Title: PULMONARY CAPILLARY TRANSIT TIMES OF ERYTHROCYTES DURING NORMOXIA OR ALVEOLAR HYPOXIA

Authors: A.E. Goetz, M.D., R. Berger, M.D., W. Lumper, M.D., P.F. Conzen, M.D., J. Hobhahn, M.D*, K. Peter, Prof.*, W. Brendel, Prof.

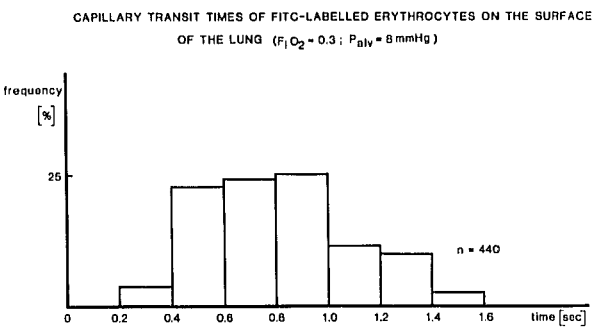
Affiliation: Institute of Surgical Research and *Institute of Anaesthesiology, Klinikum Großhadern, Ludwig-Maximilians-Universität, Marchioninistr. 15, 8000 Munich 70, Bavaria, FRG

Introduction: The red blood cell capillary transit time (RBC-CTT) from terminal pulmonary arterioles to collecting venules is of paramount importance for an effective gas exchange in the lungs (1). Besides capillary recruitment this parameter is considered as a major reserve of the pulmonary capillary bed to increase the capacity for gas exchange. This conclusion is based on two assumptions: I) a minimum time of 0,25 sec is necessary for complete oxygen saturation (2); II) indirect measurements and videodensitometric evaluations of the arteriolar-venular passage of a fluorescent plasma-marker revealed mean transit times between 1,0 and 12,7 sec during rest, and to $\leq$ 0,5 sec during exercise (1,3). Thus a reserve is still given by the potential red cell velocity increase under normoxic conditions. However, during alveolar hypoxia an increase of a dye transit has been reported (4). Since direct and detailed measurements of RBC-CTT and of the heterogenity of this parameter have not been performed so far it is still unclear if the lower limit of the reserve to increase gas exchange has been approached or exceeded. We therefore analyzed during normoxia and during alveolar hypoxia the RBC-CTT using intravital fluorescence videomicroscopy.

Methods: 20 healthy male Sprague-Dawley rats were anesthetized by intraperitoneal injections of pentobarbital-sodium (50 mg/kg b.w.). The animals were intubated and ventilated mechanically. Tidal volume and respirator rate were adjusted so that arterial pH was near 7,34. FiO_2 was 0,3. The tracheal tube was connected to a pressure-transducer to monitor airway-pressure changes continously. For measurement of heart rate and systemic pressures catheters were implanted into the ascending aorta and vena cava superior. For detecting the transpulmonary pressure gradients catheters were advanced into the pulmonary artery and the left atrium via a thoracotomy in the third left intercostal space. A circular thoracic window was implanted into the right thoracic wall after partial resection of the fourth rib and attached to the thoracic wall by a polyacryl adhesive. Thus the pulmonary microcirculation could be visualized using fluorescence videomicroscopy after i.v. application of fluorescein-isothiocyanate (FITC)-labelled red cells. 10 animals were studied during normoxic ventilation. In separate experiments 10 animals were studied during normoxia und during alveolar hypoxia. In these studies hypoxic ventilation was induced by addition of nitrogen to the inspired gas until an arterial pO_2 of 40 mm Hg was attained. The videomicroscopic images of identical microvascular areas were recorded on videotape via a high-sensitivity tv-camera. During videorecordings ventilation has to be interrupted for a maximum period of 20 sec. at alveolar pressures of 8 - 9 mmHg. The videotapes were later analyzed offline frame-to-frame at magnifications of 1200x to measure the RBC-CTT. For statistical analysis the Wilcoxon matched pairs signed rank test was used. Values are expressed as mean $\pm$ SD. $p < 0,01$ (**) was considered statistically significant.

Results: At pulmonary artery pressure (PAP) of 20,0 $\pm$ 2,5 mmHg, left atrial pressure (LAP) of 2,1 $\pm$ 0,8 mmHg and alveolar pressure (P_{alv}) of 9,2 $\pm$ 2,7 the frequency distribution of RBC-CTT given in Fig. 1 was obtained.

Pressure measurements in the second group of animals did not differ significantly from the previous group during normoxia. During alveolar hypoxia PAP was increased significantly ($p < 0,01$) by 40 % whereas LAP and P_{alv} remained unchanged. The RBC-CTT with alveolar hypoxia was significantly reduced (Fig. 2). The minimum transit times during alveolar hypoxia were 0,23 sec.



CAPILLARY TRANSIT TIME OF FITC - LABELED RED CELLS DURING HYPOXIC VENTILATION

Fig. 1

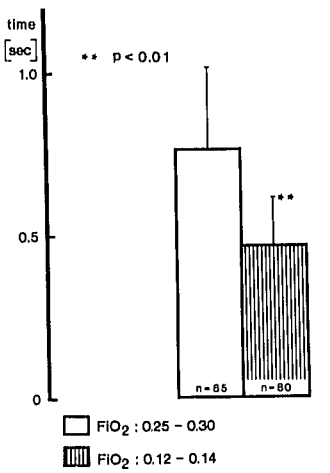


Fig. 2

Conclusions: The mean transit time of labelled red blood cells corresponds to earlier estimates and to dye transit time measurements in the lower lung of dogs, whereas they are markedly below the values in the upper lung of dogs (1,3). These findings and the present data suggest that the vertical gradient of RBC-CTT is relatively small within the rat lungs and pulmonary blood flow distribution within this species is remarkably uniform. Thus the results obtained from the surface of rat lungs indeed reflect microhemodynamic changes of the whole lungs. Furthermore, these studies indicate that a substantial part of the pulmonary gas-exchange reserve still exists, in particular during normoxia and during alveolar hypoxia as well, even if a few of the transit times are approaching the minimum time required for sufficient oxygenation of erythrocytes. Moreover it should be taken into account that oxygen uptake starts already in small arterioles (5).

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