LITERATURE CITED


LIBERATION OF HISTAMINE AND SEROTONIN AND VASCULAR PERMEABILITY IN AN ACUTE ASEPTIC INFLAMMATORY FOCUS

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Degranulation of mast cells of a peritoneal suspension and of the mesentery of the small intestine and liberation of histamine and serotonin in albino rats with acute aseptic peritonitis were shown to begin during the first minute after injury and to reach a maximum at the fifth minute. By the 15th minute the concentrations of the free amines had fallen sharply and did not differ significantly from the initial levels. The dynamics of the immediate phase of increased vascular permeability corresponded to the dynamics of the free amines. The most marked increase in vascular permeability was observed at the 10th-15th minutes. By the 20th minute it was appreciably lower. Preliminary exhaustion of histamine and serotonin reserves reduced the degree of disturbance of vascular permeability only during the first 15 min after application of the inflammatory agent. It is concluded that histamine and serotonin cause disturbance of vascular permeability in acute aseptic peritonitis chiefly during the first 15 min after injury.

KEY WORDS: acute aseptic inflammation; mast cells; histamine; serotonin; vascular permeability

The principal mediators of the microcirculatory changes that characterize the initial phase of inflammation are histamine and serotonin. However, the duration of the period within which the action of these amines is the determining factor in the increased vascular permeability in a focus of acute inflammation has not yet been established.

Most of the data on the role of histamine and serotonin in the immediate phase of increased vascular permeability are based on their pharmacodynamic action. The dynamics of the mediators in the focus of inflammation directly after application of the inflammatory agent has not been studied.

The object of this investigation was to determine the functional state of the mast cells of a peritoneal suspension and of the mesentery of the small intestine, the liberation of histamine and serotonin from them, and the changes in vascular permeability in the peritoneal cavity of albino rats in the course of acute aseptic peritonitis.

According to data in the literature [8, 10, 11], the mast cells are the sole source of detectable quantities of histamine and serotonin in the peritoneal cavity of albino rats.

**EXPERIMENTAL METHOD**

Experiments were carried out on 194 noninbred female albino rats weighing 150-220 g. Acute aseptic peritonitis was induced by intraperitoneal injection of a mixture of 0.05 ml turpentine and physiological saline (1:10). The animals were decapitated 1, 5, 15, and 30 min and 1, 2, and 5 h later, a peritoneal suspension was obtained [13], and it was immediately kept in the cold.* The mast cells were stained with neutral red and examined in a Fuchs-Rosenthal chamber under a magnification of the microscope of 400 ×. Their absolute and relative numbers and the percentage of degranulated mast cells were determined.

Mast cells in the mesentery of the small intestine were stained with toluidine blue [12] and also with safranine and alcian blue [14] and examined under a magnification of the microscope of 400 ×. The number of mast cells was counted in 100 fields of vision of the microscope and the percentage of degranulated cells calculated.

The histamine and serotonin concentrations were determined by modified fluorimetric methods of Shore and Snyder [1, 5] in the cellular and extracellular fractions of the peritoneal washings after removal of the turpentine and centrifugation of the washings at 350g and 4°C for 15 min [8]. The concentrations of the amines were expressed in micrograms per rat.

The state of permeability of the peritoneal vessels at various times after injection of the turpentine was judged from the concentration of intravenously injected (5 min before determination) trypan blue (0.75-1 ml of a 1% solution) in the peritoneal washings [2]. To obtain the washings, 5 ml of Tyrode solution was injected intraperitoneally. The concentration of dye in the washings was determined colorimetrically and expressed in g/ml washings.

To exhaust the reserves of histamine and serotonin bidistilled water was injected intraperitoneally in a volume of 10 ml/100 g body weight [9, 15].

**EXPERIMENTAL RESULTS AND DISCUSSION**

Marked degranulation of the mast cells of the peritoneal suspension and mesentery of the small intestine (81.14 ± 5.51 and 57.64 ± 8.67% respectively, compared with 1.20 ± 0.33 and 0.92 ± 0.26% in the control) was observed 1 min after injection of turpentine and was accompanied by liberation of histamine and serotonin, with an increase in their concentrations in the extracellular fraction and a decrease in the cellular fraction (Tables 1 and 2). The absolute and relative numbers of mast cells in the peritoneal suspension at this time did not differ significantly from the control (992 ± 10³ ± 225 ± 10³ and 2.73 ± 0.49% in the control; 725 ± 10³ ± 164 ± 10³ and 2.34 ± 0.66% in the experiment).

No mast cells could be found in the peritoneal suspension 5 min after injection of turpentine as a result of their complete degranulation. The number of degranulated mast cells in the mesentery reached 65.90 ± 7.45% and the concentrations of free histamine and serotonin were maximal and exceeded the control level by 4.6 and 3.3 times respectively. However, by the 15th minute after injury the concentration of the free amines in the inflammatory focus no longer differed significantly from that in the control. At subsequent times of investigation (until the fifth hour) the concentration of the free amines showed no significant change. The level of intracellular amines continued to remain very low (Tables 1 and 2).

The permeability of the peritoneal vessels was sharply increased 5 min after injection of turpentine, when it was more than 4 times higher than in the control (Fig. 1). In the period between the fifth and 15th minutes it rose steadily and reached a maximum by the 10th to 15th minute, when it was 7 times higher than in the control. By the 20th minute a significant increase in vascular permeability was observed, although at this time and later during the investigation it continued to remain higher than in the control. For instance, 1-2 h after injection of the inflammatory agent the vascular permeability was 3 times higher than in the control.

*The times of decapitation of the animals after injection of turpentine are given in the text and in the tables.*