Alveolar–Arterial O_2 Tension Difference in Monkeys under Captivity in Cages (33496)

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The difference in the oxygen tension between alveolar gas and arterial blood is an important measurement in the study of pulmonary gas exchange. The alveolar oxygen tension is always higher than the arterial oxygen tension. The alveolar–arterial oxygen difference (A—a DO_2) is due to three factors: uneven ventilation–perfusion ratio ($\dot{V}_A/\dot{Q}$) venous admixture to the pulmonary circulation and uneven diffusion-perfusion relationship. Under physiologic conditions, at normoxia, the ventilation–perfusion component comprises a major portion of A—a DO_2 gradient.

Since there is definite evidence of regional differences in $\dot{V}_A/\dot{Q}$ in the lung of an erect man (1), one would expect the effects of postural changes on the A—a DO_2. Studies by Riley *et al.* (2) indicate that A—a DO_2 is greater in erect position than in supine position in acute experimental conditions. In their elegant study, they showed that the immediate postural effects from upright to supine position were reduction of functional residual capacity and physiologic dead space along with the increase of pulmonary capillary blood flow at the apex of the lung. Diurnal variations in ventilation–perfusion relationship in man has also been established (3). Recently Cardus (4) reported significant increase of A—a DO_2 after 10 days of recumbency in man. The object of our study was to investigate the effects of prolonged partial immobilization on A—O_2 in monkeys.

Methods. Nine cynamologus (5 male and 4 female) monkeys (*M. irus*) weighing 2–4 kg were used for this study. Routine clinical, laboratory, chest X-ray studies and tuberculin tests were done on them to ensure their good physical conditions. They were placed in individual cages (24 × 18 × 20 in.) placed on a horizontal surface. They were supplied with regular monkey diet and water. They were first allowed to become acclimated for at least 2 months before any studies were undertaken. Arterial blood samples were drawn from femoral arteries of supine animals at six different intervals during an entire 10-month period following the initial period of acclimatization. The blood samples were drawn under light analgesia with intramuscular injections of phencylidine hydrocholoride (Sernylan, Parke Davis Co., Philadelphia) in doses of 1.0–1.5 mg/kg. Arterial blood samples were analyzed for gas tensions and pH by pO_2, pCO_2 and pH electrodes (Radiometer, Copenhagen). Alveolar pO_2 values were calculated by alveolar gas equation assuming a respiratory quotient of 0.8. The following form of alveolar gas equation was used.

$$p_AO_2 = p_IO_2 - \frac{p_aCO_2}{R} + (1-R)\cdot F_IO_2 \cdot \frac{p_aCO_2}{R}.$$

Results. Table I shows the means and standard deviation values of the parameters taken at six different intervals during the entire 10-month period. The six intervals were initial (0 month), 2.5, 3, 5, 8, and 10 months. The calculated mean A—a DO_2 values at those successive intervals were 2, 4.5, 6.4, 9.3, 20.3, and 21.5 mm, respectively.

Discussion. The calculated mean A—a DO_2 values progressively increase with the time of the duration of cage captivity. The assumption of $R = 0.8$ may introduce minimal uncertainty in the calculated A—a DO_2 values. The initial A—aDO_2, at the beginning of the investigation, was only 2 mm. At the end of the eighth month, the mean A—a DO_2 value became more than tenfold when compared to the initial value. The slope of rise of A—a DO_2 declined after 8 months. The values in Table I indicate that the increase in A—a DO_2 values with time is due to lowering of p_aO_2 values observed in successive determinations. All the p_aO_2 obtained after 2

TABLE I. Means and SD Values for Arterial Blood for Nine Monkeys at Different Intervals.

	1	2	3	4	5	6
p_aO_2	99 ± 5	91.5 ± 6.2	89.6 ± 5.5	92.7 ± 8.2	84.7 ± 4.2	83.5 ± 5.6
p_aCO_2	41.6 ± 2.2	44.5 ± 1.6	46.0 ± 4.6	39.3 ± 3.3	37.4 ± 3.8	40.4 ± 2.4
pH	7.40 ± 0.02	7.42 ± 0.013	7.40 ± 0.025	7.38 ± 0.073	7.378 ± 0.073	7.371 ± 0.052

months are significantly lower when compared to the initial mean value of 99 mm Hg ($p<0.05$). The p_aCO_2 values obtained between the second and fourth month appears slightly higher than the same obtained during the first determination. Subsequent p_aCO_2 values were either identical or slightly lower than the initial value. The arterial pH values show a downward tread during each successive determination except the second and third determinations.

Since it appears that the lowering of p_aO_2 values contributes a major component of the magnitude of A—a DO_2, I shall emphasize my discussion on the possible mechanisms of arterial hyposemia in our investigation. Slight hypoventilation observed in our second and third determinations may explain a portion of the increase of A—a DO_2 only during those periods. But since the p_aCO_2 values in the subsequent determinations are normal, arterial hypoxemia cannot be due to hypoventilation in our studies. Diffusion abnormality is unlikely the major mechanism for this arterial hypoxemia since the values were obtained at rest. Increase in the "venous admixture" component and altered ventilation–perfusion relationship appear to be the likely causes of this rising A—a DO_2. Unfortunately, I do not have any studies of the arterial blood gas breathing 100% oxygen (5) to quantitate the "shunt" component. It is possible and quite likely that a monkey being secluded in the cage for such a prolonged period has progressive and consistent poor perfusion in the upper lobes and overperfusion of the lower lobes. This would then cause a grossly uneven $\dot{V}_A/\dot{Q}$ relationship which can explain the arterial hypoxemia and hence, the progressively increasing A—a DO_2. It is possible that monkeys in jungles prevent the worsening of the preexisting uneven $\dot{V}_A/\dot{Q}$ relationship by their frequent and acrobatic activities. A monkey in a cage is in a state of incomplete immobilization. It is possible that prolonged and incomplete immobilization in monkeys may present a similar picture as is observed in man only 10 days after recumbency. The general downward trend of the p_aCO_2 and pH values suggest mild metabolic acidosis due to possible accumulation of metabolites secondary to poor tissue perfusion of the dependent parts related to prolonged partial immobilization.

So far, there is no published report of this sort of study on experimental animals. In view of these physiologic studies, it is mandatory that a control group should be used for comparison for any stressed group under study.

Summary. The A—a DO_2 values increase in monkeys in captivity in the cages. Uneven ventilation–perfusion relationship is possibly the major mechanism leading to increased venous admixture to the pulmonary circulation. Increase in A—a DO_2 with period of cage captivity is primarily due to progressive arterial hypoxemia resulting from increased venous admixture.

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