State Photographic Chemical Research Project, USSR) emulsion. After exposure for 21 days the preparations were treated in the usual way [4, 5] and stained with Carazzi's hematoxylin. The index of labeled nuclei (ILN) was determined by counting the labeled nuclei in 1000-1500 cells of the longitudinally divided crypts and villi. The number of crypt cells was determined as the product of the number of cells in a column of the crypt (longitudinal sections through the crypts) and the number of cells in the crypt in transverse sections [6, 10].

EXPERIMENTAL RESULTS

Calculation of ILN in the jejunum and ileum of the same control animals showed that the level of proliferation in the ileum was somewhat higher than in the jejunum (after 30 min ILN for the jejunum was

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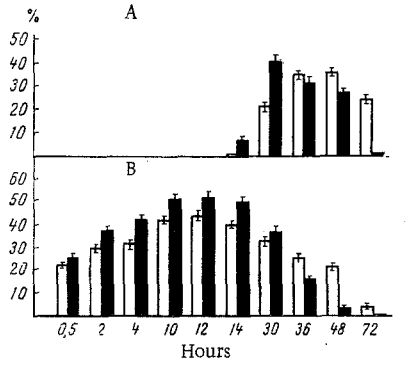

Fig. 1

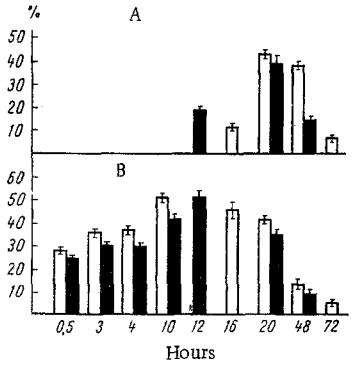

Fig. 2

Fig. 1. Index of labeled nuclei for epithelium of the jejunum in S. typhimurium infection. A) epithelium of villi; B) epithelium of crypts. Unshaded columns – control; shaded columns – infection. Abscissa, time after injection of thymidine-H^3 (in h); ordinate, percentage of labeled nuclei.

Fig. 2. Index of labeled nuclei for epithelium of ileum in S. typhimurium infection. Legend as in Fig. 1.

TABLE 1. Cell Population of Crypts of Small Intestine

	Number of cells in crypt			
	jejunum		ileum	
	control	experiment	control	experiment
In longitudinal section (A)	33,0±0,6	35,2±1,1	33,2±0,5	44,9±2,4
In transverse section (B)	22,0±0,8	22,1±0,6	21,3±0,4	20,5±0,4
Total number of cells (A × B) . . .	726,00	777,92	707,16	920,45

20.89 ± 0.83%, and for the ileum 28.43 ± 0.95%), and this was accompanied by a higher rate of migration of the cells in the ileum (Figs. 1 and 2).

The number of proliferating crypt cells was increased in the jejunum of the experimental rats at all times of the investigation. An earlier migration of cells with labeled nuclei was observed from the zone of proliferation in the crypts to the villi (14 h after injection of thymidine-H^3 in the experimental animals and 16 h after its injection in the control). Labeled cells also disappeared considerably earlier from the cells with villi; after 72 h, for instance, ILN for the villi of the control animals was 25.12 ± 1.34%, while in the experimental animals only solitary cells remained with labeled nuclei on the villi.

The calculation of the number of crypt cells showed a very small increase in the experimental animals (Table 1). ILN for the ileum of the control animals was slightly higher than ILN for the crypt of the experimental animals (Table 1), although cells with labeled nuclei also departed sooner from the villi. For instance, 48 h after injection of thymidine-H^3, 23.40 ± 2.20% of labeled cells still remained on the villi of the control animals, compared with 15.5 ± 1.50% in the infected animals. Only solitary cells with labeled nuclei remained after 72 h in the experimental series, whereas in the control series 7.40 ± 1.10% of these cells remained.

In the ileum the number of crypt cells showed a considerable increase, due to a significant increase in length of the crypts. Comparison of the values of ILN with the calculated number of crypt cells shows that only a relative increase had occurred in the number of proliferating crypt cells in the ileum. In the control, for instance, ILN of the crypts of the ileum was 28.43 ± 0.95% (30 min after injection of thymidine); i.e., presumably 198 of the 707 crypt cells were labeled (Table 1), whereas in the experimental animals ILN was 24.77 ± 0.92%; i.e., 230 of the 920 crypt cells (Table 1) had incorporated thymidine-H^3 into their nuclei, showing an increase in the absolute number of proliferating crypt cells.

Infection thus causes an increase in the proliferative activity of the intestinal epithelium which is more marked in the jejunum. A marked increase in the rate of migration of cells from the crypts to the

villus and an increase in the rate of migration of enterocytes along the villi, followed by their desquamation, also are observed.

The increase in proliferative activity in the jejunum took place chiefly on account of an increase in the number of proliferating cells without any increase in their total number, whereas in the ileum the population as a whole was increased.

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