MORPHOLOGICAL PECULIARITY OF EXPERIMENTAL DYSENTERIC INFECTION IN CATS IN RELATIONSHIP TO THE DOSE AND THE NUMBER OF MICROBIAL CELLS ADMINISTERED

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Previous investigations [1, 2] have shown that repeated administration of very small doses of microbes may cause dysenteric infections in cats. It was assumed that fractional administration of culture material leads to a cumulative intoxication which causes pathological changes in the intestine, which, in turn, permit the dysentery organisms to penetrate into the intestinal wall and to establish infectious processes.

In order to establish the significance of cumulative toxic-invective irritations in the production of dysenteric infection in cats, we have undertaken to find the minimal dose of culture material, the introduction of which in fractional doses would cause disease in cats, while the introduction of the total number of the microbial cells in a single dose would not have results.

The present investigation was undertaken with a view to elucidate the peculiarities of pathomorphological changes in the intestine and in intra- and extramural nerve centers of experimental animals in relationship to the dose and the number of the microbial cells administered.

METHODS

Pathomorphological investigations were conducted on 39 cats, in 3 series of experiments. Each series of experiments consisted of 2 groups. Animals in one group received the infective dose in a single administration, and in the other the same number of microbes in 5 administrations with 24 hour intervals, each administration consisting of $^1/_5$ of the total dose. Infections were always made perorally on an empty stomach. Various doses of culture material (2.5 million to 5 billion microbial cells per kg live weight) were investigated.

RESULTS

Cats which received 2.5 - 5 million Sonne type dysentery microbes in single administrations, as a rule, did not become sick.

Cats which were infected during 5 days with doses of 500 thousand microbial cells per day developed a disease, which, according to its course, clinical picture, form of development, and results of bacteriological and pathomorphological examinations, very much resembled dysentery in man. Symptoms of the disease were evident after 3 - 4 inoculations, i.e. before the animals received the total dose. The animals became weak and did not feed well. Stools became more frequent, fluid, with mucus and blood, with tenesmus and weakening of the sphincters. Cats lost weight, in some cases up to 30 - 40% of their original weight. Rectal temperatures rose by 0.5 - 2°C. In most sick cats the number of leucocytes in peripheral blood rose considerably. Dysentery organisms were isolated repeatedly during the entire course of the disease. A higher agglutinin titer was noted in all sick cats.

Of 39 animals subjected to pathomorphological investigations, 8 died and 31 were killed at different periods after infection. This allowed the study of pathomorphological changes beginning with 1 day to 32 days after infection.

As a result of peroral introduction of Sonne type dysentery microbes in different doses, there arose in small and large intestines of experimental animals, generally, an identical pathological process, whose nature and severity were determined by time elapsed between the beginning of the infection to the death of the animal, the infecting dose; the number of administration of microbial cells and the individual characteristics of the animal.

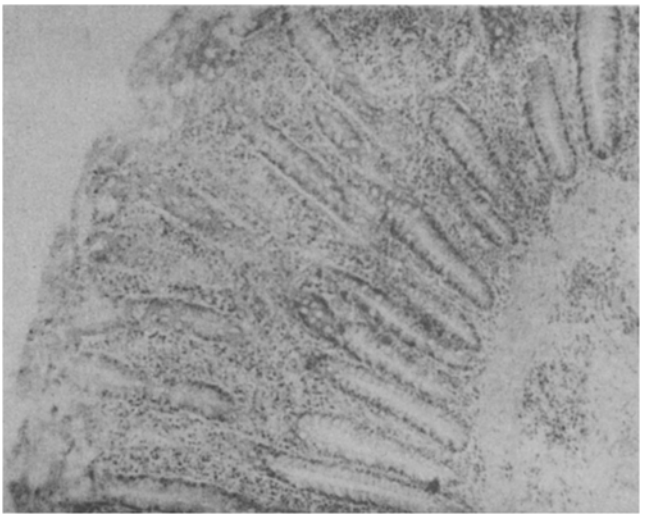

Fig. 1. Mucosa of the large intestine of cat after five administrations of a total of 1 billion microbial cells. Superficial necroses. Inflammatory infiltration of the base of the mucosa. Edema, lymphoid cell focal and perivascular infiltrates in the submucosa. Hematoxylin-eosin. Magn. 100×.

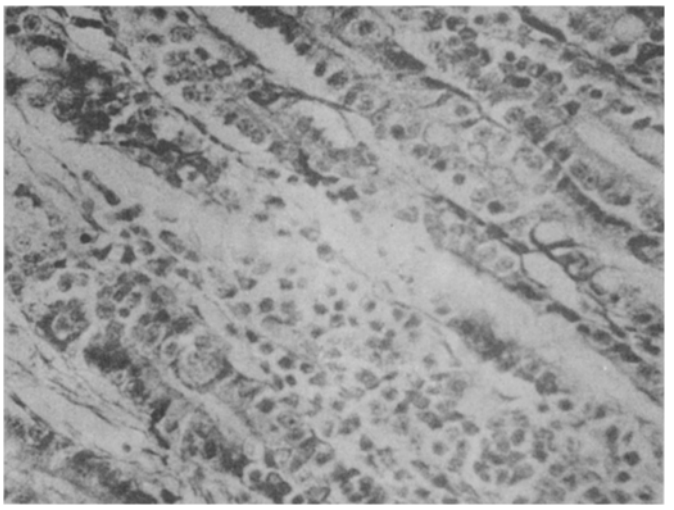

Fig. 2. Mucosa of the large intestine of cat after five administrations of a total of 1 billion microbial cells. Sharp edema and mucifaction of the epithelium of the crypts of Lieberkuhn. The base of the mucosa is infiltrated by plasma cells and histiocytic elements. Hematoxylin-eosin. Magn. 400×.

Dividing our experiments into groups allowed us to compare the morphological changes caused by different infecting doses. Changes in the intestine increased with the infecting dose. Doses of 5 billion microbial cells per kg live weight caused greater changes in the small and large intestines than smaller doses.

As a result of our investigations we were able to demonstrate the relationship of the nature of the inflammatory process to the number of introductions of infective material. A single administration of the infective dose led to a short disease and the development of an inflammatory process in the intestines of animals; with the introduction of large numbers of microbial cells this process was very sharply defined. Repeated administrations of infective material in fractional doses caused a longer disease; the pathological process in the intestine was longer, with changes of phases of the inflammatory process.

The sharpest changes were found in animals which received 5 billion microbial cells per kg. It was in this series of experiments that best comparisons of morphological changes in the intestines of cats, which received the infective material in single and in multiple doses, were made. In addition to the intestines, sharp changes were noted in extramural and intramural nerve centers.

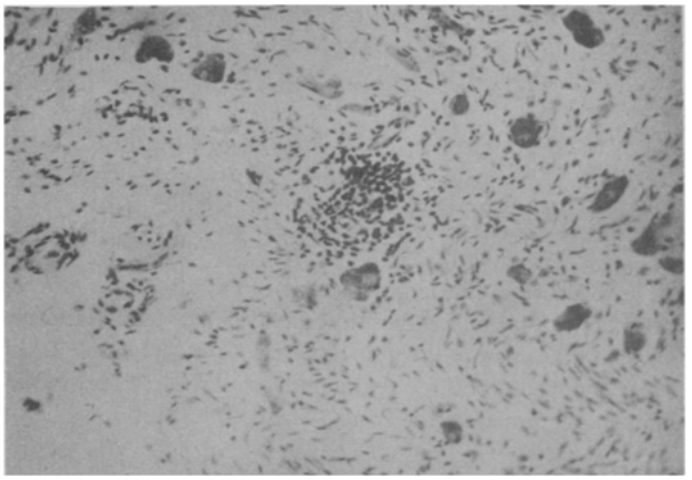

Fig. 3. Solar plexus in the intestine of cat after five administrations of a total of 1 billion microbial cells. Degeneration of nerve cells and perivascular focal lymphoid cell infiltrate Nissl's thionin. Magn. 200×

Changes in the intestines in the first 2 groups, in which the animals received the infective material in single and in fractional doses during 5 days (the total dose was the same in both cases), were different in intensity and in extent. These changes depended on the time elapsed between the beginning of infection to the death of the animal.

In these groups of animals the inflammatory changes in the intestines during the first 2 - 5 days were diffuse in character, both in their extent throughout the length of the intestinal tract, and in penetration into all the layers of the intestinal wall. The mucosa was edematous, hyperaemic, with areas of desquamation and of superficial necrosis; the base of the mucosa and the villi was infiltrated by neutrophils, lymphoid and plasma cells and local histiocytic elements. In the submucosa there developed an edema of varying intensity and either diffuse or focal round cell infiltration, localizing around blood vessels; in some cases there were minute hemorrhages and in most cases fibroid swelling and edema of vascular walls. At the same time there were small infiltrates in the muscular layer; these were mostly found at the border between the longitudinal and the circular layers.

At later periods (6, 8, 10 days after infection) the pathological process in the intestines of the first group of animals, in which they were infected by a single dose, became decreased. In the intestines of animals of the second group (in which they were infected with 5 fractional doses) the process increased in severity and generally became localized in the large intestine, in which the changes were more pronounced than in the small intestine. Superficial lesions were seen more often (Fig. 1). The mucosa was strongly adematous, hyperaemic, while the epithelial cells in the crypts of Lieberkuhn were very mucous, desquamated in places, and sometimes found in groups in the lumen

of the crypts. The infiltration of the base of the mucosa became stronger (Fig. 2), as well as that of the villi. The number of neutrophils in the infiltrate decreased in relation to the period elapsed from the time of infection, and large numbers of lymphoid and plasma cells and histiocytic elements appeared. In the submucosa the edema remained the same or sometimes increased somewhat,and many perivascular and focal lymphoid cell infiltrates were found.

Thus, the pathological process in the intestine of animals, which received the infective dose in a single administration, did not differ during the first days after infection from the process in the intestine of cats which received a similar total dose in fractional administrations and had a diffuse character. However, at later periods we noted in cases of single-dose inoculations a lessening of the pathological process, while in cases of repeated inoculations an increase of the inflammatory process and its tendency to localize in the large intestine, where it became most pronounced.

In the intramural nerve centers and in the solar plexus (Fig. 3) there were degenerative changes in the ganglion cells; these were shrinkage of cells, karyorexis, karyolysis and pyknosis of nuclei, vacuolization of the cytoplasm tigrolysis or lateral distribution of the tigroid substance; in some cases there were empty spaces where the cells were destroyed. A true neuronophagy took place.

In cases of one-dose infections these changes were of sharper focal nature; in cases of multiple subinfective doses the majority of nerve cells were degenerate, while in the stroma of the nerve centers we found changes in the blood vessels and perivascular focal round cell infiltrates. These described changes in the intra- and extramural nerve centers, apparently, are conducive to the lengthening of the inflammatory process in the intestinal wall and to the transition of the acute inflammation to a chronic one.

These investigations indicate that in the pathogenesis of the infectious process in experimental dysentery the toxic factor plays a definite part, while at later periods it is the allergic factor, as a result of the first penetration of the infection into the organism. The pathological process which arose as a result of this, later decreases if the organism does not receive new infective material. In cases of repeated fractional infections (with the same total dose), the pathological process, which arose as a result of the first introduction of infective material, increases. This leads to a real disease with a typical clinical and morphological picture.

The morphological picture of the disease is governed by the infecting dose and by the number of administrations of microbial cells.

SUMMARY

A study was made of peculiarities attending the pathomorphological changes in the intestine, intra- and extramural nerve ganglia of cats in relation to the dose and the number of microbial cell administration.

Some cats were infected once with a total dose, others repeatedly, fractionally (with the same sum total dose). Different doses were tested. As demonstrated, single administration of dysentery culture in a dose of 2.5 - 5 ml was incapable of inducing the infection. Fractional administration of the microbes (each dose containing 500,000 microbial bodies) provoked a disease resembling dysentery in man by its course, clinical picture, bacterioscopic and pathologico-morphological data. Pathological processes occurring as a result of the first administration of infective material declines in the absence of reinforcement; in case of repeated infection – it increases in intensity.

LITERATURE CITED

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