

## EFFECT OF HISTAMINE ON THE CUTANEOUS CAPILLARY CIRCULATION AND OXYGEN TENSION IN THE SUBCUTANEOUS CELLULAR TISSUE AT VARIOUS AGE PERIODS

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Local injection of 0.1 ml 0.1% histamine gives a greater increase in  $pO_2$  and a greater further increase in  $pO_2$  in response to inhalation of oxygen in elderly persons than in persons aged 18-35 years. The same dose of histamine leads to a greater increase in the number of functioning skin capillaries in the elderly.

A disturbance of vascular reactivity is the frequent cause of development of regional hypoxic states of circulatory origin in elderly and old people [8]. The study of responses of capillaries, at which level oxygen is exchanged between the blood and tissues, to regulatory influences at different age periods and of the significance of these responses to the oxygen supply to the vascularized tissues is therefore of great theoretical and practical importance.

Injection of histamine was used as the function test for the assessment of age differences in the effects of humoral factors on the terminal circulation. The effect of histamine on the cutaneous capillary circulation and on the oxygen tension in the subcutaneous cellular tissue in young and elderly subjects was studied.

### EXPERIMENTAL

The oxygen tension ( $pO_2$ ) was determined in the subcutaneous cellular tissue of the left forearm by a polarographic method [3] during test inhalation of oxygen for 10 min. Histamine solution (0.1 ml) in a dilution of  $10^{-3}$  g/ml was injected subcutaneously at a distance of 0.8-1 cm from the tip of the exposed electrode, when the  $pO_2$  level, which had risen during the inhalation of oxygen, had returned to its initial value. After  $pO_2$  had become stabilized at its maximal level after injection of histamine (which required about 15 min) a further test inhalation of oxygen for 10 min was carried out. The indices of the increase in  $pO_2$  during the oxygen test against the background of histamine injection were calculated relative to the  $pO_2$  level in the subcutaneous cellular tissue determined after injection of histamine and before the oxygen test. Altogether, 16 clinically healthy persons aged 60-74 years and 7 healthy persons aged 18-35 years, forming the control group, were investigated.

The effect of histamine on the cutaneous capillary circulation was studied in 20 clinically healthy persons aged 60-79 years and 15 healthy persons aged 18-35 years (control group). The state of the terminal circulation was recorded by studying the capillaroscopic picture of the nailbed of the left index finger by an optical microscopic method. The results were recorded objectively by photomicrography.

Statistical analysis of the results was carried out by the difference method.

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TABLE 1. Dynamics of pO<sub>2</sub> in Subcutaneous Cellular Tissue during Oxygen Inhalation Test in Different Age Groups and before and after Local Injection of 0.1 ml 0.1% Histamine (M ± m)

Index	Young subjects		Elderly subjects	
	before hist-amine injec.	after hist-amine injec.	before hist-amine injec.	after hist-amine injec.
Latent period of increase in pO <sub>2</sub> (in sec). . . . .	19,1±2,01	19,9±2,34	23,9±3,04	14,8±1,59
Time taken to reach half of level of maximal increase in pO <sub>2</sub> (in sec). . . . .	115,7±31,78	133,3±15,97	152,5±24,21	193,7±22,34
Incr. in pO <sub>2</sub> during first minute of inhalation (in mm Hg). . . . .	11,1±2,08	9,7±2,08	7,3±1,64	14,5±2,74
Incr. in pO <sub>2</sub> during first 2 min (in mm Hg). . . . .	21,6±4,16	20,1±4,47	13,4±2,52	27,2±3,97
Incr. in pO <sub>2</sub> during inhalation (in mm Hg). . . . .	42,4±11,62	50,7±11,27	33,1±4,48	74,6±12,37
Time taken to reach maximal level of pO <sub>2</sub> (in sec). . . . .	400,3±48,91	410±42,27	519,9±26,04	564,1±22,85
Latent period of decr. in pO <sub>2</sub> after inhalation of oxygen (in sec). . . . .	22,7±4,49	18,4±3,24	35,8±4,42	29,8±4,11
Duration of decr. in pO <sub>2</sub> (in sec). . . . .	336,2±102,7	389,4±102,7	475,4±31,7	786,1±180,69

## EXPERIMENTAL RESULTS

After local injection of histamine the pO<sub>2</sub> level in the subcutaneous cellular tissue of the young subjects was  $53.2 \pm 5.76$  mm Hg (initial value  $46 \pm 6.14$  mm Hg), while in the elderly subjects the corresponding values were  $35.7 \pm 4.67$  and  $51.1 \pm 7.07$  mm Hg. In the age groups studied, the increase in pO<sub>2</sub> in the subcutaneous cellular tissues in response to inhalation of oxygen also was increased under the influence of histamine (Table 1).

Meanwhile, the latent period and duration of the decrease in pO<sub>2</sub> in the subcutaneous cellular tissue with the change from the inhalation of oxygen to inhalation of air showed no significant change in either the young or the elderly age groups (Table 1). This means that histamine had no significant action on the intensity of oxygen consumption by the subcutaneous cellular tissue or on the increase in the pO<sub>2</sub> level induced by it, and also that the increase in pO<sub>2</sub> in the subcutaneous cellular tissue during inhalation of oxygen was due to an improvement in the oxygen supply to this tissue.

The elevation of the initial pO<sub>2</sub> level and the increase in pO<sub>2</sub> produced by the action of histamine during inhalation of oxygen in elderly persons were significantly greater (Fig. 1) than in subjects aged 18-35 years (Table 1). In addition, in the elderly subjects, by contrast with the control group, during inhalation of histamine the latent period of increase in pO<sub>2</sub> during inhalation of oxygen was distinctly shortened and the rise in pO<sub>2</sub> during inhalation for 1-2 min was increased (Table 1), i.e., indices reflecting the state of capillary-tissue diffusion of oxygen all showed an increase [3, 12].

The cause of the age differences in the action of histamine on the pO<sub>2</sub> level became clear when the effect of this substance on the cutaneous capillary circulation was examined in people of different ages. A clear reaction to histamine was observed in all subjects. The capillaroscopic background became pinker than before because of dilatation of the arterioles of the subpapillary plexus. In 80% of the young subjects and in all the subjects aged 60-79 years the cloudiness of the background of the field of vision was increased because of an increase in capillary permeability. The diameter of both the arterial and the venous limbs of the capillaries was increased. The capillary blood flow was accelerated in 90% of subjects. An increase in the number of functioning capillaries was characteristic.

The age differences in the effect of histamine on the cutaneous capillary circulation consist of an increase in the latent period of the response in subjects aged 60-79 years, a decrease in the rate of its development, prolongation of the response, and a large increase in the number of open capillaries.

The principal way in which histamine is inactivated in man is by methylation followed by the action of diamine oxidase [4]. Since the activity of several enzymes falls during aging [5, 6, 9, 11], inactivation of the injected histamine was presumably retarded. This assumption is confirmed by the prolongation of the response of the cutaneous microcirculation to histamine (Fig. 2). It has also been shown that during aging

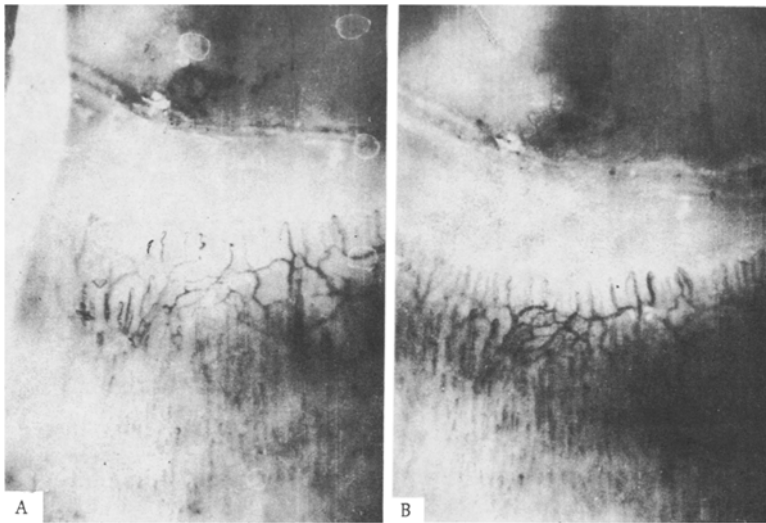


Fig. 1

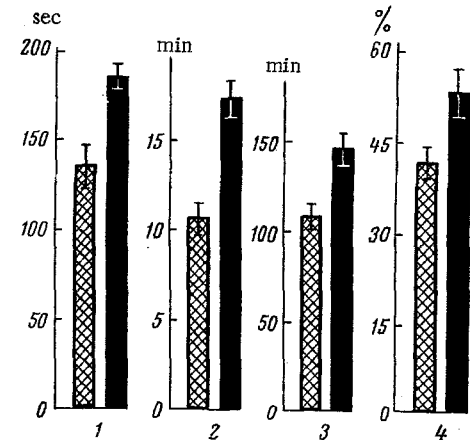


Fig. 2

Fig. 1. Capillarograms of nailbed of left ring finger before (A) and after (B) local injection of histamine: A) background of field of vision transparent, capillary branches spastic in form, intermediate limbs dilated. Nine functioning capillaries in 1 mm of the field of vision. Capillaroscopy: background of field of vision pale pink, capillary blood flow granular, moderately slow B) background of field of vision slightly clouded. Dilatation of arterial and venous branches of capillary loops. Clear intensification of pattern of subcapillary venous plexus. Fourteen functioning capillaries in 1 mm of field of vision. Capillaroscopy: background of field of vision much pinker than before, capillary blood flow homogeneous and moderately fast.

Fig. 2. Effect of local injection of histamine on cutaneous capillary circulation at different age periods: 1) latent period of response; 2) rate of development of response; 3) duration of response; 4) increase in number of functioning capillaries. Shaded columns represent young subject, black columns represent elderly subject.

nervous influences on structures and function are weakened [7] while the sensitivity of the blood vessels to histamine increases in the course of their denervation [2]. Finally, in elderly and old persons, thyroid function is depressed [1, 10]. Meanwhile, in athyreosis the action of histamine on the blood vessel wall is strengthened [2].

All these factors are evidently responsible for the more marked changes in the cutaneous microcirculation in elderly persons during injection of histamine.

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