increase in the cyclic AMP concentration in the CSF also is observed [10]. Bacterial pyrogens are known to have an indirect action, through the formation of endogenous pyrogens [4]. In the present experiments with pyrogenal, therefore, theophylline could enhance the pyrogenic action of endogenous pyrogen formed under the influence of pyrogenal, and able to penetrate into the brain. Theophylline also raises the cyclic AMP concentration not only in the brain, but also in other organs and tissues. Since cyclic nucleotides are universal biological regulators of cell metabolism [3], it is perfectly possible that when the cyclic AMP level is raised, endogenous pyrogen formation is increased under the influence of pyrogenal.

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BLOOD ANTIDIURETIC ACTIVITY AND PHARMACOLOGICAL CORRECTION OF THE HYPOTHALAMIC-NEUROHYPOPHYSEAL SYSTEM AFTER THERMAL TRAUMA

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An essential role in the pathogenesis of burns is played by the neurohypophyseal hormone vasopressin [10]. Some workers largely attribute the development of the oliguria and anuria which follow burns to the release of large quantities of antidiuretic hormone (ADH) from the neurohypophysis into the blood stream as a result of nociceptive stimulation induced by burn trauma. Meanwhile the view has been expressed [9] that a key place in the mechanisms of disturbance of the excretory function of the kidneys is occupied by circulatory disorders due primarily to a reduction in the circulating blood volume because of extensive plasma loss and the escape of fluid from the blood vessels into the tissues of burned subjects. However, as Kochetygov [4] points out, the fact must be borne in mind that the reduction in the circulating fluid volume during the development of burns is in turn a powerful stimulus to the increase in ADH secretion. This, in the writers' view, creates the conditions for a prolonged rise in the blood vasopressin concentration in burned subjects. Morphological investigations of the hypothalamic-neurohypophyseal system [6] have shown that its response to thermal trauma is phasic in character; however, the changes in antidiuretic activity (ADA) of the blood in the course of burns have so far received little study.

KEY WORDS: thermal trauma; hypothalamic-neurohypophyseal system.

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TABLE 1. Changes in Antidiuretic Activity of Blood Plasma (in %) and 24-h Diuresis (in ml) of Rabbits in Response to Burn Trauma (M ± m)

Experimental conditions	Group of animals					
	control		with injury to anterior part of hypothalamus		with injury to posterior part of hypothalamus	
	ADA	diuresis	ADA	diuresis	ADA	diuresis
Before burns	+ (19,3±7,5)	114±19	+ (4,3±4,6)	173±31	— (49,3±10,0)	120±41
After burns						
2 h	— (50,0±11,1)*	—	— (49,0±4,4)*	—	— (88,0±5,7)‡	—
1 day	— (49,3±10,7)*	36±9†	+ (20,9±3,6)‡	25±14*	— (29,5±10,7)	17±7‡
2 days	+ (42,7±15,3)	57±16	— (18,8±4,4)‡	34±13†	+ (17,6±9,4)†	88±23
1 week	— (37,4±2,6)*	37±13†	— (28,3±2,3)†	38±11†	— (28,3±9,3)	49±16‡
2 weeks	— (22,4±6,2)†	43±28	— (26,1±5,5)†	34±25†	— (39,0±12,7)	—

Legend. 1. A minus sign before parentheses denotes antidiuretic reaction, plus sign a diuretic reaction of the plasma. 2. *$P < 0.001$, †$P < 0.01$, ‡$P < 0.05$ compared with initial data.

The object of this investigation was to study the blood vasopressin concentration in burned rabbits (intact and with reactivity modified by preliminary injury to the anterior and posterior zones of the hypothalamus [2]), by a method of biological assay, and also to study the effect of pharmacological blockade of activity of the hypothalamic-neurohypophyseal system on the course of burns.

EXPERIMENTAL METHOD

Experiments were carried out on 18 male rabbits weighing 2-2.5 kg. Six rabbits served as the control, in seven rabbits a focus of injury 2-3 mm in diameter was produced bilaterally by means of a stereotaxic apparatus in the anterior part of the hypothalamus in the region of the supraoptic and preoptic nuclei (stereotaxic coordinates from Marsala and Fifkova's atlas [5]: AP −4; D, S 1.5; V −2), and in five rabbits similar injuries were produced in the posterior hypothalamic nuclei (AP +2.5, D, S 1; V −3). At the end of the experiments the location of the destructive lesions in the brain was verified morphologically. A burn affecting 12% of the skin surface was inflicted by means of an electric heater (100°C, exposure 30 sec, 1 week after the last injury to the hypothalamus). The depth of the burn corresponded to IIIB degree. The plasma ADA of the rabbits were determined by biological assay based on the percentage inhibition of diuresis of rats (males weighing 150-200 g), kept in a state of hyperhydration and alcohol-pentobarbital anesthesia [7, 13]. A similar burn was inflicted on 23 rats (males weighing 200-250 g), of which 11 served as the control, and the other 12 received an intraperitoneal injection of ethyl alcohol, which blocks the activity of the hypothalamic supraoptic nuclei, in a dose of 0.2 ml/100 g body weight, in a 25% dilution with physiological saline, immediately and again 24 h after burning. The 24-h diuresis was determined in all animals.

EXPERIMENTAL RESULTS

Mean values of the plasma ADA of the rabbits during the 2 weeks before burning are given in Table 1. In all groups of animals studied the dynamics of the plasma ADA was phasic in character. Three periods of change in the blood vasopressin concentration of the rabbits after burning can be distinguished: 1) an increase immediately after burning; 2) a decrease on the 1st-2nd day; 3) a second increase, but not reaching the level of the first period. This course is evidently due to the phasic character of the response of the hypothalamic-neurohypophyseal system to burn trauma and, in particular, the phasic character of liberation of ADH into the blood stream. The mechanism of the diuretic phase, observed on the 1st-2nd day after burning, may be connected with temporary exhaustion of the neurohypophyseal depot, inhibition of ADH secretion by the previous high concentrations of the hormone by a negative feedback mechanism, and also depression of hypothalamic stimulation during this period of time. The characteristics of the changes in plasma ADA in response to thermal trauma, described above, correspond on the whole to the dynamics of development of the oliguria after burns (Table 1), but no clear quantitative correlations could be found. This suggests that a disturbance of the neurohumoral regulating system is one of the mechanisms, but not the only cause of the disturbances of kidney function after burns.

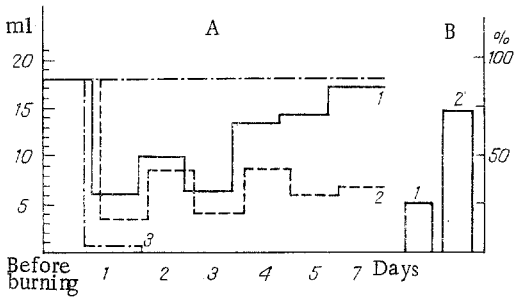

Fig. 1. Effect of blocker of antidiuretic hormone on development of oliguria in rats after burns. 1) Blocker; 2) control; 3) animals which died. Abscissa, time after burning (in days); ordinate: A) diuresis (in ml); B) number of dying animals (in %).

Meanwhile, as the results of investigation of the plasma ADA of the rabbits show, modification of the animal's reactivity by preliminary injury to the anterior and posterior zones of the hypothalamus led to a qualitatively different response of the hypothalamic-neurohypophyseal system to burn trauma. For instance, whereas in animals with injury to the anterior zone of the hypothalamus, just as in the control rabbits, thermal trauma caused a shift of plasma activity mainly toward the "antidiuretic" side (indicating stimulation of functional activity of the hypothalamic-neurohypophyseal system), in rabbits with a posterior hypothalamic lesion the response was opposite in character. Before burning the plasma of this group of animals, by contrast with the previous group, had marked antidiuretic activity, which was enhanced even more immediately after burning. Later, however, the plasma ADA fell below its initial level. This suggests inhibition of liberation of ADH into the blood stream. Hence in this case there was a predominant lowering of the activity of the hypothalamic-neurohypophyseal system compared with the initial state. The mechanism of this phenomenon may be due to increased excitability (with simultaneous depression of activity) of structures of the posterior zone of the hypothalamus after their partial injury [1, 2]. Against this background a stressor agent (burns, for instance, evokes marked activation of the posterior part of the hypothalamus [1, 2], which inhibits activity of the anterior hypothalamus reciprocally [3, 12], and, in particular, it evidently inhibits ADH secretion in the supraoptic nuclei.

The writers showed previously [2] in experiments on 385 rabbits (116 with injury to the anterior and 126 with injury to the posterior part of the hypothalamus) that the mortality after burns in animals with injury to the anterior hypothalamus is significantly higher (60%) than in rabbits with injury to the posterior hypothalamus (30%), if the burn trauma is of equal severity. This can be taken to be somehow connected with the decrease in activity of the hypothalamic-neurohypophyseal system in response to thermal injury described above. The results of experiments with injection of ethyl alcohol, which blocks activity of the hypothalamic supraoptic nuclei, into burned rats are in agreement with this hypothesis. Eight of the 11 control animals died on the 1st or 2nd day after burning, with a picture of persistent anuria (Fig. 1). The three surviving rats developed oliguria with some tendency toward an increase in diuresis on the 2nd day after trauma. Three of the 12 treated rats died, but with signs of oliguria. The decrease in diuresis on the 1st-2nd day after burns in the nine surviving animals of this group was less marked than in the control, and starting with the first week after burning a significant increase in diuresis was observed, although it still remained below the initial level (Fig. 1). Statistical analysis of the results [8] showed that the differences both in survival and in the volume of diuresis between the control and experimental groups of animals are significant ($P < 0.05$). In the control rats surviving on the 2nd day after burning, just as in the control burned rabbits (Table 1), a tendency was observed for the diuresis to increase, indicating that the character of the response of the hypothalamic-neurohypophyseal system was similar in character in the animals with burns.

The results thus demonstrate the phasic and prolonged character of liberation of ADH into the blood stream in response to burn trauma. The decrease in activity of the hypothalamic-neurohypophyseal system, in the writers' view, is a favorable factor increasing the resistance of the animal to thermal injury.

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CYTOPHOTOMETRIC STUDY OF TOTAL PROTEIN DYNAMICS IN GASSERIAN GANGLION NEURONS IN KERATITIS

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Cytophotometric studies have shown that the functioning of neurons is accompanied by changes in their nucleic acid and protein content. This rule applies not only under physiological [1, 3-4, 9-10], but also under pathological conditions. For example, changes in the protein content in Gasserian ganglion neurons have been described in experimental traumatic pulpitis [8].

Since the trigeminal nerve participates in the regulation of functions of the cornea and other structures of the eye, the writers postulated that neurons of the Gasserian ganglion, one of the main structures in the trigeminal nerve system, may undergo structural and metabolic changes after injury to the peripheral portion of the reflex arc. Such a situation evidently arises in keratitis, induced by neurogenic, traumatic, bacterial, viral, chemical, and physical factors. To test this hypothesis the investigation described below was undertaken to determine the total protein content in neurons of the Gasserian ganglion during the development of keratitis due to burns.

TABLE 1. Mean Relative Percentages of Different Groups of Cells in Control and in Rabbits with Various Stages of Burn Keratitis

Group of cells	Control	Stage I	Stage II	Stage III	Stage IV
1	14	17	4	4	13
2	51	48	31	33	42
3	33	33	45	44	28
4	2	2	20	19	17

KEY WORDS: Gasserian ganglion; total protein; keratitis.

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