No significant differences in the relative proportions of LDH fractions were observed in the medullary RF between groups of rats distinguished by the response of their BP to emotional stress (Fig. 3).

Some distinguishing features of energy metabolism in the mesencephalic RF in control rats and in rats with a different time course of BP during emotional stress were thus found by a microbiochemical method of determination of LDH isozyme levels. It is difficult now to identify the concrete cause of these changes. However, it is important to note that significant lesions in the walls of the blood vessels were found [1, 2, 5] in this same part of the mesencephalic RF in the same model of emotional stress. It was suggested by the authors cited that these vascular lesions are associated with changes in metabolism of the neurons, glia, and endothelium of the intracerebral vascular network, caused by emotional stress.

The results of the present investigation confirm this hypothesis and demonstrate the specific character of carbohydrate metabolism in the mesencephalic RF both in the control and in emotional stress.

LITERATURE CITED

1. T. I. Belova and G. Jonsson, Byull. Éksp. Biol. Med., No. 7, 3 (1983).
2. T. I. Belova and G. Jonsson, Usp. Fiziol. Nauk, 16, No. 2, 61 (1985).
3. H. Maurer, Disc Electrophoresis [Russian translation], Moscow (1971).
4. O. L. Serov and Yu. S. Nechaev, Biokhimiya, No. 6, 1117 (1972).
5. T. I. Belova and G. Jonsson, Acta Physiol. Scand., 116, 21 (1982).
6. R. D. Cahn, N. O. Kaplan, L. Levine, and E. Lurilling, Science, 136, 962 (1962).
7. N. O. Kaplan, Brookhaven Symp. Biol., 17, 131 (1964).
8. R. Kvetnansky and L. Mikulaj, Endocrinology, 87, 738 (1970).
9. M. Palkovits, Brain Res., 59, 449 (1973).

GENERAL AND LOCAL RESPONSES OF THE PROTEOLYTIC SYSTEM IN EXPERIMENTAL PNEUMONIA

A. V. Kubyshkin

UDC 616.24-002-092.9-092:616.153.1:577.152.344-074

KEY WORDS: proteases; antiproteases; lungs; inflammation.

The role of the system of proteolytic enzymes and their inhibitors in the pathogenesis of inflammation in the lungs has been the subject of much research in recent years [7, 8, 11, 13]. The development of an imbalance in the proteases–inhibitors system has been demonstrated in the lungs during chronic inflammation [3, 6, 9, 10]. However, relations between the principal components of the system in the serum and the inflammatory process in the lungs during acute inflammation and during its transition into the chronic stage have not yet been studied.

The aim of this investigation was to compare the proteolytic and antiproteolytic potentials of the blood serum and bronchoalveolar secretion during the development of experimental pneumonia.

EXPERIMENTAL METHODS

Inflammation in the lungs was produced in 98 albino rats, initially weighing 150-200 g, by the introduction of a Kapron thread, 0.2 mm in diameter and 2.5-3 cm long, into the trachea. Considering that the pneumonia simulated by this method can be evaluated both as acute (until 1-2 months) and as chronic (over 2 months) stages of the process [2], the investigations were

---

Department of Medical Climatology and Clinical Physiology, I. M. Sechenov Research Institute of Physical Methods of Treatment and Medical Climatology, Yalta.

(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 10, pp. 400-402, October, 1986. Original article submitted March 5, 1985.

0007-4888/86/0010-1334$12.50

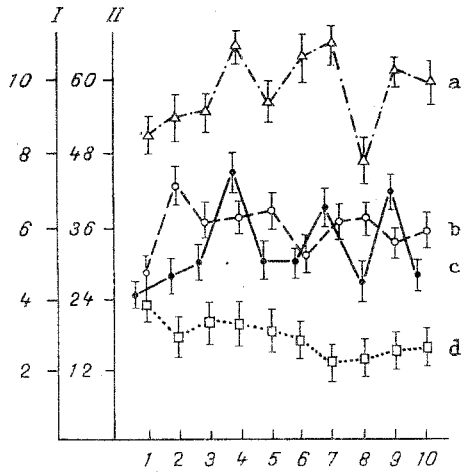

Fig. 1

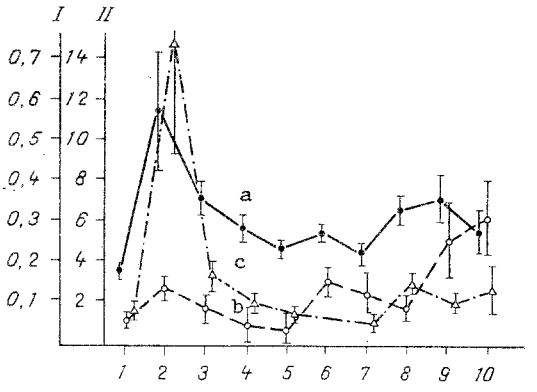

Fig. 2

Fig. 1. Time course of changes in EA and activity of principal proteolysis inhibitors in rat blood serum during development of experimental pneumonia. Abscissa, duration of inflammation: 1) control, 2) 1 day, 3) 3 days, 4) 1 week, 5) 2 weeks, 6) 1 month, 7) 2 months, 8) 3 months, 9) 4 months, 10) 6 months. Ordinate: I) α_2-MG and TASTI activity (in inhibition units – IU/ml); II) EA activity (in μmoles BAEE/ml/h) and α_1-PI activity (in IU/ml). a) TASTI, b) α-PI; c) EA; d) α_2-MG.

Fig. 2. Time course of changes in protein concentration and proteolytic activity of BAW of rats during development of experimental pneumonia. Ordinate: I) protein concentration (in g/liter); II) TLA and ELA (in mU/ml). a) Protein; b) TLA; c) ELA. Remainder of legend as for Fig. 1.

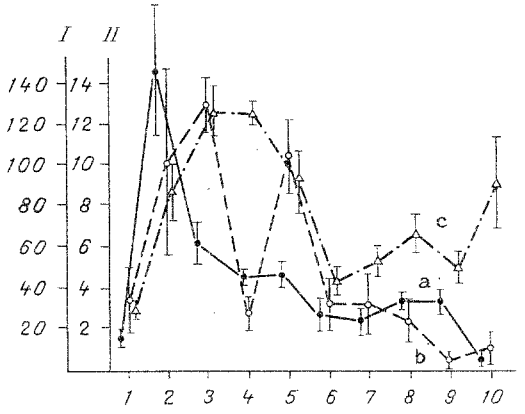

Fig. 3. Time course of changes in parameters of inhibitory potential of BAW from rats during development of experimental pneumonia. Ordinate: I) ATA (in mIU/ml); II) ASI and α_2-MG levels (in mIU/ml). a) ATA; b) ASI level; c) α_2-MG level. Remainder of legend as for Fig. 1.

conducted 1 and 3 days, 1 and 2 weeks, and 1, 2, 3, 4, and 6 months after its induction. At each time six to ten animals were investigated. The control consisted of 21 rats with no inflammation of their lungs. Blood for testing was obtained by catheterization of the right ventricle of the rats under thiopental anesthesia. The animals were killed by exsanguination, the heart-lung complex was removed, and bronchoalveolar washings (BAW) were obtained by irrigating the lungs with 10 ml of 0.9% NaCl solution in 8-10 aliquots.

Esterase activity (EA) [1], activity of proteinase α_1-inhibitor (α_1-PI), and α_2-macroglobulin (α_2-MG) [5], and of thermostable and acid-stable trypsin inhibitor (TASTI) [4] in the blood serum were determined. The protein concentration and trypsin- and elastase-like activity (TLA and ELA, respectively) and the level of acid-stable inhibitors (ASI) [6] were measured in BAW after centrifugation at 5000 rpm. To determine free antitryptic activity (ATA) and α_2-MG activity, 0.5-1 ml of washings were taken for analysis, and the subsequent determination was carried out as described for blood serum [5].

EXPERIMENTAL RESULTS

The parameters studied showed regular changes during the development of inflammation in the lungs. The α_1-PI and EA levels in the blood serum rose sharply and TASTI activity reached maximal values after a gradual increase on the 7th day of the investigation (Fig. 1). Marked changes in these parameters continued for 1 or 2 months of development of inflammation, after which they became less pronounced. After 3 and 6 months no significant increase in EA and TASTI activity was observed. Toward the end of the investigation, α_1-PI activity also fell to the upper limits of normal, whereas the α_2-MG level was lowered at all times of the investigation, and the decrease was significant after 2 weeks of inflammation.

The protein concentration was increased threefold, TLA twofold, and ELA ninefold in BAW only 24 h after introduction of the thread into the trachea (Fig. 2). An increase of activity also was observed in the inhibitor system: ATA was increased ninefold and the ASI and α_2-MG levels more than twofold (Fig. 3). However, at times corresponding to the acute stage of the inflammatory process, activity of the inhibitors remained stable and at a high level, 2-4 times higher than in normal animals, whereas protease activity did not go beyond the limits of control values. Later, toward 3 months of development of inflammation, ELA was doubled, and TLA was 5 times higher than the normal value after 4-6 months. Under these circumstances ATA 6 months after the beginning of inflammation was reduced by 3.5 times and the ASI level fell close to zero. Only α_2-MG activity remained at higher values than in the control at all times of the investigation.

The results show that activity of the inhibitors in the blood serum and bronchoalveolar secretion is increased during acute inflammation in the lungs, whereas during chronic pneumonia the inhibitory potential falls. Analysis of correlation between changes in the parameters of the proteases—inhibitors systems in the blood serum and BAW during the development of bronchopulmonary inflammation showed that correlation is strong between α-PI and ATA ($r = 0.86$) and also between ATA and the protein concentration ($r = 0.88$) in the washings. This fact, first, confirms the view that α-PI, which reaches the alveoli by transudation from the serum [12], plays a leading role in the protection of the alveolar structures of the lungs; second, it enables the reduction of α_1-PI activity in the serum to the control level during chronic pneumonia to be interpreted as evidence of relative deficiency of the inhibitor [3, 9], since ATA of the bronchoalveolar secretion virtually ceases to be determinable under these circumstances. However, the absence of correlation between the remaining parameters of the blood and BAW is evidence that, during clinical investigations, the state of components of the protease-inhibitory system must be analyzed actually in the bronchoalveolar structures in order to obtain a more accurate estimate of the participation of proteolytic enzymes and their inhibitors in the pathological process.

The authors are grateful to Professors V. A. Protsenko and V. G. Bokshe for useful advice during the planning of this investigation and discussion of its results.

LITERATURE CITED

1. O. A. Gomazkov, N. V. Komissarova, L. V. Bol'shakova, and N. N. Teplova, Kardiologiya, No. 6, 25 (1972).
2. L. I. Gorbatsevich, Problems in Pulmonology [in Russian], No. 7, Leningrad (1978), p. 289.
3. G. O. Kaminskaya, N. L. Zhukova, and L. V. Ozerova, Ter. Arkh., No. 10, 74 (1984).
4. V. F. Nartikova and T. S. Pashkina, Biokhimiya, No. 2, 282 (1968).
5. V. F. Nartikova and T. S. Pashkina, Vopr. Med. Khim., No. 4, 494 (1979).
6. O. G. Ogloblina, L. V. Platonova, L. V. Myasnikova, et al., Vopr. Med. Khim., No. 3, 387 (1980).
7. O. G. Ogloblina, Vopr. Med. Khim., No. 1, 3 (1984).
8. N. V. Putov, I. V. Pokhodzei, and L. A. Kolodkina, Ter. Arkh., No. 3, 144 (1985).

9. N. V. Syromyatnikova, G. O. Kaminskaya, T. A. Kochegura, and N. L. Zhukova, Sov. Med., No. 10, 74 (1984).
10. A. G. Khomenko, G. O. Kaminskaya, Ya. A. Pylluste, et al., Ter. Arkh., No. 3, 60 (1983).
11. J. E. Gadek, G. W. Hunninghake, G. A. Fells, et al., Bull. Eur. Physiopath. Resp., 16, 27 (1980).
12. J. E. Gadek, G. A. Fells, R. L. Zimmerman, et al., J. Clin. Invest., 68, 889 (1981).
13. R. A. Stockley, Clin. Sci., 64, 119 (1983).

EFFECT OF TEMPORARY HYPOVOLEMIA ON EARLY POSTRESUSCITATION CENTRALIZATION OF THE CIRCULATION AND SURVIVAL OF ANIMALS RECOVERING AFTER CLINICAL DEATH

A. Ya. Evtushenko, L. A. Shalyakin, and A. S. Razumov

UDC 616-036.882-036.82-092.9-07:616.12-008.3-02:616.151.11-021.6

KEY WORDS: postresuscitation period; centralization of the circulation; hypovolemia.

The writers showed previously that centralization of the circulation takes place in the initial stage of the postresuscitation period, and that the intensity and duration of this response correlates postively with the severity of the state before recovery [1].

The aim of this investigation was to study the effect of temporary exclusion of part of the blood volume from the circulation on cardiac output, the distribution of its principal fractions, and the survival rate of animals recovering from clinical death.

TABLE 1. Cardiac Output and Its Principal Fractions in Postresuscitation Period (M ± m)

Parameter	Experimental conditions	Initial value	Postresuscitation period								
			min						h		
			3	5	10	15	20	30	1	2	3
CO, ml/kg	Experiment	140±7,3	140±15,3[c]	117±9,6[c]	91±8,8[a, c]	97±11,8[a,c]	110±11,5	115±13,5[b]	154±26,7	120±20,9	93±20,4[b]
	Control	162±9,3	264±17,9[a]	256±19,8[a]	203±28,7[b]	172±16,8	132±14,7	143±8,6[b]	139±8,9[b]	116±12,1[a]	100±9,8[a]
Supradiaphragmatic fraction, ml/(min·kg)	Experiment	70±9,3	86±12,8[c]	68±11,0[c]	50±9,9[c]	48±9,4[b, c]	58±11,4	58±8,8	90±19,5	43±8,6[a]	35±8,5[a]
	Control	77±6,3	168±16,7[a]	167±14,9[a]	119±19,5[b]	100±10,3[b]	72±10,6	73±7,9	62±6,1	47±6,5[a]	36±5,2[a]
Subdiaphragmatic fraction, ml/(min·kg)	Experiment	70±8,0	52±7,4[b, c]	49±6,8[c]	41±4,8[a, c]	49±4,6[a, c]	52±5,4[b]	57±7,8[bd]	64±12,9	77±12,9	58±12,2
	Control	85±5,3	96±10,5	89±8,3	84±13,3	72±9,5	60±6,4[a]	70±4,4[a]	77±6,2	69±7,1[b]	64±6,9[a]
CCC, units	Experiment	0,50±0,03	0,63±0,06[b]	0,58±0,07	0,54±0,09	0,49±0,06[d]	0,52±0,06	0,50±0,04	0,58±0,05[c]	0,36±0,02[a]	0,38±0,03[b]
	Control	0,47±0,02	0,64±0,03[a]	0,65±0,03[a]	0,59±0,04[a]	0,58±0,03[a]	0,54±0,03[b]	0,51±0,03	0,45±0,03	0,40±0,03[b]	0,36±0,03[a]

Legend. a) $P < 0.05$-0.001 (Student's test); b) $P \leq 0.05$-0.01 (Wilcoxon's test) compared with initial data; c) $P < 0.05$-0.001 (Student's test); d) $P \leq 0.05$-0.01 (Wilcoxon–Mann–Whitney test) compared with control.

Department of Pathological Physiology, Kemerovo Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 10, pp. 402-404, October, 1986. Original article submitted September 12, 1985.

