The cholesterol molecule is known to occupy an area of 38 A^2, the phosphatidylcholine molecule in the presence of cholesterol an area of 58 A^2, and according to the equation D = 3V/S, where V is the total encepsulated volume and S the total surface area of lipid [9], it can be calculated that the mean diameter (D) of single lamella liposomes is 450-540 A, in good agreement with the results of the microscopic investigation.

Ultrasonic treatment is thus not essential for reverse-phase evaporation. The freezing and thawing procedure facilitates transformation of the amorphous gel-like system formed with high concentrations of lipids after phase reversal into a suspension of liposomes 0.2-1.5 μ in diameter, containing 10-14 μl of aqueous phase/μmole phospholipids. By increasing the lipid concentration, up to 70-80% of the total volume of the aqueous phase can be incorporated into liposomes. Since incorporation of hydrophilic compounds into liposomes is largely determined by the encapsulated volume, this method can be recommended for the production of liposomal forms of other therapeutic preparations.

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INEQUALITY OF LUNG VENTILATION DETERMINED BY TRANSCUTANEOUS MEASUREMENT OF pO_2 IN ARTERIAL BLOOD DURING OXYGEN INHALATION

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The simplest and most accessible method of discovering inequality of lung ventilation is oxyhemometric determination of the oxygen desaturation time of arterial blood after inhalation of oxygen [1, 3, 8, 9]. However, by this method adequately clear results can be obtained only in patients in whom the oxygen saturation of the arterial blood is depressed during inhalation of air [9]. The practical value of the parameter studied in that case (the blood desaturation time) is considered to be doubtful because of the great variability and poor reproducibility of this parameter [7, 8]. A more informative parameter during inhalation of pure oxygen is the partial pressure of oxygen in arterial blood (p_aO_2). However, dynamic and continuous measurement of p_aO_2 is fraught with technical difficulties (catheterization of arteries, the need to use special catheter electrodes, and so on). For continuous determination of p_aO_2 the writers have used the method of transcutaneous determination of the partial pressure of oxygen in arterial blood (Tcp_aO_2), first suggested by Huch et al. [11]. The degree of inequality of lung ventilation was estimated from the time of lowering of p_aO_2 (blood desaturation time) after inhalation of oxygen.

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EXPERIMENTAL METHOD

The value of p_aO_2 was determined transcutaneously by means of an SM 361 Oxymonitor (from Hellige, West Germany), fitted with a Huch electrode, the three separate platinum cathodes of which were buried in glass and surrounded by a circular silver anode (which also serves as heating device for the electrode). The electrode, heated to 45°C, creates a local skin temperature of about 43°C, sufficient for dilatation of the subepidermal capillaries, and it induces hyperemia and arterialization of the capillary blood beneath it. Molecular oxygen diffuses through the avascular epidermis and through the Teflon membrane of the electrode to the cathode, where it is reduced. The partial pressure of oxygen (pO_2) measured by such an electrode correlates closely with p_aO_2; in adults the mean Tcp_aO_2 is 10-12% lower than pO_2 of the corresponding arterial samples [6, 10, 11]. The investigation was carried out in the morning, under basal metabolic conditions, with the air temperature in the room at 22-24°C. After preliminary calibration of the electrode *in vitro* it was fixed to the slightly moistened skin by means of self-adhesive rings (in the subclavicular region). After stabilization of the reading (Tcp_aO_2) the subject began to inhale moistened pure oxygen (96%) through a mask (with mouthpiece) for 9-10 min until the peak level of p_aO_2 was reached, after which he switched to inhalation of room air, and the time of return of Tcp_aO_2 from the peak level to its original value (the blood desaturation time) was recorded. Altogether 12 healthy subjects and 25 patients with chronic nonspecific lung diseases (CNLD), aged from 25 to 70 years were studied. The bronchial patency and lung volumes, and other parameters of respiratory function were determined by whole-body plethysmography, using the "Pulmorex" apparatus (from Fenyer and Gut, Switzerland). To verify the primary data, inequality of ventilation of the lungs was determined by oxyhemometric and capnographic (the LB-3 capnograph, from Beckman, USA) methods and also by the helium dilation method of the POOL apparatus. All measurements were made twice. The results were subjected to statistical analysis. Reproducibility was determined by calculating standard deviations (σ) of the results of repeated measurements with a 95% confidence interval (1.96 σ) [4].

EXPERIMENTAL RESULTS

The initial mean level of Tcp_aO_2 in normal subjects was 72.5 ± 2.2 mm Hg, but after the beginning of inhalation of oxygen it rose gradually (on average to 430 ± 20 mm Hg), and at the 6th minute it flattened out on a plateau. On the change to inhalation of room air, Tcp_aO_2 fell gradually to its initial level. The desaturation time of the arterial blood varied from 3.5 to 4.8 min, with a mean value of 4.3 ± 0.14 min. During repeated measurements on the same subject, high reproducibility of the results was observed (5.6%).

In patients with CNLD the initial Tcp_aO_2 level was 69 ± 1.9 mm Hg. After oxygen inhalation Tcp_aO_2 increased (on average to 340 ± 1.96 mm Hg) and reached its peak level after 8-12 min. On the switch to inhalation of room air, the blood desaturation time of individual patients varied from 5.6 to 14 min (mean 8 ± 0.75 min). During repeated measurements on the patients good reproducibility of the parameter also was observed (4.8%). After the beginning of oxygen inhalation the curve rose, and after 6 min it flattened out on a plateau at 480 mm Hg. After the switch to inhalation of room air Tcp_aO_2 fell quickly and returned to its initial level after 4 min. In patient Kh., a man aged 54 years with chronic obstructive bronchitis, after the beginning of inhalation of oxygen it rose gradually, and did not reach its peak value until the 11th minute. After switching to inhalation of air, Tcp_aO_2 also fell slowly, and reached its initial level only after 10 min. A similar pattern was observed in patient M., a man aged 58 years with chronic bronchitis and emphysema of the lungs. In this case the desaturation time of the arterial blood was 12 min.

According to these investigations, the desaturation time of arterial blood both in normal subjects and in patients correlated highly with the helium mixing time in the lungs, determined on the POOL apparatus (coefficient of correlation r = 0.92). As regards the oxygen desaturation time of arterial blood, determined by the oxyhemometric method, great variability was observed with poor reproducibility of the measured parameter (standard deviation 11%).

The equality of ventilation is expressed most accurately by the ratio of alveolar ventilation to alveolar volume [2, 9]. This value is determined by the rate of flushing out of inert gas from the lungs or the rate of its mixing in the lungs. The method we suggest for determining inequality of ventilation is based on the principle of clearance of the lungs (in this case from oxygen) during respiration in an open system. If the degree of inequality of ventilation of the lungs is high, after inhalation of oxygen the time of return of p_aO_2 to its initial level is considerable (6-14 min). The reason is that oxygen, having filled the

poorly ventilated regions of the lungs, is flushed out of them over a long period of time and its partial pressure in the alveoli of these regions falls only gradually and slowly to its initially low values [9]. It is generally considered that an increase in the desaturation time, just as in the saturation time, depends mainly on inequality of pulmonary ventilation [1, 9], but it may be influenced by several factors the volume of alveolar ventilation and the functional reserve capacity of the lungs [3].

However, our experience has shown that for practical purposes the degree of inequality of ventilation can be determined sufficiently informatively by the use of the graph of the true time for p_aO_2 to fall to its initial level after oxygen inhalation.

Since oxygen is a biologically active gas, the level of change of p_aO_2 during inhalation of oxygen may be highly informative also for estimating disturbance of ventilation-perfusion ratios in the lungs and judging the increase in percentage of blood shunted inside the lungs.

The suggested method of determining inequality of ventilation of the lungs by transcutaneous continuous measurement of the arterial blood desaturation time (after oxygen inhalation), based on the principle of clearance of the lungs from oxygen, is an absolutely harmless, accurate, and reliable method, requiring no complex equipment for the use of inert gases (radioactive substances), and it can be recommended as a diagnostic method reflecting inequality of ventilation of the lungs. Meanwhile, if changes in the level of Tcp_aO_2 during inhalation of air and pure oxygen are recorded graphically, in some cases it is possible to draw conclusions regarding disturbances of ventilation-perfusion relations in the lungs.

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