the bioantioxidant class to protect the myocardium, in the writers' opinion, is very promising.

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### EFFECT OF HYPEROXIA ON THE OXYHEMOGLOBIN DISSOCIATION CURVE AT DIFFERENT AGES

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KEY WORDS: old age, oxygen, action on the body, blood gases, oxyhemoglobin dissociation curve.

The widespread use of oxygen therapy in geriatric practice [8] on the one hand, and the frequent absence of a therapeutic effect [15] or even the occurrence of side effects during its use in elderly and old patients [3], on the other hand, necessitate a penetrating study of the effect of oxygen on the senile organism. Investigation of the effect of hyperoxia on the respiratory function of the blood, which plays a major role in the maintenance of gaseous homeostasis of the body, is particuly interesting in this connection. The aim of this investigation was to study parameters of the oxygen transport function of blood in elderly subjects during inhalation of oxygen.

# EXPERIMENTAL METHOD

The investigation was conducted on nine clinically healthy elderly subjects (aged 60-74 years) and on nine young subjects (aged 19-32 years) who formed the control group. As the model of hyperoxia, the subjects inhaled a gas mixture containing 95% oxygen and 5% nitrogen for 20 min from the closed circuit of a SG-1M spirograph. The oxygen content in the working

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TABLE 1. Parameters of Oxyhemoglobin Dissociation Curve (in mm Hg) during Hyperoxia Compared with the Initial Level in Young (A) and Elderly (B) subjects

| am-  | Oxyhemoglobin dissociation curve in native blood  |   | Standard oxyhemoglobin dissociation curve                         |  |  |  |
|--|---|---|---|--|--|--|
| Param<br>eter  | A   | В   | A   | В  |  |  |
| $\begin{array}{c} P_{10} \\ P_{20} \\ P_{30} \\ P_{40} \\ P_{50} \\ P_{60} \\ P_{70} \\ P_{80} \\ P_{90} \\ P_{95} \\ P_{100} \end{array}$ | $ \begin{array}{c c} -0.4 \\ -1.0 \\ -1.3 \\ -1.4 \\ -1.9* \\ -2.0* \\ -2.3* \\ -2.4* \\ -2.2 \\ -1.4 \\ -3.1 \end{array} $ | -0,3<br>-0,6<br>-0,6<br>-0,3<br>-0,4<br>-0,1<br>0,1<br>0,2<br>2,2<br>-0,8 | -0.5 -1.1* -1.4* -1.2** -1.7** -1.8** -2.2** -2.1* -2.1 -1.5 -3.1 | $\begin{array}{c} -0.6 \\ -0.9 \\ -1.0 \\ -1.0 \\ -1.1 \\ -1.2 \\ -0.9 \\ -0.9 \\ -1.3 \\ 2.1 \\ -2.8 \end{array}$ |  |  |
| Legen  | id *P ≤ (   | 0.05: **P   | < 0.01.   |  |  |  |

TABLE 2. Parameters of Arterial and Venous Blood Gas Composition (in mm Hg) for Young and Elderly Subjects during Hyperoxia

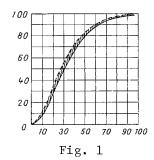
|   | Young subjects   |   |                                  | Elderly subjects   |   |                                  |
|---|--|---|----------------------------------|--|---|----------------------------------|
| Parameter   | $M\pm m$   | magnitude<br>of shift from<br>initial level | significance<br>of shift         | $M\pm m$   | magnitude<br>of shift from<br>initial level | significance<br>of shift         |
| Arterial blood  | $252\pm16,09$  | 156,7                                       | <0,01                            | 194,6±18,05  | 113,6                                       | <0,01                            |
| pCO <sub>2</sub><br>Venous  | $35,3\pm1,93$  | 0,8   | >0.05                            | $41,6\pm0,2$   | 2,9   | < 0.05                           |
| pO <sub>2</sub> pCO <sub>2</sub> Arteriovenous difference of pCO <sub>2</sub> | $\begin{array}{c} 40.5 \pm 1.24 \\ 44.5 \pm 1.58 \\ 212.9 \pm 16.4 \\ 9.23 \pm 1.63 \end{array}$ | 7,3<br>0,93<br>150,6<br>1,4                 | <0,01<br>>0,05<br><0,01<br>>0,05 | $36,9\pm1,71$ $51,4\pm1,17$ $157,7\pm17,68$ $9,1\pm0,91$ | 6,1<br>3,23<br>107<br>0,5                   | <0,01<br><0,05<br><0,01<br>>0,05 |

cylinder of the spirograph was monitored by means of an MMG-1 oxygen analyzer, which was connected to the spirograph at the point of attachment of the gas analyzer to determine the residual volume of the lungs. Before the test and 19-20 min after its beginning, arterial blood samples were taken to determine the partial pressures of oxygen  $(pO_2)$  and carbon dioxide  $(pCO_2)$ , samples of venous blood were collected to determine  $pO_2$  and  $pCO_2$ , and the oxyhemoglobin dissociation curve was plotted.  $pO_2$  was determined polarographically by means of a Clark's electrode.  $pCO_2$  was calculated from the value of pH by computer. Measurements were made on a micro-Astrup apparatus (from Radiometer, Denmark). The oxyhemoglobin dissociation curve was obtained with a DCA-1 apparatus (Radiometer, Denmark). The technique of blood taking and analysis of the oxyhemoglobin dissociation curve was described perviously [7, 9].

# EXPERIMENTAL RESULTS

Analysis of the oxyhemoglobin dissociation curve in native blood and of the standard (reduced to pH 7.4) oxyhemoglobin dissociation curve showed that values of  $pO_2$  in young subjects corresponding to all levels of oxygen saturation examined were reduced. The fall of  $pO_2$  was significant over the range  $P_{50}$ - $P_{80}$  during analysis of the dissociation curve in native blood and within the range  $P_{20}$ - $P_{80}$  during analysis of the standard dissociation curve (Table 1). This state of affairs implies a shift of the oxyhemoglobin dissociation curve to the left (Fig. 1). In the elderly subjects there was virtually no shift of the dissociation curve in native blood (Table 1; Fig. 2). Meanwhile the standard oxyhemoglobin dissociation curve of the elderly subjects revealed a small shift to the left, but this was not significant (Table 1).

During inhalation of oxygen the value of pCO<sub>2</sub> in arterial and venous blood of the young subjects was virtually unchanged (Table 2). This agrees with the observed absence of change in the ventilation [5] and gas exchange [1] levels in normal subjects during hyperoxia. In elderly people pCO<sub>2</sub> increases in arterial and venous blood during inhalation of oxygen (Table 2), evidently on account of a decrease in pulmonary ventilation [5].



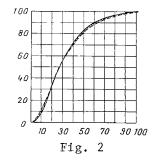


Fig. 1. Oxyhemoglobin dissociation curve in native blood from young subjects in initial state (continuous line) and during hyperoxia (broken line). Abscissa  $pO_2$  (in mm Hg); ordinate, hemoglobin oxygen saturation (in %).

Fig. 2. Oxyhemoglobin dissociation curve in native blood from elderly subjects in initial state (continuous line) and during hyperoxia (broken line). Legend as to Fig. 1.

The shift of the oxyhemoglobin dissociation curve to the left in young subjects during hyperoxia can be explained as follows. Hydrolysis products are known to stimulate the formation of 2,3-diphosphoglycerate (2,3-DPG) in erythrocytes [13]. Since glycolysis is inhibited in the body during hyperoxia because of the Pasteur effect, this means that less 2,3-DPG is formed and its concentration in the erythrocytes falls. This probably leads to an increase in the affinity of hemoglobin for oxygen and a shift of the oxyhemoglobin dissociation curve to the left. Since the Pasteur effect becomes much weaker with age [2], this explains the very small increase in the affinity of hemoglobin for oxygen and the shift of the dissociation curve to the left in old age- Under real conditions, however, this very small shift to the left can no longer be determined because of the increase in pCO<sub>2</sub> and the associated Bohr effect.

Besides its beneficial physiological effect (correcting hypoxemia), oxygen may also have a toxic action on the body, and the degree of the side-effects is known to depend on the oxygen concentration in the inspired air [4, 12, 14]. The shift of the oxyhemoglobin dissociation curve to the left, signifying an increase in the affinity of hemoglobin for oxygen and interference with the giving up of oxygen to the tissues in young subjects can thus be regarded as an adaptive response, safeguarding the tissues against an excessive increase in their  $p0_2$ .

The effectiveness of this mechanism is revealed by the much greater increase in the arteriovenous difference of  $pO_2$  in the young than in the old subjects during inhalation of oxygen (Table 2). Age differences in the increase in the arteriovenous difference of  $pO_2$  cannot be explained by the slowing of the blood flow that is characteristic of hyperoxia [4, 11], since the dynamics of the venoarterial  $pCO_2$  difference was not significant and was the same in both age groups (Table 2). A factor responsible for the high value of the arteriovenous difference of  $pO_2$  in young subjects under normoxic conditions, such as the higher position of the point of the artery of the oxyhemoglobin dissociation curve at which the giving up of oxygen to the tissues begins [9], likewise cannot be of practical importance, because during hyperoxia  $PAO_2$  in both groups of subjects was considerably above 200 mm Hg. Consequently, the cause of the greater increase in the arteriovenous difference of  $pO_2$  in young subjects during hyperoxia is an increase in the affinity of hemoglobin for oxygen, as a result of which the giving up of oxygen to the tissues is accompanied by a greater fall of  $pO_2$  in the blood than in elderly subjects.

It might be supposed that an increase in the affinity of hemoglobin for oxygen in young subjects should lead to an increase in the association of hemoglobin with oxygen in the lungs. However, it was in the region of high values of hemoglobin oxygenation (starting from 90%) that the increase in affinity of hemoglobin for oxygen was not significant. Regulation of the rate of association of hemoglobin with oxygen likewise is less important than regulation of the rate of oxyhemoglobin dissociation. In fact, whereas the rate at which oxygen is given up by the blood is not high (50% of the oxygen is given up by erythrocytes in 0.75-0.9 sec), and it is considerably influenced by the affinity of hemoglobin for oxygen, the

association of oxygen with hemoglobin takes place 10 times faster and 50% saturation of the erythrocytes with oxygen takes 0.08-0.09 sec [10]. This rate is quite sufficient for normal saturation of the erythrocytes with oxygen, and changes in it within certain limits will not affect this process.

The affinity of hemoglobin for oxygen is thus increased in young subjects during hyperoxia, and this is reflected in a shift of the oxyhemoglobin dissociation curve to the left, and the tissues are protected against an excessive increase in  $p0_2$ , which could have serious consequences. In elderly subjects the affinity of hemoglobin for oxygen under standard conditions does not increase significantly, and under real conditions it does not change at all.

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# POSTSTRESS RIGIDITY IN THE LEFT VENTRICULAR MYOCARDIUM

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Under the influence of emotional-painful stress (EPS) a unique syndrone of poststress rigidity has been shown to develop in the arterial myocardium: the atrial muscle responds to an equal applied load by an increase in length which is less by 33-50% than in the control; this is accompanied by depression of the tension developed by the atrium during isometric contraction [1, 8]. The question of the importance of this phenomenon for cardiac function remains unanswered, for it was not known whether poststress rigidity and the accompanying disturbances of contractile function are realized in the mycardium of the ventricles of the heart, which play the decisive role in its pumping functions.

The aim of this investigation was to study the extensibility and contractile function of the papillary muscles of the left ventricle of animals exposed to stress and to compare the disturbances found with those observed in the atrial myocardium.

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