PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

EFFECT OF SODIUM SALICYLATE ON THE DIGESTIVE ORGANS

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We tested a number of pharmaceuticals in order to produce an example of experimental hepatitis. The administration of carbon tetrachloride to dogs produced severe intoxication with a purulent process at the place of administration. In 100% of the cases, the administration of atophan led to the formation of ulcers in the stomach, and sometimes in the duodenum as well, along with liver disease [1, 3, 4].

Some investigators observed pathological changes in the digestive organs during intake of sodium salicylate [2, 5, 6, 7, 8]. We calculated that it should be possible to obtain a more successful experimental example of hepatitis by selecting suitable doses and times of action of sodium salicylate, than by the administration of carbon tetrachloride or atophan.

The present investigation was carried out on 13 rats and 6 dogs.

Sodium salicylate was administered to rats through a probe using 0.05-0.1 g per kilogram of weight in 0.5% water solution. Dogs were given sodium salicylate 1-2 times a day using 0.1-0.2 g per 1 kg of the animal's weight in a mixture of milk and water at a concentration of 0.5-1.5%. The duration of the administration of the sodium salicylate varied from 2 to 18 days.

The shape of the glycemic curve when the animals were given glucose (2 g per kg of the animal's weight) and the results of blood bilirubin determinations served as indicators of the functional deterioration of the liver. The positive benzidine test for blood in the feces served as an indicator of the inflammatory process in the mucosa of the digestive tract. After autopsy of the animals, detailed histological investigation of the digestive organs was carried out.

Results of Histological Investigation of Rat Liver.

Sodium salicylate was administered to rats no. 1, 2, and 3 for 2 days. Insignificant hyperemia of the stomach, intestines, liver and pancreas was observed in all the rats. No histological changes of these organs were found.

Sodium salicylate was administered to rats no. 4 and 5 for 5 days, to rats no. 6 and 7 for 8 days. Significant hyperemia of the blood vessels and capillaries of the liver was observed in all the rats. The liver cells were compressed by the capillaries which were enlarged and full of blood. The protoplasm of the liver cells had a broken up and vacuolated appearance; lysis of the nucleus was observed in many cells. Fatty inclusions were found in the liver cells of rats no. 5, 6, and 7. Lipoid inclusions in the form of brown granules were observed in some leucocytes.

Sodium salicylate was administered for 14 days to rats no. 8, 9 and 13, for 18 days to rats no. 10, 11 and 12. The histological picture of the liver was the same as that of the preceding group.

Results of Histological Investigation of the Digestive Tract of Dogs.

Dog no. 1 (weight 7 kg) was given 0.1 g per 1 kg of weight of sodium salicylate from January 15 to February 6 at intervals of 1-2 days. In all, 7 g were given in the course of 20 days. On the 7th day blood appeared in the feces. On February 6 the dog was dissected. The stomach was very atonic. An ulcer 1.5 x 1 cm^2 with degenerated edges and with bloodclots on the bottom was found in the intermediary zone of the posterior wall. A broad band of surface erosion extended from it around the intermediary zone. Defects of the mucosa were present at the pyloric sphincter and duodenum. The gastric and duodenal mucosa was very hyperemic. The gastric mucosa, especially in the pyloric region, was covered with a considerable amount of mucous which was brown in color.

On histological investigation of the mucosal layer of the fundal region of the stomach it was possible to observe in various sections of it a hyperemia of the blood vessels of the submucosal layer and of the mucosa itself, enlargement of the neck regions of the gland tubes and a considerable depletion of mucoid secretion in the parietal cells in individual areas of the mucosa; in other areas (lesser curvature) intensive mucoid secretion was observed. The chief cells of the majority of gland tubes were of short cubical shape and were reminiscent of indifferent epithelial cells. The lining cells had a normal appearance. A distince swelling of the submucosal layer, infiltration of stroma of the mucosa, moderate mucoid secretion by the glandular elements and, here and there, hypertrophy of the gland tubes could be observed in the pyloric region. The walls of the blood vessels of the submucosal layer were thickened in the pyloric as well as in the fundal region. An ulcer of the posterior wall of the intermediary zone was found. The bottom of the ulcer was formed of a degenerated edematous submucosal layer which was slightly infiltrated with neutrophilic leucocytes. The vessels of the submucosal layer were dilated and filled with blood (condition of stasis). One side of the ulcer was formed from the mucosa of the intermediary zone, the other of the degenerated pyloric zone (Fig. 1). An ulcer was also located at the transition of the pyloric region into the duodenum. Brunner's glands were evident, individual groups of them lined by low cuboidal epithelium and distended like cysts. Mucoid secretion was poorly evidenced (Fig. 2).

In the pyloric region was found erosion, the bottom of which was formed of the muscularis mucosa and, here and there, of the submucosal layer. Mucoid secretion was in satisfactory evidence in the pyloric glands.

In the liver, considerable hyperemia was found, the vessels were often surrounded by accumulations of leuco-lymphatic elements. The hepatic cells were granular in appearance. In the hepatic cells, stained yellow, fatty inclusions were found; lipoid inclusions of a brown color were observed in the leucocytes (Geldman's method). Drops of fat were in the bile ducts. The stroma was infiltrated with leucocytes (Fig. 3).

Similar results were obtained with dogs no. 3 and 5. One of them received sodium salicylate for 4 days, the other for 12 days (0.2 g per 1 kg of weight each). The dissection was carried out after 2 days in the first case, in the second 12 days after the salicylate was stopped.

Dissections of dogs no. 2, 4, and 6 were carried out longer periods of time after the sodium salicylate was stopped (from 27 to 35 days). Dog no. 2 (weight 9.5 kg) received 0.1 g of sodium salicylate per 1 kg of weight for 14 days. Blood was found in the feces on the 9th day. The dog was dissected 27 days after the sodium salicylate was stopped.

Dog no. 4 (weight 9.8 kg) received 0.2 g per 1 kg of weight of sodium salicylate from January 3 to January 15, 1953. On the 8th day blood was found in the feces. The dog was dissected on March 1, 1953 (33 days after the salicylate was stopped).

Dog no. 6 (weight 15 kg) received 0.1 g per 1 kg of weight of sodium salicylate from March 17 to April 1. On the 6th day blood appeared in the feces. On April 28 the dog was dissected (27 days after the sodium salicylate was stopped).

Hyperemia of the mucosa of the stomach, of the duodenum, of the pancreas and of the liver was observed in all of these dogs. No defects of the gastric and duodenal mucosa were found.

During histological investigation of the stomach were observed: uniform thickness of the mucosa with a regular disposition of gland tubes, hyperemia of the blood vessels of the submucosal layer and mucosa, edema of the submucosal layer and mucosa at the border of the muscularis mucosa, considerable mucoid secretion in the parietal cells (especially on the lesser curvature), small granules of mucous in the chief cells and pycnosis of the nuclei in a small number of lining cells.

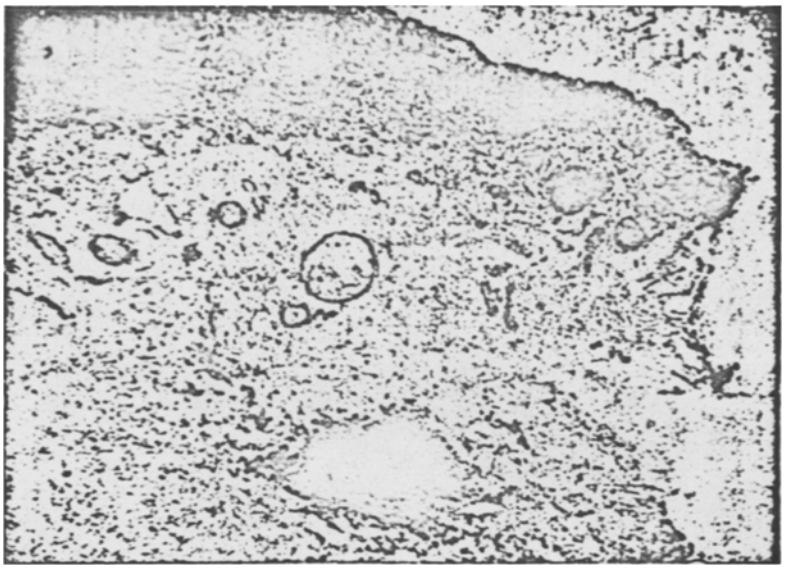

Fig. 1. Edge of the ulcer of the posterior wall of the intermediary zone (in dog no. 1). Hemorrhagic area in the edematous submucosal layer. Enlargement x 12.

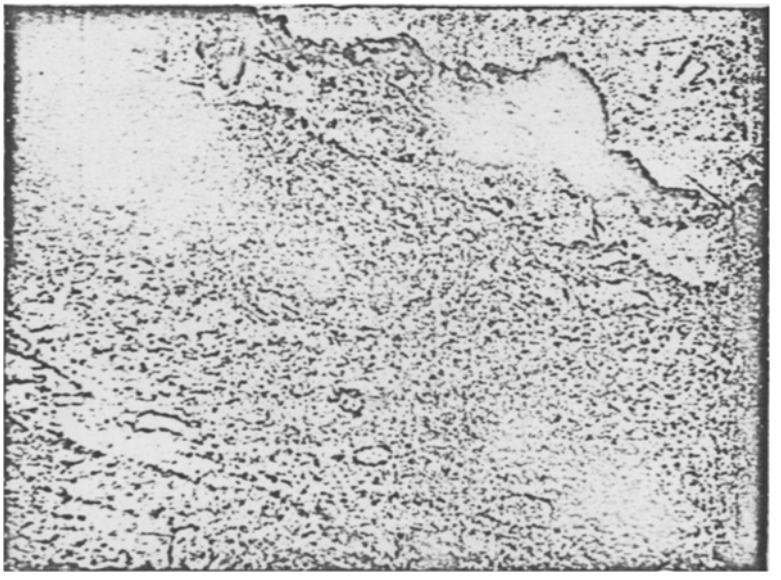

Fig. 2. Bottom of the ulcer of the posterior wall of the intermediary zone (in dog no. 1). Distince edema of the submucosal layer, detached necrotic substance above. Enlargement x 12.

In the pyloric region the mucosa was of average height with rather loosely placed gland tubes whose epithelium extensively secreted mucous secretion. In individual areas of the mucosa, proliferation of the epithelium of the gastric depressions and individual gland tubes were also observed. Considerable histological changes were found in the liver, similar to those described above.

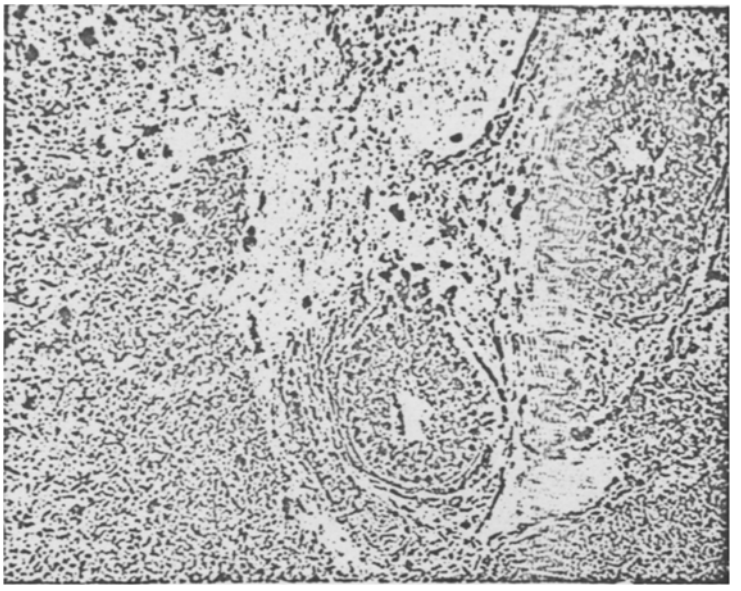

Fig. 3. Considerable leucocytic infiltration of the hepatic parenchyma and extensive fatty infiltration of the bile duct epithelium in dog no. 4. Enlargement x 140.

In the pancreas the following changes took place: hyperemia of the blood vessels; zymogenic cells diminished in size; zymogenic granules almost completely absent; dark, pyknotic cell nuclei. Some of the islands of Langerhans were diminished in size and seemed to contain nuclei only; others, fewer in number, were represented by light formations of considerable size.

Considerable changes in the carbohydrate metabolism occurred under the influence of sodium salicylate. A smaller and later rise of the blood sugar concentration was observed than normal. The blood sugar content did not return to the original levels for several hours. No changes were observed in the bilirubin content of the blood.

Sodium salicylate caused changes in the behavior of the experimental animals also. Thus, for example, rats became sluggish already on the 2-3rd day after it was administered, refused to eat, sat passively in a corner of the cage, etc. Similar changes were also observed in the behavior of dogs.

The appearance of gastritis and toxic hepatitis during the administration of sodium salicylate to experimental animals, it seems to us, can have some significance in clinical medicine where sodium salicylate is applied widely.

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