12. F. Hammersen, Symposium on Capillary Exchange and the Interstitial Space: Proceedings, Berlin (1972), pp. 43-63.
13. G. Hauck, Bibl. Anat., No. 12, 356 (1973).
14. J. M. Williamson, J. Physiol. (London), 202, 326 (1969).
15. S. Yamada, Jpn. J. Physiol., 36, 619 (1986).

CHANGES IN THE LUNGS IN THE EARLY PERIOD OF CLOSED CHEST INJURY IN RATS

V. I. Kulitskaya, M. A. Sapozhnikova,
M. V. Barinova, T. V. Korotkova,
T. V. Fedichkina, and T. D. Finogenova

UDC 617.54-001-039.11-06:
616.24-091.8]-092.9

KEY WORDS: trauma; carbon dioxide; chest.

The CO_2 concentration in arterial blood depends mainly on the state of the external respiratory system [4, 8]. The high oxygen consumption in the lungs found in the early post-traumatic period of closed chest injury and also the fact that the value of p_aO_2 can be influenced by activation of free-radical lipid oxidation in the lungs [2, 3] suggest that metabolic processes in the lungs may be involved in regulation of the arterial blood CO_2 concentration.

The aim of this investigation was to study the time course of metabolic processes and their morphological expression in the lungs in the early period after closed chest trauma, in the injured and uninjured lung separately, in order to discover the importance of these processes in the changes in the arterial blood CO_2 concentration.

EXPERIMENTAL METHOD

Experiments were carried out on 130 male Wistar rats weighing 200-250 g. A contusion of the lung was inflicted by means of a spring-operated pistol, in the right half of the chest [2, 3]. The CO_2 concentration in the end-portion of the expired air (f_ACO_2) was recorded in rats, fixed in the prone position, on an MKh-6202 gas analyzer. Blood was taken by puncture from the left and right ventricles for determination of pO_2 and pCO_2 on a "Corning" gas analyzer (England). Values of p_ACO_2, the CO_2 concentration in arterial and mixed venous blood (C_aCO_2, C_vCO_2) [4], the difference between p_vCO_2 and p_ACO_2 ($p_{v-a}CO_2$), and the difference between C_vCO_2 and C_aCO_2 ($C_{v-a}CO_2$) were calculated. The rats were decapitated and the concentrations of protein [5], total lipids [10], and glucose [1] were determined in the right and left lung (RL and LL), and morphologic and electron-microscopic investigations also were undertaken. Sections through RL and LL were stained with azure-eosin, orcein, and picrofuchsine. Material for electron microscopy was fixed in paraffin and 1% osmic acid solution by Palade's method and embedded in Araldite. Semithin sections were stained with toluidine blue. Ultrathin sections were cut on an LKB 8-8800 III Ultrotome (Sweden) and stained with uranyl acetate and lead citrate. The material was examined in the ÉVM-100L electron microscope. To analyze the state of the lung over a period of time, parameters obtained in intact rats and 1 and 2 h and 1 and 7 days after trauma were studied. The results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

The upper and middle lobes of RL were injured as a result of trauma. No mechanical injuries were found in LL. Arterial hypoxemia developed in the rats during the first hours

Laboratory of Experimental Pathology, Department of Pathomorphology, N. V. Sklifosovskii Emergency Aid Research Institute, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. K. Permyakov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 108, No. 10, pp. 417-420, October, 1989. Original article submitted December 14, 1987.

 0007-4888/89/0010-1400 $12.50

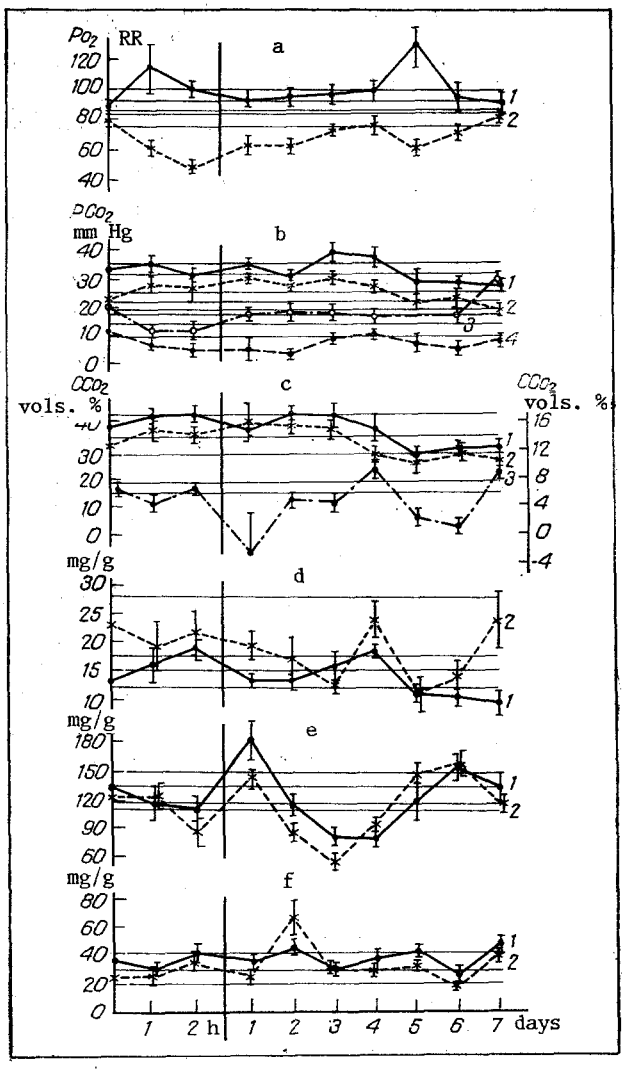

Fig. 1. Changes in gas exchange in lungs and concentrations of glucose, protein, and total lipids in injured RL and intact LL in early post-traumatic period of closed chest trauma in rats (M ± m). Abscissa, time after contusion of chest; ordinate, a: 1) respiration rate (RR), cycles/min, 2) p_aO_2; b: 1) p_vCO_2, 2) p_aCO_2, 3) p_ACO_2, 4) $p_{v-a}CO_2$; c: 1) C_vCO_2, 2) C_aCO_2, 3) $C_{v-a}CO_2$; d: glucose concentration in RL (1) and LL (2); e: protein concentration in RL (1) and LL (2); f: total lipid concentration in RL (1) and in LL (2).

and 5 days after trauma (Fig. 1a, 2), but it was not present at any other time of observation. A fall of p_aO_2 occurred during the period of quickening of respiration (Fig. 1a, 1). The time course of the changes in p_aCO_2 and C_aCO_2 in the acute period of trauma showed no correlation with changes in the character of pulmonary ventilation. Arterial hypercapnia was discovered 1 and 3 days after trauma, when the respiration rate returned to its initial level. The appearance of arterial hypercapnia, 24 h after trauma of the chest, for example, cannot be explained by a considerable increase in the inflow of CO_2 into the lungs (p_vCO_2 and C_vCO_2) and simultaneous impaired elimination of CO_2 from the lungs (p_ACO_2), for the above parameters at this period did not differ statistically significantly from the corresponding parameters for intact rats (Fig. 1b, c). According to the values of $p_{v-a}CO_2$ and $C_{v-a}CO_2$, removal of CO_2 from the lungs was minimal 1 and 6 days after trauma. The mean value of $C_{v-a}CO_2$ after 24 h was actually negative, for the mean value of C_vCO_2 was a little below the mean value of C_aCO_2 (Fig. 1c, 3). The value of p_ACO_2 did not differ significantly from that of p_ACO_2 of intact rats, but was sharply increased 7 days after trauma: it was statistically significantly higher than the value of p_ACO_2 of intact rats and p_aCO_2 (Fig. 1b, 3).

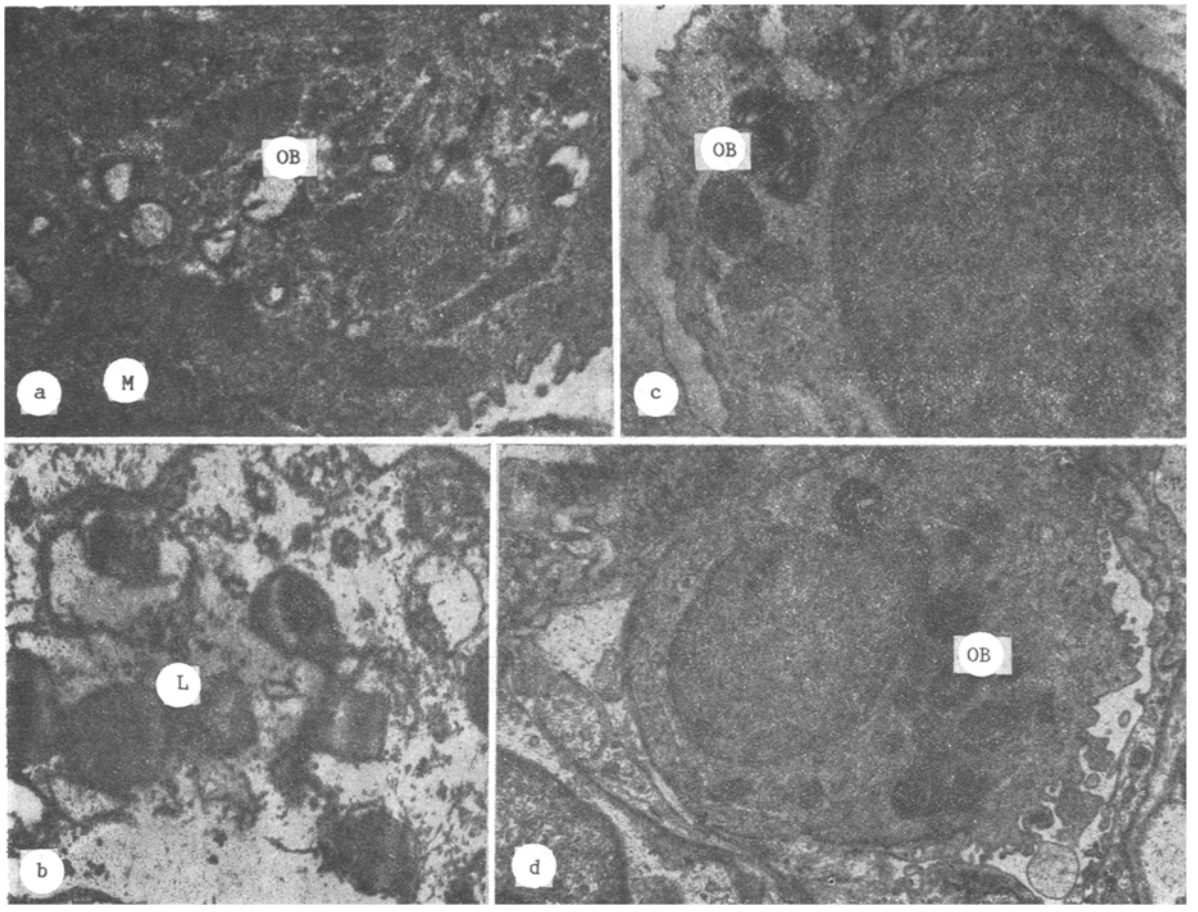

Fig. 2. Electron-microscopic changes in LL in early period after chest trauma. a) Fragmentation and vacuolation of osmiophilic bodies (OB) and increase in size and number of mitochondria (M) and condensation of their matrix in type II alveolocytes toward end of 1st day after trauma. 12,000 ×; b) enlargement of lipid inclusions (L) in cytoplasm of type II alveolocytes 2 days after trauma. 18,000 ×; c) decrease in number of osmiophilic bodies and destruction of cristae of mitochondria in type II alveolocytes 5 days after trauma. 20,000 ×; d) increase in number of osmiophilic bodies with high osmiophilic density in type II alveolocytes 7 days after trauma. 12,000 ×.

These results suggest that CO_2 may be formed in the lung tissue itself and enter the arterial blood and the lung capillaries. We know that CO_2 formation in tissues depends on access of O_2 and on the nature of the substrate oxidized [6]. In the acute period of chest trauma, phasic changes in concentrations of proteins, lipids, and glucose were found in the poorly (RL) and well (LL) ventilated areas of the lungs. During the first week after trauma two waves of consecutive accumulation, first of carbohydrates (after 2 h and 4 days), and then of proteins (1st and 6th days), and later still of lipids (2nd and 7th days) were observed in both lungs. The period of accumulation of substrates was followed by a period of restoration of their concentration up to (glucose and lipids) or below (proteins) that found in intact rats. More marked accumulation of total lipids was observed in the intact LL, and of glucose in the injured RL compared with concentrations of these substrates in LL and RL of intact rats (Fig. 1d, e, f). In LL, in the early post-traumatic period, a tendency was noted for the glucose concentration to fall, besides the times of glucose accumulation mentioned above, when it was restored to the same level as in LL of intact rats.

The simultaneous change in the concentrations of the substrates in RL and LL in the early post-traumatic period was evidently due to changes in their entry into the lungs in the venous blood [8, 10]. However, differences in concentrations of glucose and lipids in RL and LL were evidently determined by differences in the supply of O_2 into the alveoli.

This suggestion was confirmed by morphological investigation of the lungs. On the side of injury (in RL) atelectases and dystelectases of different extent were found. Electron-microscopically, a decrease in the number of osmiophilic bodies, their displacement to the periphery of the cell, and the release of individual osmiophilic bodies into the lumen of the alveoli were observed in type II alveolocytes in RL. In the intact LL, signs of an increased functional load on the structures of the air-blood barrier appeared, in the form of enlargement of the mitochondria of the type II alveolocytes and condensation of their matrix. Considerable accumulation of the lipid inclusions was observed 2 and 7 days after trauma in the cytoplasm of the type II alveolocytes (Fig. 2). However, accumulation of lipids, and in particular of fatty acids (FA), reduced the ability of the alveolocytes to synthesize their own FA [11], and also inhibited protein synthesis in them [12]. Glucose may partly suppress this inhibitory effect, and together with lactate, it is utilized in the lungs for FA synthesis [11, 12]. That may be why the accumulation of total lipids in the lungs of the intact rats and in rats after trauma to the chest was accompanied by a fall in the glucose concentration and products of aerobic degradation of glucose were utilized in the lungs for protein synthesis [7].

Some correlation was found between accumulation of substrates in the lungs in the acute period of chest trauma and the CO_2 concentration in the arterial blood and p_ACO_2. Thus accumulation of proteins (1st and 6th days) was accompanied by an increase in the total CO_2 concentration in the arterial blood up to or even above the CO_2 concentration in mixed venous blood during active elimination of CO_2 from the alveoli. CO_2 formation in the lungs evidently took place in areas with reduced ventilation, perhaps mainly in RL, or otherwise the CO_2 formed would have been eliminated through the alveoli. A sharp excess of p_ACO_2 over p_aCO_2 which we observed (on the 7th day) cannot be explained by the laws of CO_2 diffusion from the blood of the pulmonary capillaries into the alveoli, according to which the value of p_ACO_2 can be only equal to or less than the value of p_aCO_2 [4, 8]. It can be tentatively suggested that it was due to the formation of CO_2 in the ventilated alveoli. In this period, the results of biochemical and electron-microscopic studies showed accumulation of total lipids in the lungs, more especially in LL. Synthesis and oxidation of lipids in the cells require large quantities of O_2 [6], and that is evidently why accumulation of total lipids in the acute period of trauma took place in areas of the lungs with intact ventilation, in LL. Accumulation of lipids in the lung cells was probably accompanied by degradation of other substrates to CO_2, which was excreted from the alveoli, increasing the value of p_ACO_2.

Thus in the acute period of chest trauma overloading not only of gas exchange [8], but also of metabolism, arises in the intact areas of the lungs, and may be accompanied by changes in their structure. The results also suggest that the CO_2 concentration in arterial blood in the early post-traumatic period of closed test injury depends not only on the character of the pulmonary ventilation, but also, at the same time, on the metabolic processes in the lung tissue itself, that depend on substrates accumulating in it.

LITERATURE CITED

1. V. K. Gorodetskii, Modern Methods in Biochemistry [in Russian], Vol. 1, Moscow (1964), p. 311.
2. V. I. Kulitskaya and M. V. Barinova, Byull. Éksp. Biol. Med., No. 8, 157 (1987).
3. V. I. Kulitskaya and G. G. Rogatskii, Byull. Éksp. Biol. Med., No. 3, 287 (1986).
4. M. Navratil, K. Kadlec, and S. Daum, The Pathophysiology of Respiration [Russian translation], Moscow (1967).
5. V. M. Predtechenskii, L. T. Borovskaya, and V. M. Margolina, Laboratory Methods of Investigation [in Russian], Moscow (1950), p. 176.
6. A. Prosser, Comparative Physiology of Animals [Russian translation], Vol. 1, Mir, Moscow (1977), pp. 349-421.
7. Teodorescu-Escarcu, General Traumatic Surgery [in Russian], Medical Publishing House, Bucharest (1972).
8. L. L. Shik, Textbook of Clinical Physiology of Respiration [in Russian], Meditsina, Moscow (1980), pp. 107-179.
9. S. K. Compton, M. Hamosh, and P. Hamosh, Lipids, 17, No. 10, 696 (1982).
10. J. Folch, J. Ascoli, M. Lees, et al., J. Biol. Chem., 191, 833 (1951).
11. C. W. Lanner, M. Arborelius, E. W. Swenson, et al., Respiration, 34, 1 (1977).
12. W. M. Maniscalco, J. N. Finkelstein, and A. B. Parhurst, Biochim. Biophys. Acta, 751, 462 (1983).

13. J. A. Martinez, R. Parrilla, and M. S. Aguso, Biochim. Biophys. Acta, 760, 175 (1983).

ROLE OF THE ENDOTHELIUM IN THE DEVELOPMENT OF REACTIVE HYPEREMIA

V. F. Sagach and M. N. Tkachenko

UDC 616.005.2].3-092:616.13].14-018.74

KEY WORDS: reactive hyperemia; endothelium.

The development of reactive hyperemia is a fundamental phenomenon found in various vascular regions of the circulation [1]. An important role in the development of reactive hyperemia is ascribed to metabolic agents secreted during previous ischemia. An important role in the formation of vascular reactions has recently been discovered for the endothelium, which is involved in the mechanism of action of various agents on blood vessels through the secretion of endothelial relaxation factors [3, 4], which has recently been identified as an endogenous nitrate [8, 10]. The endothelium has been shown to take part in the development of vasomotor reactions to a change in the velocity of the blood flow [2]. It very probably has a role also in the development of postocclusive vasodilatation.

The aim of this investigation was to study whether the endothelium is involved in the development of reactive hyperemia.

EXPERIMENTAL METHOD

Experiments were carried out on 22 dogs weighing 15-20 kg, anesthetized with chloralose and urethane (0.05 and 0.5 g/kg, respectively, intravenously). The following series of experiments were carried out: I) to study the effect of chemical removal of the endothelium, II) to study the effect of blocking biosynthesis of derivatives of the cyclooxygenase pathway of arachidonic acid metabolism, III) to study the effect of lipoxygenase blockade, and IV) the effect of guanylate cyclase blockade on reactive hyperemia in the system of the femoral artery. The reaction was reproduced after circulatory arrest (compression of artery and vein) for a period of between 5 and 120 sec. Changes in blood flow were determined with the aid of an RK-2 electromagnetic blood flowmeter and recorded on a multichannel automatic writer. The reaction was recorded in the initial state, after which the endothelium was removed or blockade carried out, and reactive hyperemia was again induced. The endothelium was removed by injecting a solution of saponin (1 mg/ml) into the system of the femoral arteries and arresting the circulation for 5 min, thereby destroying the endothelial cells and selectively inhibiting endothelium-dependent relaxation [14]. Cyclo-oxygenase was blocked by intravenous injection of a solution of indomethacin (3 mg/kg), lipoxygenase by intravenous injection of quercetin solution (10 mg/kg), and guanylate cyclase by intravenous injection of a solution of methylene blue (4 mg/kg). Possible changes in reactivity of the vascular smooth muscles under the influence of the above chemical agents were monitored on the basis of the response to injection of papaverine (4 mg in 1 ml physiological saline). The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The postocclusive increase in blood flow depended strictly on the duration of preceding occlusion. This reaction was considerably reduced after chemical removal of the endothelium with saponin (Fig. 1). For instance, whereas in the animals before treatment with saponin the peak blood flow after its arrest varied from 24.4 ± 2.9% after occlusion for 5 sec to 167.4 ± 25.8% of the initial blood flow after occlusion for 2 min, after treatment

Department of Physiology of the Circulation, A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR, Kiev. (Presented by Academician of the Academy of Medical Sciences of the USSR B. I. Tkachenko.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 108, No. 10, pp. 421-423, October, 1989. Original article submitted May 3, 1988.

 0007-4888/89/0010-1404 $12.50