MORPHOLOGY AND FUNCTION OF THE CECUM IN EXPERIMENTAL ESCHERICHIOSIS

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The study of morphologic changes in different parts of the intestine in escherichiosis still remains an urgent problem, partly because of the wide distribution of this disease and partly because some aspects of the pathogenesis and local immune reactions require further investigation. In experimental escherichiosis the morphological changes in the small intestine have been described in sufficient detail, but the situation is less satisfactory with regard to the large intestine [2, 5, 7]. This applies in particular to the cecum, in which the writers previously demonstrated a high concentration of immunocompetent tissue, located mainly in its distal part [6, 8]. The cecum and, in particular, its vermiform appendix, also are known to play an important biological role as an immunocompetent organ of the digestive system. We have studied morphological and functional changes in the distal part of the cecum in experimental escherichiosis.

EXPERIMENTAL METHOD

Experimental escherichiosis was produced by the method described previously [1]. Mice receiving physiological saline perorally served as the control. Pieces of the distal part of the cecum were removed 15 and 30 min, and 1, 3, 6, 8, 14, and 24 h, and also 1 and 2 weeks after infection. The material was fixed in a 1% solution of acetic acid in ethanol or in a 10% solution of neutral formalin and embedded in paraffin wax. Paraffin sections were stained with hematoxylin and eosin, by the methods of Brachet and Grimelius, and with toluidine blue; the PAS reaction was carried out. To detect immunoglobulin-containing cells, an immunoenzymic method was used [3]. The relative percentage of interepithelial lymphocytes (IEL), the total density of cellular infiltration (TDCI) in the lamina propria of the mucous membrane, and the number of plasma cells (PC), of immunoglobulin-containing cells (IGCC), and endocrine cells (EC) per unit area was determined by a morphometric method. The mast cell (MC) population was characterized by a complex morphometric approach [4]. The results were analyzed by Student's test. Ultrathin sections were examined in the JEM-100B electron microscope (Japan).

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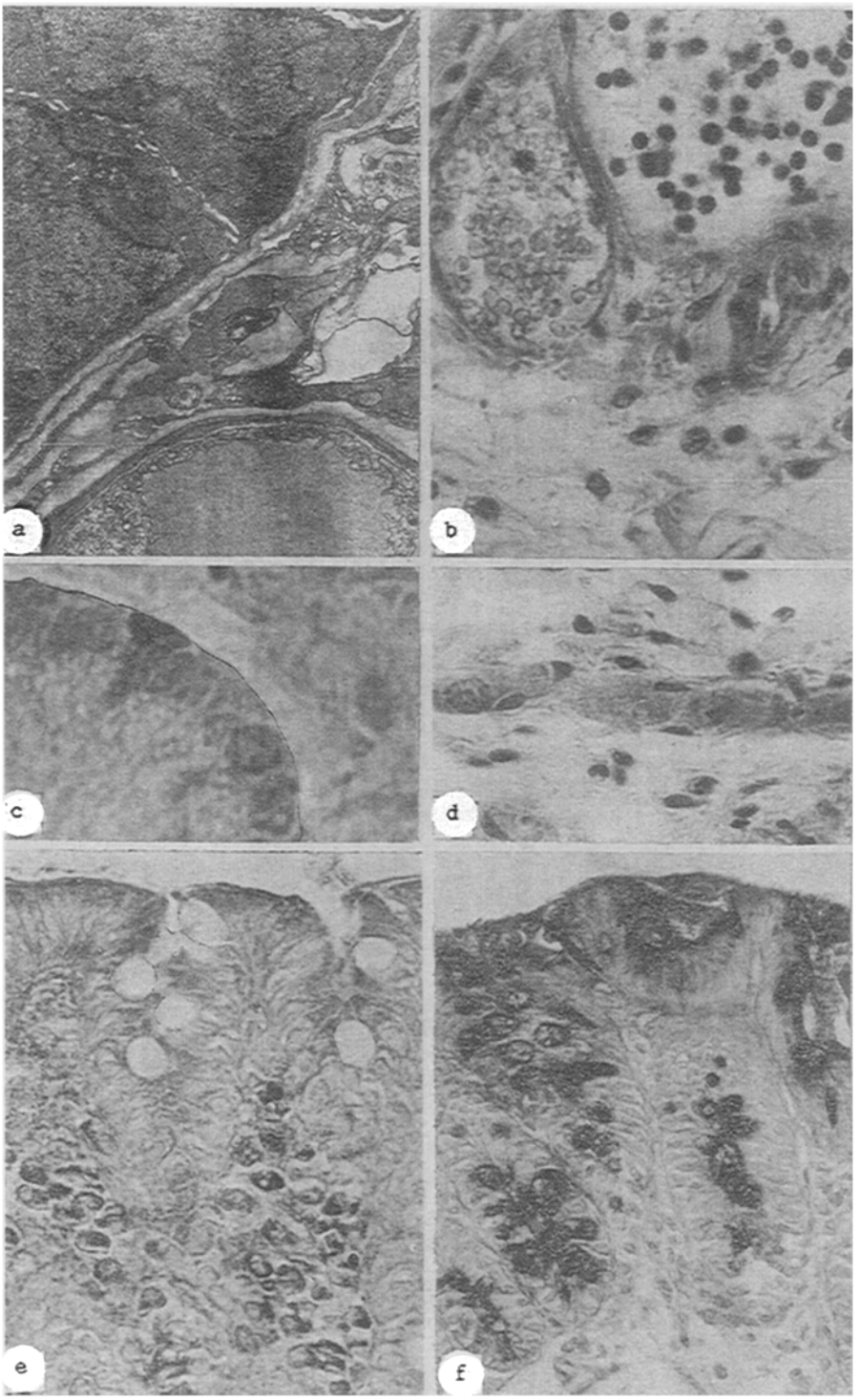

Fig. 1. Morphologic and functional changes in wall of cecum in experimental escherichiosis at different times after infection: a) moderate widening of intercellular spaces of epitheliocytes, 30 min after infection. 10,000×; b) dilatation of blood vessels and lymphatics, 1 h after infection. Hematoxylin and eosin. 130×, c) endocrine cell in crypt of cecum, 1 h after infection. Grimelius' stain. 130×; d) Dystrophy with karyolysis and plasmolysis of individual ganglion cells of intermuscular nervous plexus, 6 h after infection. Hematoxylin-eosin. 130×; e) immunoglobulin-containing cells of lamina propria of mucous membrane, 14 h after infection. Immunoperoxidase method. 120×; f) increase in mucus formation on surface of mucosa, 24 h after infection. Stained with Schiff reagent. 100×.

TABLE 1. Morphometric Parameters of Cells and Tissues of Distal Part of Cecum in Experimental Escherichiosis (M ± m)

Cells, etc	Control	Periods of infection					
		1 h	6 h	14 h	1 day	1 week	2 weeks
TDCI	13142±424	18067±1103***	14949±427***	17545±890***	18632±631***	18403±566**	16848±253**
PC	6022±778	7134±218	8180±297*	8135±403	8815±492**	10868±460***	9271±513**
IGCC	2022±770	2106±215	3049±112*	5851±316***	6176±506	7067±433**	5378±278***
EC	28±5	17±3	15±3	14±2**	11±2***	19±4	22±2
MC	50,5±3,4	45,8±5,1	55,2±3,4	38,8±6,9	36,5±7,7	38,8±3,1	37,3±5,9
IEL	2,64±0,5	3,2±0	2,7±0,06*	2,96±0,03*	3,86±0,4	3,1±0,15	2,6±0,1*
GC	12,9±3,2	16,8±10,3	16,7±2,5	23,2±5,3	22,6±3,4	20,5±4,1	17,4±6,5

Legend. GC) Goblet cells, *$p < 0.05$ compared with previous period, **$p < 0.05$ compared with control, ***$p < 0.05$ compared with control and previous period.

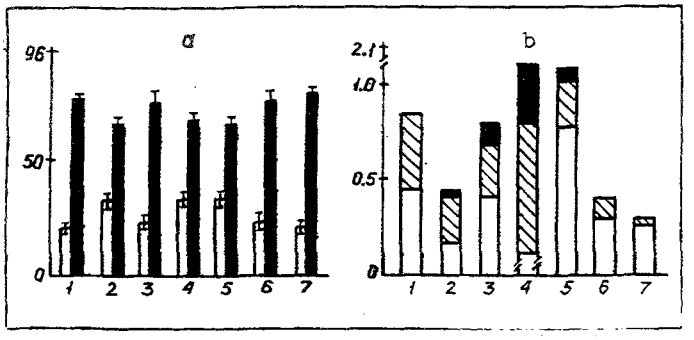

Fig. 2. Morphometric criteria of state of mast cell population of cecum in experimental escherichiosis: 1) control animals; 2) 1 h, 3) 6 h, 4) 14 h, 5) 24 h, 6) 1 week, 7) 2 weeks after infection; a) relative frequency of dark (black columns) and pale (unshaded columns) cells; b) degranulation index and relative frequency of its forms; unshaded part of columns represents mild form of degranulation, obliquely shaded – moderate, black – strong degranulation.

EXPERIMENTAL RESULTS

During the first hour after infection mainly ultrastructural changes were found in the epithelial cells (Fig. 1a). In the very earliest stages (15 min–1 h) the changes mainly affected the microvilli, the terminal zone, and the cytoplasm of the brush-border epitheliocytes; slight widening of the intercellular spaces was observed, and was more marked in the basal part of the cells. Even at this early stage edema, dilatation of blood vessels and lymphatics (Fig. 1b), and infiltration of the lamina propria of the mucous membrane (LPMM) had developed (Table 1). LPMM was infiltrated mainly by lymphocytes and plasma cells, with a few macrophages and polymorphonuclear leukocytes; 30% of the plasma cells were IGCC, but their number at this period of infection was only a little higher than in the control. The study of the mast cell population revealed the following changes: the number of cells with moderately severe and severe forms of degranulation was increased, whereas the degranulation index and the heparin saturation index were reduced (Fig. 2). The number of EC was slightly reduced, and besides cells packed with granules there were many degranulated cells (Fig. 1c).

Edema and stasis of erythrocytes were still present 3-6 h after infection. Dystrophic changes, vacuolation of the cytoplasm and, in some cases, karyolysis and plasmolysis of individual ganglion cells were observed in cells of the nervous plexuses (Fig. 1d). The total density of cellular infiltration was considerably reduced, but the number of PC and IGCC showed a significant increase compared with the previous time ($p < 0.05$). The MC population as before was dominated by degranulated forms with a relative increase in the number of strongly and mildly degranulated forms among them.

Between 8 and 14 h after infection a further increase in the density of cellular infiltration of LPMM was noteworthy, but the increase was due entirely to IGCC (71.9 ± 11.9%; Fig. 1e) compared with 33.6 ± 9.3% in the control. The number of EC at this time was significantly less than in the control ($p < 0.05$). It must also be pointed out that the degranulation index of MC was maximal at this time, mainly on account of cells with moderately severe and severe forms of degranulation.

Between 18 and 24 h, although no statistically significant changes took place in TDCI and of LPMM, the number of PC in it was greater than in the control. IGCC accounted for 70.1 ± 15.3% of them. Abundant mucus formation also was observed on the surface of the mucosa, where it gave a bright PAS-positive reaction (Fig. 1f). The MC degranulation index was reduced, and 92.0 ± 9.0% of the degranulated forms were cells with moderately strong and weak forms of degranulation.

During the next 2 weeks after infection slight edema in the submucosa still remained. The blood vessels were moderately dilated and congested. The total density of cellular infiltration of LPMM was reduced and did not differ significantly from the control. The increased number of PC and IGCC was replaced toward the end of the 2nd week by a very small decrease. Meanwhile the number of EC increased toward the end of the 2nd week. The MC degranulation index was minimal toward the 2nd week compared with other times of infection, and cells with moderate and weak forms of degranulation accounted for 100% of all degranulated cells. At the same period an increase in the number of IEL and PC continued to be observed.

The pathological process developing in the cecum is thus characterized, even in the earliest stages of experimental escherichiosis, by a distinct inflammatory reaction affecting its distal part, and comprising a combination of morphological changes. With the range of pathomorphologic and cytochemical reactions studied it was possible to establish the immune trend of the pathological process in the distal part of the cecum in experimental escherichiosis. The possible role of the distal part of the cecum as a source of B cells or as an organ for their maturation is confirmed by the presence of immunoglobulin-containing and plasma cells, and the fact is becoming increasingly evident that this part of the intestine is part of the APUD-system of the body, influencing the complex system of self-regulatory mechanisms of immunity.

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