ON THE PATHOGENESIS OF TYPHOID FEVER INTOXICATION IN DOGS
AT VARIOUS STAGES OF GROWTH

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(Received November 5, 1954. Presented by Academician A. D. Speransky)

A.D. Speransky and his coworkers established the role of the nervous system in the pathogenesis of a number of infections, both under experimental conditions and through clinical observations. The importance of the nervous system in the process of development of the principal symptoms of disease is shown most clearly by experimental analysis of toxin intoxication at various stages of growth.

The work of our laboratory has established that the absence of so-called typical symptoms of a disease during toxin poisoning at an early age is due to the inactivity of those reflex mechanisms which produce these symptoms in adults [1-4].

The problem which was attacked in the present investigation was the characterization of some principal symptoms of typhoid poisoning in dogs at various stages of growth, especially with respect to the intestines.

EXPERIMENTAL METHOD

The experiments were conducted on: 38 adult dogs; 3 puppies 5 days old; 2, 8 days old; 3, 14 days old; 2, 18 days old; 2, 22 days old; and 4 puppies 3-4½ months old. We used a diphtheric antigen, which had been prepared at the Gamaleia Institute of Epidemiology and Microbiology, in order to produce the typhoid intoxication. It was a concentrate of the entire culture: the liquor and killed bacteria. We were able to use two antigens which had been prepared from two different varieties of typhoid bacteria. We established the lethal dose of Antigen No. 1, the more toxic one, to be 10 mg/kg; the lethal dose of Antigen No. 2 was 15-20 mg/kg. The antigens, which had previously been dissolved in physiological salt solution, were introduced subcutaneously and, in a few experiments, intravenously. We observed the clinical condition of the animals carefully; we took electrocardiograms to register changes in heart action and noted changes in breathing and temperature. After the animals died or were killed a certain length of time after introduction of the antigen, the pathological anatomy of the intestinal tract was studied.

EXPERIMENTAL RESULTS

Adult dogs die during the first, or more rarely, the second, 24 hours after the administration of a lethal dose of the antigen. The first signs of recuperation appear on the third day (with Antigen No. 1) and in some cases on the second day (chiefly with Antigen No. 2) after introduction of a sublethal dosage. In only an hour or more, depending on the dosage and method of administration, vomiting begins (more frequent with Antigen No. 2). Later, diarrhea, usually bloody, is observed (especially true with Antigen No. 1). During the acute stage of the intoxication the temperature rises to 40°. Prolonged bradycardia occurs in adult dogs.

Animals whose intoxication was not lethal were killed from several hours to five days after the first symptoms of illness. Autopsy revealed the typical progress of changes in the lymphatic system of the intestines which has been described for human typhoid fever. During the first hours after administration of the toxin, es-
especially of a lethal dose, swelling of Peyer’s patches and solitary glands could be observed, together with hyperplasia of the lymphatic tissues, i.e., the first stage of proliferative inflammation. Peyer’s patches were swollen the whole length of the intestines, especially in the region of the ileum and, slightly less, in the duodenum. The first stage was replaced by the second—necrosis, followed by ulceration and sloughing of the necrotic tissue.

The area of the patch became deeper as a result of the necrosis, reaching the serosa in individual cases. 24 hours and, in individual cases, two days later, autopsy revealed extensive necrotization and ulceration, together with swelling of Peyer’s patches (Fig. 1). When sublethal doses of the antigen had been administered (especially in the case of No. 1), hyperemia was evident primarily in the ileum and duodenum. On introduction of lethal and, especially, larger doses, swelling of the mucosa and a very evident diffuse hyperemia of it throughout the length of the intestine could be observed. The intestine became soft and practically fell apart under the scissors. In these cases, the hyperemia was evident in the area of the lower part of the stomach and, to a lesser extent, in the large intestine. The liver, and especially the spleen, were full of blood. Petechial hemorrhage was observed in the lungs and, occasionally, in the

Fig. 1. Upper portion of the jejunum of an adult dog (weight, 12 kg), two days after intoxication produced by administration of 10 mg/kg of typhoid fever Antigen No. 1.

Fig. 2. Ileum and mesenteric lymph glands of an adult dog (weight, 9 kg), 5½ hours after the beginning of intoxication produced by administration of 10 mg/kg typhoid Antigen No. 2.

Fig. 3. Duodenum of an adult dog (weight, 7.5 kg), two days after the beginning of intoxication produced by administration of a dose of 7.5 mg/kg of typhoid fever antigen to the atropinized animal.