The antiarrhythmic action of TT can also be exhibited in the case when arrhythmias in the late stage of infarction are due to the circulation of excitation. It has recently been shown that in dogs in the late stage of infarction, cells of the working myocardium generate a sodium-dependent action potential which, spreading at reduced speed over the nonhomogeneous myocardium, can induce circulation of excitation [11]. In that case a decrease in the velocity of conduction of excitation as a result of a decrease in the sodium current under the influence of TT can lead to a conduction block and can stop the arrhythmia.

It can be concluded that the fact that arrhythmias can be abolished by the action of TT, a specific blocker of the fast inward sodium current, discovered by this investigation will help to reveal the true causes of development of arrhythmias and of the antiarrhythmic effect of drugs in the late stage of myocardial infarction.

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ACTIVATION OF LIPID PEROXIDATION DURING PAINFUL EMOTIONAL STRESS

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Accumulation of primary and secondary lipid peroxidation (LPO) products were investigated by ultraviolet spectrophotometry and fluorescence of Schiff bases in various tissues of Wistar rats subjected to painful emotional stress (PES). The quantity of LPO products was shown to increase under the influence of PES mainly in the heart, and also significantly, although to a lesser degree than in the heart, in skeletal muscles and brain. The increase in content of hydroperoxides in all the organs studied was smaller than the increase in the content of fluorescent Schiff bases, the end products of LPO.

KEY WORDS: painful emotional stress; lipid peroxidation.

The role of emotional stress in the etiology of human diseases is widely known, but the actual metabolic link through which the harmful action of high concentrations of catecholamines and glucocorticoids in stress is effected requires further study. One of the main mechanism of injury to cell structures is activation of lipid peroxidation (LPO) [2, 3]. It was shown recently that after painful emotional stress (PES) an increase

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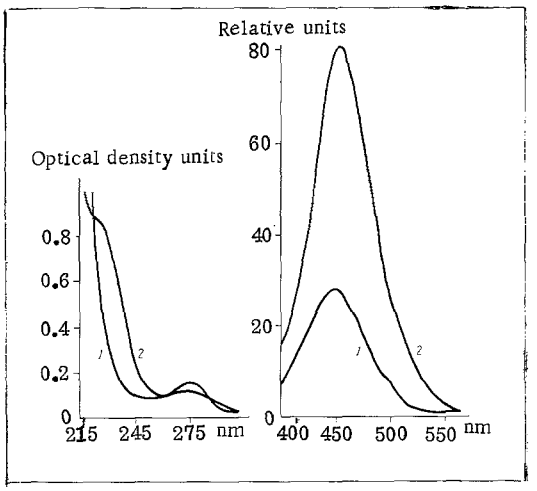

Fig. 1 Fig. 2

Fig. 1. Typical absorption spectra of heart muscle lipids from rats before and after PES. 1) Lipids isolated from heart muscle of control animals; 2) lipids isolated from heart muscle of animals exposed to PES. Abscissa, wavelength (in nm); ordinate, optical density (in optical density units).

Fig. 2. Characteristic fluorescence emission spectra of heart muscle lipids of rats before and after PES. 1) Lipids isolated from heart muscle of control animals; 2) lipids isolated from heart muscle of animals exposed to PES. Abscissa, wavelength (in nm); ordinate, intensity of fluorescence (in relative units).

in the intensity of chemiluminescence of lipids isolated from heart muscle is observed and, on this basis, it was concluded that LPO is activated during stress [5, 7]. However, measurement of chemiluminescence is not a direct quantitative method of estimating the contents of LPO products in tissues [3]. In the present investigation primary molecular products of LPO (hydroperoxides of polyene lipids) and of the end products of LPO (fluorescent Schiff bases) were therefore determined in the brain, heart, and skeletal muscles of rats exposed to PES.

EXPERIMENTAL METHOD

Male Wistar rats weighing 170-200 g were used. PES was produced in the form of an anxiety neurosis by Desiderato's method [11]. The main features of this model of PES are: First, the presence of conflict between an established conditioned reflex of avoidance of electric shock by jumping on a platform and unconditioned nociceptive stimulation of that platform, and second, sustained expectation of a painful electric shock. Lipids were isolated from the brain, heart, and gastrocnemius muscle by Folch's method [12]. Accumulation of hydroperoxides in polyene lipids was estimated from the ultraviolet absorption spectrum of a solution of lipids in methanol–hexanol (5 : 1), characteristic of diene conjugates, assuming that the molar coefficient of extinction at $\lambda_{max} = 232$ nm is 2.1×10^4 $M^{-1} \cdot cm^{-1}$ [8]. The absorption spectra of the lipids were recorded on a Shimadzu MPS-50L spectrophotometer. The end products of LPO – products of interaction between short-chain dialdehydes and aminophospholipids – were recorded as fluorescence spectra of solutions of the lipids in chloroform with the fluorescence excitation maximum at 360 nm and emission maximum in the region of 420-440 nm [10] on an Aminco–Bowman spectrofluorometer. Before each series of measurements the instrument was calibrated against a standard solution of quinine sulfate (1 μg/ml in 0.1 N H_2SO_4).

EXPERIMENTAL RESULTS

Typical UV absorption spectra (Fig. 1) and emission spectra of fluorescence (Fig. 2) of solutions of lipids isolated from the heart muscle of the control animals and animals exposed to PES are illustrated in

TABLE 1. Accumulation of LPO Products in Tissues of Wistar Rats Exposed to PES (M ± m)

Test object	Lipid hydroperoxides, optical density units		Accumulation of hydroperoxides following PES nmoles/mg lipids	Fluorescence of Schiff bases, relative units	
	control ($n=10$)	PES ($n=11$)		control ($n=10$)	PES($n=11$)
Heart muscle	0,35±0,05	0,90±0,05	26,2*	19,1±2,9	95,5±20,8
Skeletal muscle	0,40±0,05	0,80±0,10	19,0†	13,0±1,7	35,3±7,3
Brain	0,15±0,05	0,25±0,05	4,8†	9,3±0,4	20,0±1,5

*$P < 0.001$.

†$P < 0.01$.

Figs. 1 and 2. As Fig. 1 showed, lipids isolated from the heart of animals exposed to PES showed the characteristic absorption spectrum of hydroperoxides of polyene lipids with maxima at 230-235 and 270-280 nm, which were virtually absent in the control. It will also be evident that the intensity of fluorescence of Schiff bases, the end product of LPO, was significantly higher for lipids in animals exposed to PES than for lipids of the control rats (Fig. 2).

The results of determination of primary LPO products (hydroperoxides) and the end product of the process (fluorescent Schiff bases) in lipids from the brain, heart, and skeletal muscle are summarized in Table 1. They show that under the influence of PES a considerable increase in the content of LPO products took place in all the organs studied. Two features attract attention. First, the content of LPO products increased under the influence of PES most of all in the heart, and also significantly, although to a lesser degree than in the heart, in the skeletal muscle and brain. Second, the increase in the content of hydroperoxides in all the organs studied was smaller than the increase in the end products of LPO (fluorescent Schiff bases). In fact, the hydroperoxide content in heart muscle increased threefold under the influence of PES, whereas the intensity of fluorescence of LPO end products increased fivefold; the corresponding increases for skeletal muscles were 2 and 2.7 times, and for brain 1.7 and 2.1 times.

After exposure to PES marked activation of LPO thus took place in the brain and skeletal and heart muscles. It has recently been shown that in the model of PES used in these two experiments of labilization, the lysosomes are observed in the heart, energy metabolism is disturbed, the blood enzyme level rises significantly [6], and the contractile function of the heart is also distrubed [7]. Since lipid peroxides have been shown to destroy membranous structures [2], it can be tentatively suggested that the above-mentioned disturbances are based on damage to biomembranes caused by the accumulation of LPO products, the existence of which was demonstrated in the present experiments.

The question of the mechanisms by means of which high concentrations of catecholamines and glucocorticoids can activate LPO during stress is still unanswered. One possible solution is that autoxidation of the excess of catecholamines observed during stress is accompanied by the generation of active forms of oxygen [9], capable of inducing LPO [1, 3]. Another possible explanation is that during the excessive intake and utilization of oxygen characteristic of stress, the power of the enzymic and nonenzymic antioxidant systems is insufficient [1], and LPO is activated in the same way as in hyperoxia [4]. Further research aimed at the experimental analysis of these alternatives is envisaged.

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INEQUALITY OF VENTILATION–PERFUSION RATIOS IN THE LUNGS AND ARTERIAL HYPOXEMIA

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A general analysis was made of the relationship between the degree of inequality of ventilation–perfusion ratios and the blood flow through poorly ventilated regions of the lungs, on the one hand, and arterial hypoxemia, on the other hand. Quantitative data on the onset of arterial hypoxemia during disturbance of ventilation–perfusion ratios were obtained.

KEY WORDS: ventilation–perfusion ratios; arterial hypoxemia; respiratory failure.

Inequality of ventilation–perfusion ratios ($\dot{V}_A/\dot{Q}$) in the lungs is known to be the commonest cause of hypoxemia (a decrease in the partial pressure of oxygen $-p_aO_2$ – and the degree of oxygen saturation of the arterial blood – HbO_2) during disturbance of external respiration [1, 2]. However, at certain degrees of inequality of $\dot{V}_A/\dot{Q}$ the partial oxygen pressure and oxygen saturation of the arterial blood are normal, as is the case, for example, in healthy human subjects in a vertical position of the body [4].

The object of this investigation was to study quantitative relations between the degree of inequality of $\dot{V}_A/\dot{Q}$ and the onset of arterial hypoxemia.

EXPERIMENTAL METHOD

Certain assumptions were made for the necessary calculations. The first assumption was that at any value of $\dot{V}_A/\dot{Q}$ in a poorly ventilated part of the lungs (i.e., in a part where $\dot{V}_A/\dot{Q}$ is below normal) the mean value of $\dot{V}_A/\dot{Q}$ remains normal (0.86) on account of an increase in $\dot{V}_A/\dot{Q}$ in the remainder of the lungs. This assumption is based on the fact that otherwise the respiratory quotient, determined from the composition of the expired air and connected with the mean value of $\dot{V}_A/\dot{Q}$ [3], would differ from the metabolic respiratory quotient, which is impossible. The second assumption was that the possible gradient between pO_2 in the alveolar air and arterial blood, due to disturbances of diffusion or contamination with venous blood, is in fact absent. In reality, in human subjects with no pathological changes in the diffusion capacity of the lungs and venous shunts, such a gradient exists and lies between 5 and 7 mm Hg. The third assumption was that the dissociation curve of the blood and the gaseous composition of the venous blood were taken to be normal. All calculations were thus aimed at determining the degree of disturbances of equality of $\dot{V}_A/\dot{Q}$ which leads to the appearance of arterial hypoxemia.

On the basis of these assumptions the gaseous composition of the alveolar air and blood flowing from two regions of the lungs (with lowered and raised values of $\dot{V}_A/\dot{Q}$) and the gaseous composition of mixed arterial blood flowing from the lungs were calculated. The calculations were done for all values of $(\dot{V}_A/\dot{Q})_1$ (from normal, namely 0.86, to 0) and for all ratios between the volumes of blood flowing through the part of the lungs where $\dot{V}_A/\dot{Q}$ was below normal and the blood flow through the lungs $(\dot{Q}/\dot{Q}_0)_1$. The calculations were carried out on the BÉSM-6 computer on the basis of programs prepared in accordance with the assumptions made above.

EXPERIMENTAL RESULTS

Samples of the principal results are given in Table 1. The first three vertical columns give data obtained for $(\dot{V}_A/\dot{Q})_1 = 0.6$ in a poorly ventilated region of the lungs, i.e., when $(\dot{V}_A/\dot{Q})_1$ was moderately reduced

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