EFFECT OF ACUTE HYPOXIC HYPOXIA ON THE THICKNESS OF THE LUNG AIR–BLOOD BARRIER

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The arithmetic mean and harmonic mean thickness of the air–blood barrier (ABB) of the lungs and the arithmetic mean thickness of its individual layers were studied by morphometric analysis of electron micrographs obtained from rats of different ages under normal conditions and after inhalation of a gas mixture of N_2 with 11.2% O_2 for 30 min. Acute hypoxic hypoxia leads to thickening of ABB, and the younger the animal the more marked the thickening observed. The relative thicknesses of individual layers of ABB differed after acute hypoxia in animals of different age groups. The results point to age differences in the mechanisms of development of arterial hypoxemia in acute hypoxic hypoxia.

KEY WORDS: air–blood barrier of the lungs; arithmetic mean thickness; harmonic mean thickness; acute hypoxic hypoxia.

Age differences in the development of arterial hypoxemia due to oxygen deficiency in the inspired air have been discovered in recent investigations [5], and the younger the animal concerned, the higher the degree of undersaturation of arterial blood with O_2. These results suggested that the age differences observed were due mainly to the diffusion properties of the air–blood barrier (ABB) of the lungs. One factor determining the ability of ABB to conduct O_2 from the alveolar air into the blood of the pulmonary capillaries is its thickness. However, the question of whether acute hypoxic hypoxia affects the thickness of ABB in the adult organism and in the early stages of its development has not been adequately discussed in the literature.

EXPERIMENTAL METHOD

Experiments were carried out on 24 laboratory albino rats of three age groups: 2 weeks, 3 weeks, and adult (10–14 weeks). Acute hypoxic hypoxia was produced by making the animals inhale a gas mixture consisting of N_2 with 11.2% O_2 for 30 min. Intact animals of the same age groups formed a parallel experimental series. After decapitation of the rats pieces of tissue were taken from the same places of the lower lobes of both lungs, fixed in glutaraldehyde and osmium tetroxide, and then embedded in Epon. Ultrathin sections stained with uranyl acetate and lead citrate were examined in the Tesla BS-513A electron microscope. Random sampling was carried out by the method described previously [1]. The arithmetic mean and harmonic mean thickness of ABB and its individual layers were determined by the use of randomly arranged lines of finite length by the method of Chalkley et al. [8] in the modification of Weibel and Knight [10]. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The results are given in Table 1. Attention is drawn to the fact that although the thickness of ABB in intact rats of the younger age groups was significantly less than in adult animals, the ratio between the individual layers of the barrier remained virtually constant throughout the chosen period of ontogenetic development. The alveolar epithelium accounted for 32-42%, the interstitial layer for 27-30%, and the capillary endothelium for 31-40% of the total thickness of ABB (Fig. 1).

After exposure to acute hypoxic hypoxia the thickness of ABB increased inversely proportional to age, which can be explained by the development of edema of the lung tissue (Fig. 2), which is more marked in the

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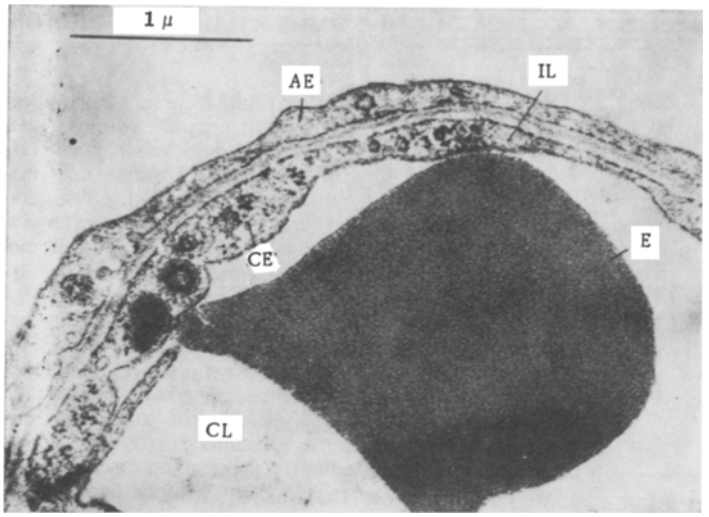

Fig. 1. ABB of lungs of 2-week-old rat under normal conditions (28,700 ×). CL) Capillary lumen; AE) alveolar epithelium; IL) interstitial layer; CE) capillary endothelium; E) erythrocyte.

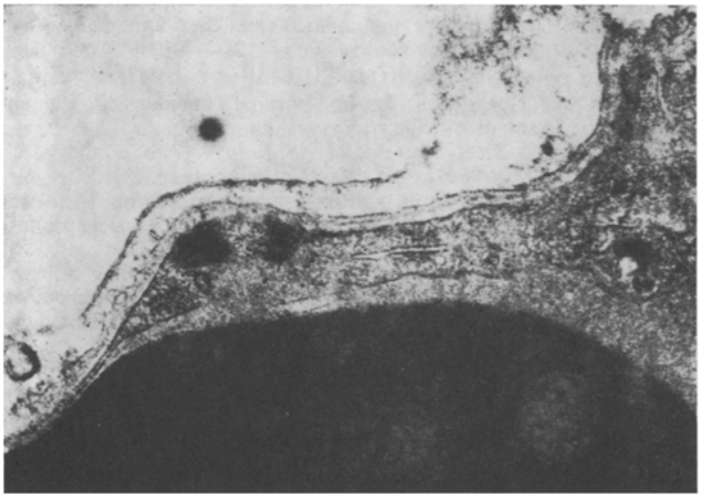

Fig. 2. ABB of lungs of 2-week-old rat after acute hypoxic hypoxia (29,500 ×).

TABLE 1. Arithmetic Mean (τ) and Harmonic Mean (τ_h) Thickness of Pulmonary ABB in Rats of Different Ages under Normal Conditions and after Acute Hypoxic Hypoxia (in μ, M ± m)

Age of rats, weeks	Experimental conditions	τ	τ_h	τ		
				epithelium	interstitial	endothelium
2	Normal	0,252±0,020	0,215±0,011	0,100±0,019	0,064±0,008	0,074±0,020
	Hypoxia	0,434±0,031	0,367±0,022	0,146±0,010	0,116±0,002	0,151±0,023
	P	<0,001	<0,001	<0,05	<0,001	<0,01
3	Normal	0,241±0,012	0,205±0,020	0,090±0,008	0,070±0,007	0,074±0,009
	Hypoxia	0,420±0,043	0,268±0,021	0,164±0,020	0,116±0,011	0,180±0,024
	P	<0,001	<0,05	<0,001	<0,001	<0,001
10—14 (Adult)	Normal	0,293±0,019	0,240±0,017	0,086±0,008	0,077±0,005	0,106±0,010
	Hypoxia	0,390±0,032	0,289±0,021	0,124±0,011	0,104±0,019	0,121±0,018
	P	<0,02	>0,05	<0,01	>0,1	>0,2

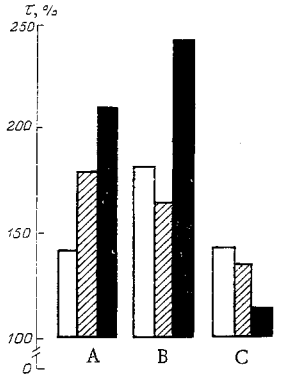

Fig. 3. Increase in arithmetic mean thickness of layers of ABB of lungs in rats of different ages after acute hypoxic hypoxia. A) Rats aged 2 weeks; B) rats aged 3 weeks; C) adult rats. Unshaded columns – alveolar epithelium; obliquely shaded – interstitial layer; black – capillary endothelium. Thickness of corresponding layer under normal conditions taken as 100%.

early stages of ontogeny [7]. The different components of ABB increased unequally in rats of different age groups (Fig. 3). According to some workers [3, 4, 9], the alveolar epithelium is more sensitive to influences of various types. This is confirmed by the results now obtained in the group of adult animals. The distinguishing features of the changes in thickness of the individual layers of ABB in the animals of the younger age groups during hypoxia were as follows. The capillary endothelium in direct contact with blood changed in the presence of O_2 deficiency in the inspired air much more strongly in young animals; its greatest increase in thickness in rats aged 3 weeks was most probably attributable to the considerable increase in the blood volume of the pulmonary vessels at that age [6]. As regards the interstitial layer, the younger the animal the more it thickened; its changes in 2-week-old rats, when the increase in blood volume of the pulmonary vessels was comparatively small [6], was evidently connected with a considerable increase in the permeability of ABB for liquid and protein in the animals of this age group during acute hypoxia [2]. The character of the changes in thickness of the alveolar epithelium is evidently due to differences in the mechanism of the direct effect of acute hypoxic hypoxia on ABB of the lungs at different ages.

On the basis of these results age differences in the development of arterial hypoxemia in the presence of a deficiency of O_2 in the inspired air can be explained. The smaller decrease in the alveolar–arterial pO_2 gradient observed previously in young animals than in adults is probably attributable to the much greater increase in the harmonic mean thickness of ABB in the early stages of ontogeny, which creates additional obstacles to O_2 diffusion from the alveolar air into the blood of the pulmonary capillaries.

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