ROLE OF AUTOINTOXICATION IN GENESIS OF HEPATORENAL INSUFFICIENCY IN THERMAL BURNS

I. K. Koryakina and R. V. Nedoshivina

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As a result of thermal injury, toxic substances inhibiting migration of leukocytes in blood cultures appear in the serum of burned animals. Burn trauma causes considerable pathological changes in kidney and liver function, leading to the development of hepatorenal insufficiency. The experimental results suggest that autointoxication is an important factor in the development of hepatorenal insufficiency after thermal burns.

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In the modern view, thermal burns are accompanied by structural and functional disturbances of the liver and kidneys [1, 3, 8-11]. In the opinion of most workers, definite changes arise in these organs even in the case of burns covering small areas. Many workers [2, 12-13] attribute the changes in the internal organs to burn autointoxication.

Our earlier investigations [5, 7] yielded results supporting the toxemia theory. A parallel was demonstrated between the toxic action of serum of burned animals and changes in kidney function and nitrogen metabolism.

The object of the present investigation was to compare the toxic properties of the serum and the pathology of the liver and kidneys after thermal injury.

EXPERIMENTAL METHOD

Experiments were carried out on 12 dogs. After the initial data had been obtained, the animals were burned with a spirit flame over an area of 15-20% of the body surface, the exposure lasting 1-2 min. Investigation of the toxic properties of the serum and changes in kidney and liver function began 4 h after the burn.

The toxic properties of the serum were investigated by using migration of leukocytes in a culture of healthy human leukocyte film as criterion [4]. The sera for testing were added to the nutrient medium of the experimental cultures, and Ringer's solution was added to the controls. Migration of the experimental

TABLE 1. Changes in Kidney Function and Toxic Properties of Serum of Animals after Burn Trauma (in percent of normal, apart from toxicity). Mean Data

Time after burning	Glomerula filtration	Renal blood flow	Filtration fraction	Reabsorption	Maximal secretion	Diuresis	Toxicity
4 h	42.3	48.5	90.6	104.3	34.2	31.6	—16
1 day	40.8	38.1	104.5	102.4	37.4	41.2	—11
2 days	59.4	52.5	128.5	101.8	52.3	53.1	—12
3 days	73.8	66.6	130.0	100.7	71.0	82.0	—10
5 days	62.2	40.7	180.7	101.6	55.9	61.7	—18
7 days	78.6	58.3	179.3	102.6	64.5	72.5	—9
9 days	92.6	93.7	102.7	101.2	80.5	90.8	—3

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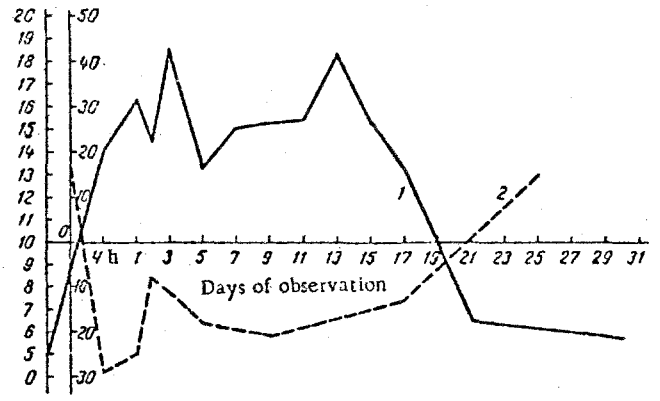

Fig. 1. Changes in toxic properties of blood serum and in excretory function of the liver of burned animals. Ordinate: migration of leukocytes in blood cultures (on the right) and percentage retention of bromsulphthalein in the blood (on the left); abscissa: days of observation. Numbers above abscissa denote increase in migration of leukocytes, those below denote inhibition of migration under the influence of test serum compared with control. 1) Retention of bromsulphthalein; 2) toxicity.

cultures was calculated as a ratio of the control, taken as 100, and expressed as the difference from a hundred with a plus or minus sign. Inhibition of leukocyte migration indicated the toxic action of the serum.

The excretory function of the liver was studied by the sulphobromophthalein method [6]. In parallel tests the kidney function was studied: spontaneous diuresis, glomerula filtration by the inulin method (a simplified version of Harrison's method), the maximal secretion, and the renal blood flow (by the diodrast method of White and Rolfe as modified by Beck, Brown, and Raaschou), tubular reabsorption of water, and plasma filtration fraction.

EXPERIMENTAL RESULTS

Four hours after burning, the serum of the burned animals had a distinct toxic action on the blood cultures, whereas before burning the serum of the same dogs stimulated migration of leukocytes. Later observations revealed that changes in the toxic action of the serum of the blood cultures occurred in two phases. The second wave of increase of its toxic action was observed on the 5th day after burning. The serum retained its toxic properties until the 25th-30th day after burning.

The whole period of delay in excretion of sulphobromophthalein from the blood thus took place against the background of marked toxicity of the serum of the experimental animals. Recovery of the excretory function of the liver coincided with disappearance of the toxic action of the serum on leukocyte migration.

Under the influence of burn trauma, all indices of kidney function likewise were disturbed (Table 1). As Table 1 shows, oliguria was observed in all the animals. Parallel with the decrease in excretion of urine, glomerula filtration was diminished. In some cases the level of glomerula filtration fell to a minimum of 15.7 ml/min 4 h after burning, indicating extreme inhibition of glomerula filtration function. After the 7th day the filtration function of the kidneys gradually began to recover.

Essential changes were found by studying the renal hemodynamics (a marked decrease in the effective renal blood flow). The renal circulation began to recover on the 9th day after burning. The most sensitive indicator of changes taking place in the kidneys after burn trauma is disturbance of the secretory activity of the tubular epithelium. In all the experiments, maximal secretion was reduced on the day of infliction of the burn. A decrease in secretory activity of the kidneys was found throughout the period of toxemia. Changes in the maximal secretion of the renal tubules coincided fairly closely with the dynamics of the toxic action of serum from the experimental animals on blood cultures: the sharp fall in maximal secretion in the first hours after burning coincided with the marked toxic effect of the serum on leukocyte migration. The changes both in maximal secretion and in toxicity of the serum were observed to occur in two phases. The most marked disturbances were found on the 1st and 5th days after burning. On the 9th day, with a decrease in toxicity of the serum, all indices of kidney function began to recover.

These experiments thus showed that the appearance of toxic properties in the serum as revealed by the blood culture method was constantly accompanied by severe changes in renal and hepatic function. This parallel appeared from the first hours after burning and persisted throughout the acute period of the disease. Two phases were observed in the variation in toxicity of the blood and pathological changes in the hepatorenal system of the experimental animals. The second wave of deterioration coincides with the onset of suppurative liquefaction of necrotic tissues at the site of the burn. The results of these experiments show that toxic products formed in the body as a result of thermal injury play an important role in the pathogenesis of hepatorenal insufficiency. The liver and kidneys respond particularly acutely to the toxic factor, because they are mainly responsible for the detoxication and elimination of foreign substances from the body. It may be concluded from these results that the toxemia plays an important role in the development of hepatorenal insufficiency after thermal injury.

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