# ULTRASTRUCTURAL CHANGES IN LIVER MAST AND PLASMA CELLS IN PREGNANT RATS WITH ENDOTOXIN SHOCK

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An important role in the pathogenesis of endotoxin shock is played by vasoactive and other biologically active substances. Their secretion into the blood stream has been shown to take

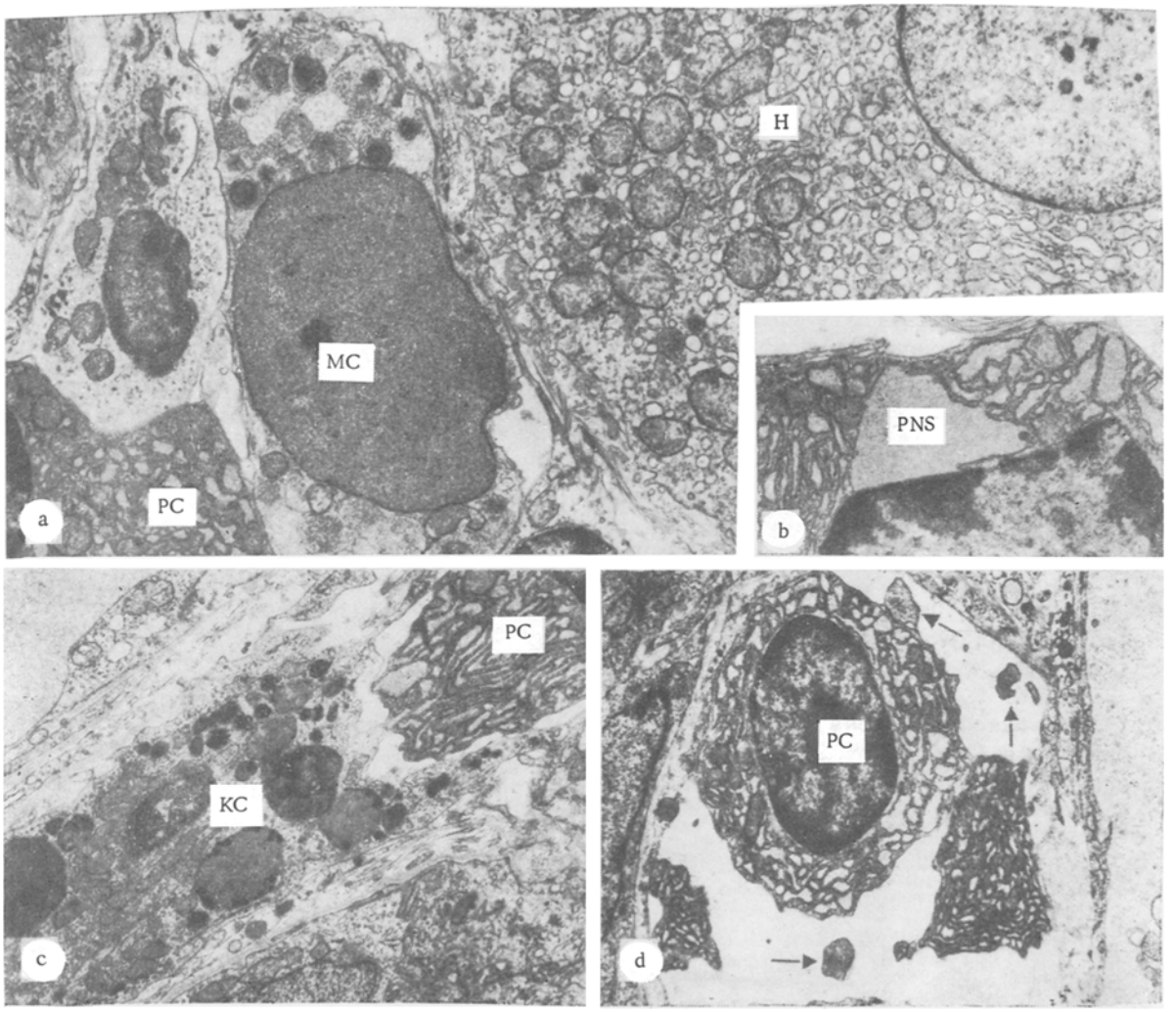


Fig. 1. Ultrastructure of mast cells (MC) and plasma cells (PC) in initial period of endotoxin shock. a) Contact between MC and PC. 8050 ×; b) local widening of perinuclear space (PNS). 11,760 ×; c) contact between PC and Kupffer cell (KC). 10,500 ×; d) clasmatosis of PC (arrows). 7140 ×. H) Hepatocyte.

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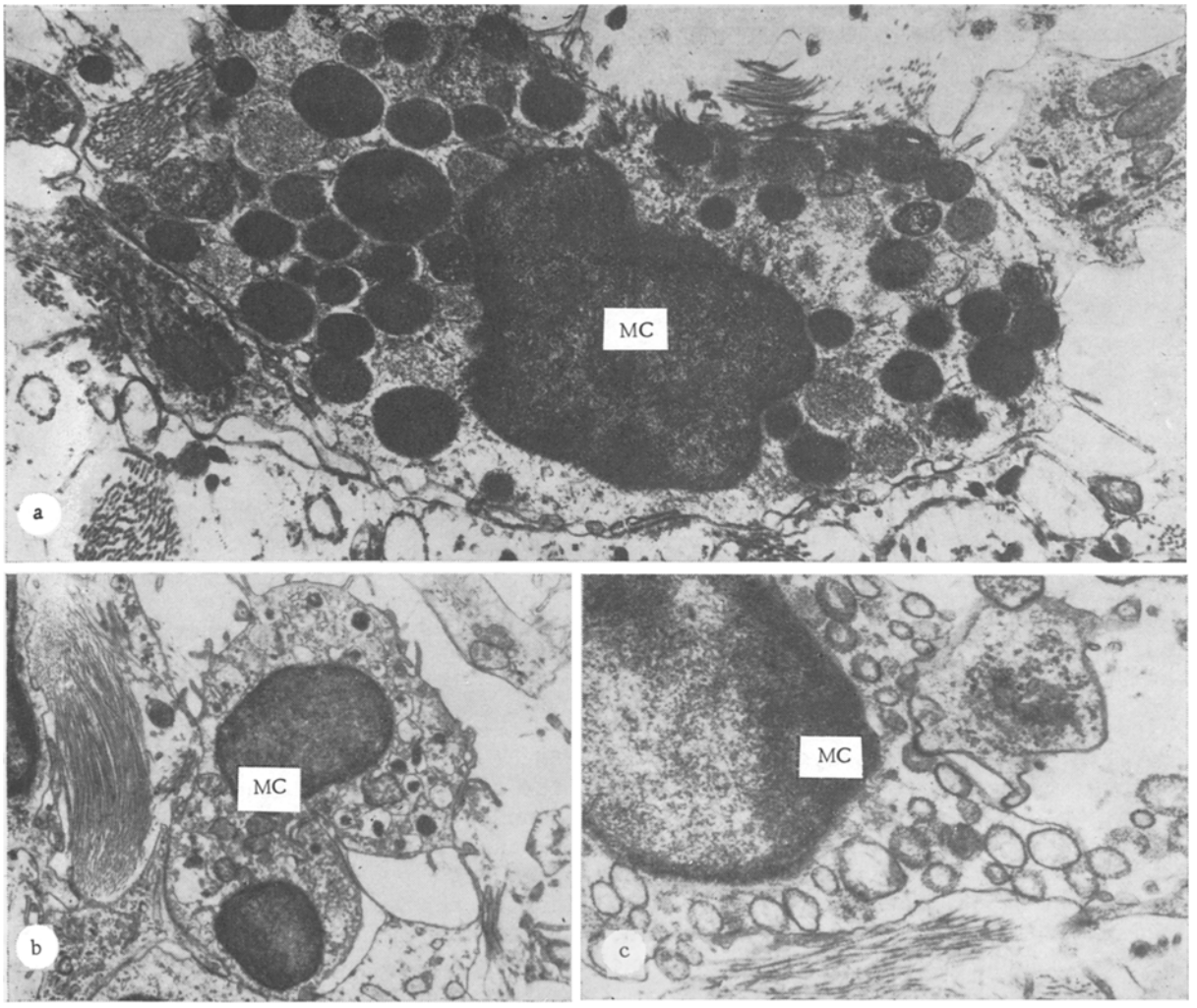


Fig. 2. Different degress of degranulation of mast cells (MC). a) Disappearance of osmiophilic matrix in center of granules (arrow): 12,880 ×; b) formation of zone of perigranular clearing: 6300 ×; c) degranulated MC. 10,500 ×.

place through stimulation of the sympathico-adrenal system and interaction between circulating endotoxin with reticuloendothelial cells, platelets, and mast cells. Mast cells frequently make contact with immunologically competent cells, especially plasma cells, and they participate in immediate-type hypersensitivity reactions [8].

Death of the animals is attributed to the development of systemic hypotension and hypofusion of vital organs, followed by the onset of irreversible changes in them [1, 2, 4, 12]. The more severe course of endotoxin shock in pregnancy depends on the weakening of the detoxicating power of the reticuloendothelial system as a result of the reduced clearance of biologically active substances and certain metabolites which are formed [11].

The aim of the present investigation was to study the character of ultrastructural changes in the mast and plasma cells of the liver in pregnant rats in the early stage of endotoxin shock.

## EXPERIMENTAL METHOD

Experiments were carried out on 15 pregnant (more than 17 days after mating) albino rats weighing 250-300 g. Shock was produced by intravenous injection of typhoid or *Escherichia coli* endotoxin in a dose of 2 mg/100 g, equivalent to $LD_{90}$ [10]. The arterial pressure was recorded in the carotid artery with a BM-101 electromanometer. Two groups of animals served as the control: group 1) five nonpregnant rats receiving endotoxin, group 2) five pregnant rats receiving physiological saline. The experimental and control animals were decapitated after 30 min. All experiments were carried out under intraperitoneal pentobarbital anesthesia. Pieces of liver were fixed in 3% glutaraldehyde solution in 0.1 M phosphate buffer, postfixed

in 1% osmic acid solution in Millonig's buffer at 4°C, dehydrated in alcohols, and embedded in Epon 812. Sections were cut on the LKB 8800 ultratome, stained on grids with uranyl acetate and lead citrate, and examined in the JEM-100S electron microscope. For light-optical investigation semithin sections were cut from the same blocks and stained with a mixture of toluidine blue and azure II.

## EXPERIMENTAL RESULTS

Intravenous injection of endotoxins into animals of the experimental and control groups led to a statistically significant fall in arterial pressure ($P < 0.05$) after 30 min. The pressure was unchanged in animals receiving physiological saline.

Pregnancy potentiated the ultrastructural changes in the liver mast and plasma cells in endotoxemia. Injection of endotoxins into nonpregnant animals led to structural changes reflecting activation of the apparatus of energy metabolism and stimulation of synthesis and release of the secretion products. Injection of physiological saline caused no ultrastructural disturbances of any kind.

In endotoxin shock plasma cells making contact with fibroblasts, and reticular, mast, and Kupffer cells could be seen in the perisinusoidal spaces of the liver of the pregnant rats (Fig. 1a, c). It is a noteworthy fact that extensive cavities of endoplasmic reticulum and regions of the widened perinuclear space, containing material of average electron density, could be observed in the plasma cells (Fig. 1b). Our observations showed that plasma cell function was considerably enhanced by injection of endotoxin, and secretory material was liberated from them through clasmatosis (Fig. 1d).

Granules of unequal electron density, reflecting the degree of liberation of mediators (labrokines, Fig. 2a), were observed in the cytoplasm of the mast cells. Intracellular lysis of the contents of the granules usually began with the formation of a zone of perigranular clearing (Fig. 2b), although sometimes the finely granular matrix disappeared in the center (Fig. 2a). In both cases large membrane profiles remained in their place. Completely degranulated mast cells were most frequently found in the pregnant rats (Fig. 2c), reflecting an extreme level of functional activity of the cells, with the result that the surrounding medium was enriched with histamine, heparin, and so on. Great importance in the mechanism of endotoxin shock is attached to a high histamine concentration in the region of the hepatic venules, causing stasis of the blood flow in them and severe hypotension, in consequence of which the microcirculation is disturbed even more and structural and metabolic disturbances arise in the hepatocytes [9].

The electron-microscopic investigation thus demonstrated conclusively that mast cells and plasma cells of the liver play a role in the early period of endotoxin shock, and the latter respond more strongly during pregnancy. These cells must evidently be regarded as a type of "unicellular gland" [3, 7]. The local and distant effects of mediators of the mast cells can be reduced to disturbance of the circulation, permeability, and blood clotting, blockade of phagocytosis, and so on, whereas the structural changes in the plasma cells correlate with their well-known role as immunocompetent cells. Interaction between cells of the perisinusoidal space and also with the intercellular matrix and the principal components of the functional element of the liver [5, 6] forms a complex system of connections that determine the character of the lesions in endotoxemia.

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