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MORPHOLOGICAL AND FUNCTIONAL REACTIONS OF PEYER'S PATCHES DURING TRAUMATIC SHOCK AND THE EARLY RECOVERY PERIOD IN DOGS

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UDC 616-001.36:611.341.001.6

Modern views on the role of the endotoxin component in the pathogenesis of shock [8-10, 12-14], the well-known views of Selye on involution of the thymicolymphoid system during exposure to stress, the clear changes in regional and distant lymph nodes under the influence of trauma [5, 6], and the complete absence of information on the response of Peyer's patches to trauma all indicate the need for a study of this problem. Interest in morphological and functional changes in Peyer's patches in the course of traumatic shock and the early recovery period after shock is due primarily to the localization of these structures, which are regional in relation to endotoxin derived from the intestine, and also to the possible role of Peyer's patches in differentiation of lymphocytes in the B-cell direction.

EXPERIMENTAL METHOD

Traumatic shock was produced by Cannon's method in albino rats. Standard shock-producing trauma was applied to the animals and, in 50-60% of cases, proved fatal. The times of investigation corresponded to periods of traumatic shock (1 — original background, 2 — erectile phase, 3 — beginning of the torpid phase, 4 — 1 h, 5 — 3 h after trauma) and the early recovery period after shock (6 — 1st day, 7 — 3rd day, 8 — 5th day after trauma). Material for histological study was fixed in Carnoy's fluid and sections were subsequently stained with hematoxylin and eosin, with methyl green and pyronine "g" by Brachet's method, and with gallocyanin for RNA. Reactions for alkaline and acid phosphatases (AlP and AcP, respectively) by Gomori's method were conducted on cryostat sections, fixed beforehand for 24 h in formalin—calcium mixture. The level of enzyme activity was judged from the intensity of the histochemical reactions.

EXPERIMENTAL RESULTS

Peyer's patches in intact animals are localized in the intestinal mucosa and submucosa and are lymphoid formations with high cell density (Fig. 1a). The pale center is somewhat eccentric in situation and displaced toward the serous membrane. The density of small lympocytes around the pale center decreases toward the intestine. Reticulum cells and various intermediate forms of cells predominate in the cupola of the patch, located above the lymphoid zone of the follicle. A few plasma cells can be seen beneath the epithelium of the cupola.

Infliction of standard shock-producing trauma led to definite changes in the cytoarchitectonics of the Peyer's patches as early as in the erectile stage of shock, characterized by dilatation and congestion of blood vessels of capillary type and increased AlP activity (Fig. 1b) in their endothelium. At the beginning of the torpid phase, development of which was judged from the appearance of shock hypotension, some decrease in the density of small lymphocytes was observed in the peripheral portions of the follicle in the Peyer's patches, against the background of microcirculatory disorders, and this was accompanied by an increase in the number of macrophages with signs of phagocytosis in the pale center (Fig. 1c) AlP activity in the macrophages of the pale center, the peripheral zones of the patch, and also in the reticulum cells of its cupola, was distinctly increased (Fig. 1d). Further development

KEY WORDS: Peyer's patches; traumatic shock; early recovery period after shock; endotoxin.

Department of Pathophysiology, Rostov Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. K. Kulagin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 4, pp. 424-426, April, 1981. Original article submitted April 28, 1980.

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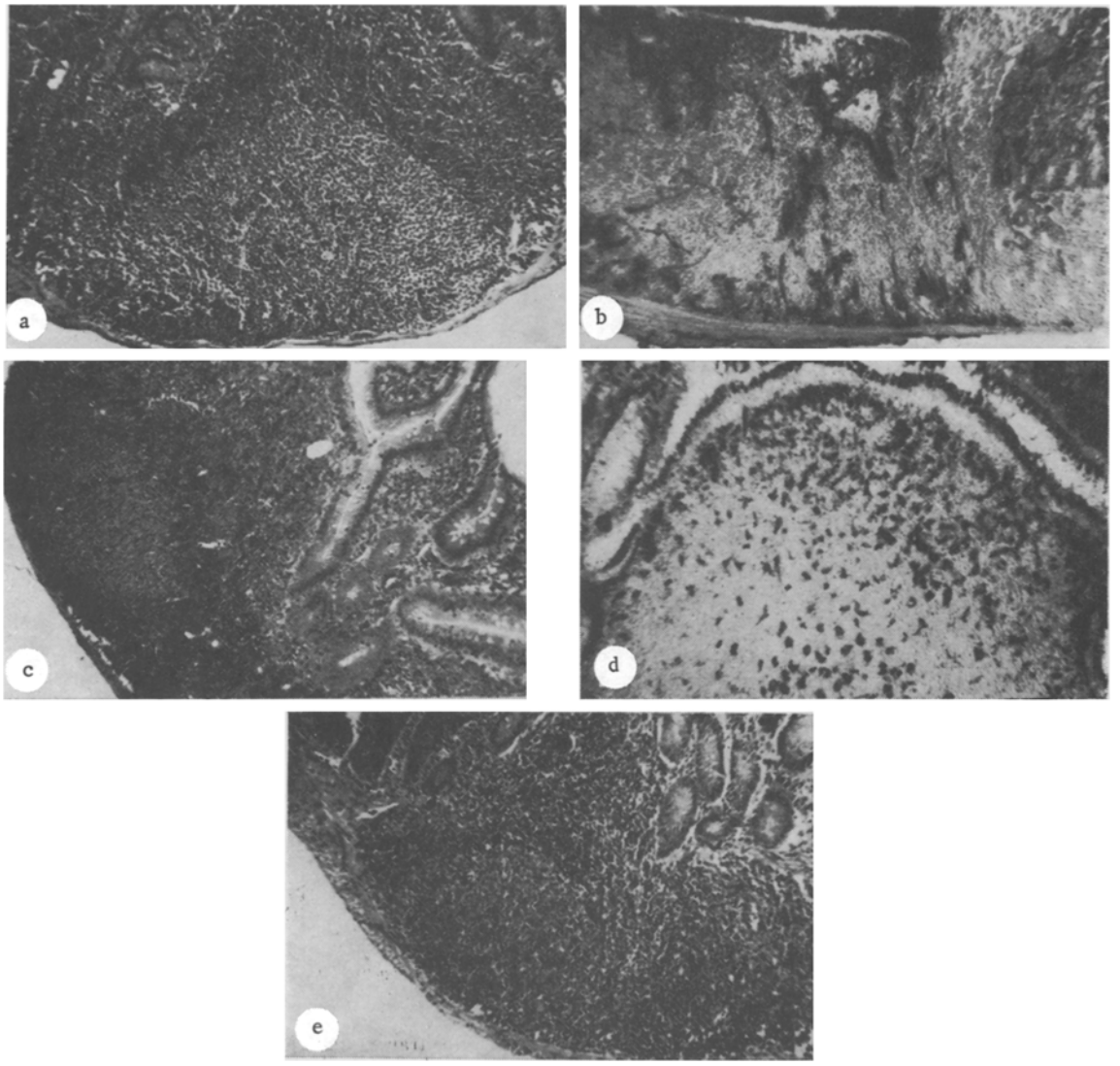

Fig. 1. Histophysiological characteristics of Peyer's patches during traumatic shock in rats: a) clearly marked zone of small lymphocytes surrounding pale center in intact rats; b) increase in AlP activity in vascular endothelium on territory of Peyer's patch, erectile phase; c) small decrease in number of small lymphocytes at periphery of follicle, beginning of torpid phase; d) increase in AcP activity in macrophages and reticulum cells of pale center and cupola of patch, beginning of torpid phase; e) reduction in density of small lymphocytes in peripheral zones of follicle, indistinctness of boundaries, torpid phase, 3 h. a, c, e) hematoxylin and eosin; b, d) Gomori's reaction; 80×.

of shock 1 h after trauma led to a clear reduction in the density of lympocytes in the marginal zones of the follicle, an increase in the number of phagocytic macrophages in the pale center, and intensified activity of hydrolytic enzymes. The greatest decrease in the density of small lymphocytes in the peripheral zones of the follicle was observed 3 h after the beginning of the experiment (Fig. 1e). The boundaries between zones of the follicle became indistinct and the lymphoid zone became very much thinner, especially in the upper part of the follicle toward the cupola of the patch. Phagocytic cells were seen in all parts of the follicle, but mainly in the pale center.

The development of nonlethal shock thus led to considerable morphological and functional changes in the Peyer's patches, manifested as vascular disturbances, which evidently reflect a special case of the general hemodynamic changes typical of shock; it was also accompanied by cellular changes characteristic of lymphoid organs during the development of stress situations [2, 7], manifested as a reduction in the density of small lymphocytes in the follicles

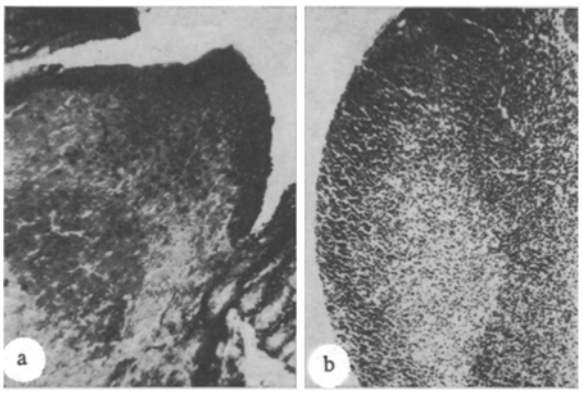

Fig. 2. Histophysiological characteristics of Peyer's patch in early period after shock. a) Increase in AlP activity in macrophages and reticulum cells of cupola of Peyer's patch, 1st day. Gomori's reaction; b) restoration of zone of small lymphocytes around periphery of follicle on 5th day. Hematoxylin and eosin. Magnification: 75×.

of the Peyer's patch. This depopulation may be accounted for both by migration of lymphocytes [1] and by their death and subsequent phagocytosis [7]. Since stress changes in lymphoid organs are usually associated with the influence of pituitary and adrenocortical hormones on them, it is natural to suggest that these cell changes in Peyer's patches in the course of traumatic shock are largely determined by changes in functional activity of the hypothalamohypophyseo-adrenal system, that are a constant feature of the development of shock [3, 4]. It was noteworthy that during the development of traumatic shock an invariable component of the response of the Peyer's patches at all times of the investigation was a high macrophagal response.

In the terminal phase of traumatic shock, with death occurring 4-5 h after trauma (the experiments were performed on dogs), changes in the Peyer's patches were more severe. Survey staining with hematoxylin and eosin revealed severe cell depopulation of the pale center and massive death of the cells in it, against the background of typical vascular changes. At the periphery of the pale center and around it, mitoses, blast cells, and a moderate number of lymphocytes were seen. In the cupola of the patches many plasma cells and transitional forms of them were noted. Many interepithelial lymphocytes were observed in the epithelium of the cupola of the patch.

The early period after shock in the rats were accompanied by different changes in the histological picture of the Peyer's patch. The decrease in density of small lymphocytes in the follicles 1 day after trauma was less marked. Lymphocytes with weakly pyroninophilic cytoplasm predominated in the lymphoid zone. In the cupola of the patch the plasma cells contained little RNA, with the exception of a few which were rich in RNA. The number of blast cells rich in RNA was reduced in the pale center. The macrophagal response remained fairly high. Activity of hydrolytic enzymes increased sharply in the macrophages and reticulum cells in the cupola of the patch (Fig. 2a). On the 3rd day the morphological and functional picture changed only a little and was practically the same as on the 1st day. On the 5th day the number of lymphocytes at the periphery of the follicle was significantly increased (Fig. 2b) but had not yet regained its initial level. The density of small lymphocytes was lowest in the central area of the lymphoid zone, in the direction toward the cupola. The macrophagal response remained fairly high. An essential factor in the response of the Peyer's patch in this period was an increase in the number of RNA-rich plasma cells in the cupola of the patch and in the number of blast cells in its pale center. Activity of hydrolytic enzymes was reduced, but not to its initial level.

The response of Peyer's patches to trauma was thus established on the basis of these investigations. This response is characterized by vascular, cellular, and enzyme-histochemical changes. The dynamics of themorphological and functional changes in the Peyer's patches is a combination of four groups of changes: 1) vascular disturbances arising immediately after trauma and manifested as dilatation of blood vessels of capillary type; 2) primary or stressor changes in the cytoarchitectonics of the Peyer's patch, recorded throughout the duration of shock and manifested as a reduction in the density of small lymphocytes in the lymphoid zone; 3) secondary changes in the cytoarchitectonics of the Peyer's patch, exhibited in the early period after shock and characterized by the beginning of repair processes and an increase in the number of plasma cells; 4) intensification of the macrophagal response and increased activity of hydrolytic enzymes, detectable throughout the course of traumatic shock and in the early period after shock. Intensification of the macrophagal response of the Peyer's patch is evidently connected with its boundary localization and is probably due to the action of an

endotoxin, for one of the distinguishing features of the effect of endotoxins of intestinal origin is their high stimulating capacity, leading to increased enzymic activity of the macrophages [11]. It is logical to assume that the increase in the number of plasma cells with a parallel increase in the number of blast cells on the 5th day after trauma is based on antigenic stimulation, associated with penetration of endotoxin from the intestine.

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