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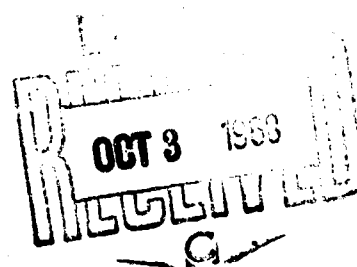
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## OXYGEN CONSUMPTION OF THE ISOLATED PERFUSED LUNG LOBE OF THE DOG

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(Pflüger's Archives of General Physiology)  
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According to Bostroem and Lochner's investigations [4] the  $O_2$  consumption of an isolated lung lobe perfused with blood from a donor dog greatly increases when the blood pressure of the donor dog is lowered by opening a vein. In their experiments this rise in the  $O_2$  consumption was so great (up to six to nine times the control value) that 10 to 30% of the total consumption of oxygen would have had to be allotted to the lung alone. Bostroem and Lochner's method was technically difficult and complicated. The  $O_2$  consumption of the lung lobe was found as the difference between the spirometrically determined  $O_2$  absorption and the  $O_2$  given off as determined by Fick's principle. The variation of their measured values is also very great.

We attempted to confirm this interesting phenomenon by a simpler method. The essential feature of our method consisted in the fact that the alveolar-capillary gas exchange was eliminated by filling the lung lobe with Ringer's solution. The  $O_2$  consumption of the lung lobe could then be determined by Fick's principle (= arterio-venous  $O_2$  content difference · perfusion).

In determining the arterio-venous  $O_2$  content difference the polarographic method of measuring the  $O_2$  pressure was used. This method is particularly well suited to measurement of a small difference in  $O_2$  content in the hyperoxic range, where the hemoglobin is practically 100% saturated with  $O_2$ .

In addition to checking the observation of increase in  $O_2$  consumption with lowered blood pressure in the donor dog, it was our objective to determine the absolute value of the  $O_2$

consumption of the lung lobe, and also its dependence on the magnitude of the perfusion and the type of the perfusion blood (arterial or venous).

#### Method

For the experiments the atelectatic left or right lung of a 9-14 kg dog was used and perfused with arterial or venous blood from an 13-27 kg donor dog.

Both dogs were pretreated with morphine (2 mg/kg subcutaneous) and then narcotized either with 80 mg/kg of chloralose given intravenously or with 1.25 g/kg of urethan (sometimes intravenously, sometimes intramuscularly). Coagulation of the blood was prevented with heparin (5 mg/kg).

The lung donor dog was killed by bleeding. Immediately afterwards the lung lobe was dissected out, attached to the experimental apparatus, and perfused. The air was removed from the lung lobe by resorption during perfusion with venous blood from the hyperoxic donor dog. The process was accelerated by having the lung donor dog breath 100% O<sub>2</sub>. To remove any remaining traces of air the lung lobe was washed well with Ringer's solution through the bronchus and then filled with 20 to 50 ml of Ringer's solution.

The experimental lung lobe was hung in a chamber filled with Ringer's solution at 37°. The blood for perfusion was conveyed from the artery or the vena femoralis of the donor dog by means of a blood pump through a temperature regulator into the artery of the lung lobe. The outflow from the pulmonary vein took place through a measuring cylinder into the jugular vein of the donor dog, which was placed correspondingly lower. The perfusion was started with the blood pump and measured at the outflow with measuring cylinder and stop watch. To prevent the collapse of the capillaries, the pressure in the pulmonary vein was set slightly positive ( $\approx$ +2 mm Hg). The blood temperature shortly before and after passage through the lung was 36.5-37.5° C.

The donor dog was given a respiratory mixture which in the experiments with arterial perfusion contained 60-85% O<sub>2</sub> in N<sub>2</sub>, but in the experiments with venous perfusion consisted of 100% O<sub>2</sub>. In order to have something like a normal CO<sub>2</sub> pressure in the perfusion blood for the lung lobe, the endexpiratory CO<sub>2</sub> content was checked in the donor dog with the URAS apparatus and kept at 4-6% CO<sub>2</sub>. Some donor dogs could be left with spontaneous breathing, some had to be given artificial respiration, and some were given a continuous infusion of succinyl cholin to suppress spontaneous respiration and then were given artificial respiration.

The O<sub>2</sub> pressure in the blood samples from the artery and the pulmonary vein of the lung lobe were measured immediate-

Table 1. O<sub>2</sub> Consumption of the Lung Lobe

Control Conditions

Exp. No.	Perfusion Blood	anarco-sis <sup>1</sup>	Weight of Lung Donor (g)	Dry Weight of Lung Lobe (g)	No. of Measurements	Perfusion (ml/min)	O <sub>2</sub> Pressure in Art. Pulm. (mm Hg)	O <sub>2</sub> Consumption of Lung Lobe <sup>2</sup>
1	arterial	U + C	11.0	9.0	5	145	554	0.025
2	arterial	U + C	10.0	9.0	4	150	338	0.034
3	arterial	U + C	9.5	8.0	5	144	477	0.019
4	arterial	U + C*	9.0	4.0	6	104	392	0.036
5	arterial	U + C*	14.0	8.5	7	100	349	0.017
6	arterial	U	9.0	6.0	5	100	519	0.030
7	arterial	U	12.0	6.0	7	100	473	0.022
Average:								0.026
8	venous	U	11.0	7.2	14	50	64	0.015
9	venous	U	19.0	6.6	8	50	89	0.021
10	venous	U*	10.5	5.8	13	50	57	0.024
11	venous	U*	9.0	4.5	12	50	86	0.030
Average:								0.023
Overall Average:								0.025
Average error of the overall average:								±0.002

<sup>1</sup>U + C - urethan-chloralose, U - urethan. -- \*Continuous succinyl cholin infusion.

<sup>2</sup>  $\left( \frac{\text{ml}}{\text{min} \cdot \text{g dry weight}} \right)$

ly after removal with the membrane-covered platinum electrode by the method of Gleichmann and Lübbers [7] at 37°. The electrode was calibrated with tonometered blood samples. In order to avoid an error conditioned by the O<sub>2</sub> consumption of the blood (which can be especially great at high O<sub>2</sub> pressures), the readings were made each time at exactly the same interval of time after the blood was taken.

All measurements of O<sub>2</sub> consumption were made within the period of 40 minutes to 3 to 5 hours after removal of the lung lobe. In the experiments with changes in the rate of perfusion the first measurements were made in each case 20 minutes after the new rate of perfusion was set. Since the values in the second measurement (10 to 15 minutes later) agreed with the values of the first measurement, a sufficiently stationary condition must have been attained. In the experiments in which

the blood pressure of the donor dog was varied, the periods lasted about one hour and the measurements were made 15-25 minutes after the blood pressure of the donor dog was set. In all experiments 3 to 7 measurements of the arterio-venous  $O_2$  pressure difference were made in each period.

Evaluation. -- The arterio-venous  $O_2$  content difference was computed as arterio-venous  $O_2$  pressure difference times the slope of the  $O_2$  fixing curve. In the experiments with arterial perfusion the  $O_2$  pressure in the pulmonary vein was always higher than 200 mm Hg. The slope of the  $O_2$  fixing curve could therefore be set equal in that case to the solubility coefficient of the  $O_2$  in the blood. In the experiments with venous perfusion the slope of the  $O_2$  dissociation curve was estimated in the range of measurement by determination of the  $O_2$  content and  $O_2$  capacity in van Slyke's apparatus and with the aid of the  $O_2$  fixing curves for canine blood given by Bartels and Harms [3]. The  $O_2$  consumption was computed as the product of the arterio-venous  $O_2$  content difference and the perfusion and adjusted to the dry weight (dried at  $90^\circ$  to the point of constant weight).

## Results

### 1. $O_2$ Consumption in Perfusion with Arterial and Venous Blood

The  $O_2$  consumption was measured on seven lung lobes with perfusion with arterial blood ( $p_{O_2} = 340-550$  mm Hg) and on four lung lobes with perfusion with venous blood ( $p_{O_2} = 55-90$  mm Hg). Table 1 shows the  $O_2$  consumption figures for control conditions (= magnitude of perfusion shown, normal blood pressure of the donor dog). These figures are averages of 4 to 14 individual measurements in each experiment. The overall average of  $O_2$  consumption is  $0.025$  ml  $O_2$ /minute·gram dry weight ( $s_{\bar{x}} = \pm 0.002$ ). Between the averages of  $O_2$  consumption in the case of arterial perfusion and that of venous perfusion ( $0.026$  and  $0.023$  ml  $O_2$ /min·g dry weight respectively) there is no significant difference.

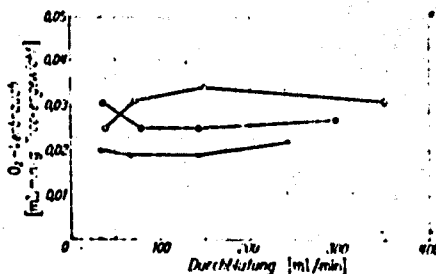


Figure 1. Relationship between  $O_2$  consumption and perfusion in the isolated lung lobe of the dog. o—o experiment no. 1; ●—● experiment no. 2; ●—● experiment no. 3. Vertical scale:  $O_2$  consumption (ml/min·g dry wt.). Horizontal scale: perfusion (ml/min).

Table 2. Relationship between Normal Blood Pressure of the Donor Dog and  $O_2$  Consumption of the Isolated Lung Lobe

Exp. No.	Perfusion (ml/min)	Blood Pressure of the Donor Dog (mm Hg)	$O_2$ Consumption of the Lung Lobe (ml/min · dry wt.)	L/N <sup>1</sup>
4	104	100	0.044	0.80
		72	0.035	0.82
		105	0.043	0.70
		55	0.030	0.86
		105	0.035	0.91
		50	0.032	0.94
		105	0.034	
5	100	91	0.017	0.82
		54	0.014	0.82
		97	0.017	1.06
		51	0.018	
6	100	86	0.019	1.32
		50	0.025	0.78
		99	0.032	0.81
		55	0.026	
7	100	92	0.021	1.10
		50	0.023	1.00
		100	0.023	1.17
		50	0.027	
			Average (n = 15):	0.92

Perfusion with Venous Blood

Exp. No.	Perfusion (ml/min)	$O_2$ Pressure in A. pulmonalis (mm Hg)	Blood Pressure of Donor Dog (mm Hg)	$O_2$ Consumption of Lung Lobe (ml/min · g)	L/N
8	50	59	95	0.014	0.93
		50	55	0.013	0.81
		70	95	0.016	1.13
		59	55	0.018	
9	50	84	90	0.012	0.92
		64	55	0.011	0.37
		94	90	0.030	
10	50	59	90	0.017	1.67
		45	55	0.028	0.90
		55	85	0.031	1.06
		51	55	0.033	
11	50	74	95	0.029	1.40
		66	55	0.030	1.00
		97	95	0.030	
			Average (n = 10):	0.98	

<sup>1</sup> L/N =  $\frac{O_2 \text{ Consumption with Lowered Blood Pressure}}{O_2 \text{ Consumption with Normal Blood Pressure}}$  . See Note.



[Note to Table 2] Overall average L/N (n = 25): 0.95;  
mean error of the overall average:  $\pm 0.05$ .

## 2. Variations in the Magnitude of Perfusion and O<sub>2</sub> Consumption

For three lung lobes the O<sub>2</sub> consumption was measured with perfusion varying in the range from 350 ml/minute ( $\approx$  normal value) to 30 ml/minute. The measured values are shown in Figure 1. These lung lobes were perfused with arterial blood. There is no recognizable connection between the magnitude of perfusion and the O<sub>2</sub> consumption.

## 3. Lowered Arterial Blood Pressure of the Donor Dog and the O<sub>2</sub> Consumption of the Lung Lobe

Eight experiments were done to test whether lowering the arterial blood pressure of the donor dog affects the magnitude of the O<sub>2</sub> consumption of the lung lobe. In the first four experiments the lung lobe was perfused with arterial blood, in the other four with venous blood. The blood pressure of the donor dog (18 to 27 kg) was lowered on the average from 95 to 55 mm Hg by drawing 150-550 ml of blood.

The measurement data are shown in Table 2. By way of analysis of a possible effect of the lowered blood pressure on the quotients L/N (= O<sub>2</sub> consumption at lowered blood pressure divided by O<sub>2</sub> consumption at normal blood pressure) was derived for all measurement periods, consecutive in each case. The overall average of 25 quotients L/N amounted to 0.95 ( $s_{\bar{x}} = \pm 0.05$ ). Thus no dependence of the O<sub>2</sub> consumption on the blood pressure reduction was found.

## Discussion

The preparation of the fluid-filled lung lobe has the advantage that determination of the O<sub>2</sub> consumption in the hyperoxic range by means of polarographic measurement of the arterio-venous O<sub>2</sub> pressure difference is relatively simple and exact. Accordingly, the spread of measurement data in our experiments was much less than in those of Bøstroem and Lochner [4], whose method was technically complicated.

In the hyperoxic range (with arterial perfusion) the measurement was relatively easy, since the arterio-venous O<sub>2</sub> pressure difference was usually 30 to 100 mm Hg. In the hypoxic range on the other hand (with venous perfusion) the arterio-venous O<sub>2</sub> pressure difference was only 1 to 6 mm Hg (even with lowered rate of perfusion of 50 ml/minute). There were also difficulties in some cases in determining the slope of the O<sub>2</sub> fixing curve. The aim of our experiments with venous perfusion was primarily to find the effect of lowered blood pressure in the donor dog on the O<sub>2</sub> consumption of the lung lobe, not to determine precisely the absolute value of the O<sub>2</sub> consumption. For that reason the noticeably good correspondence of the ab-

Table 3. Summary of Measurements of  $O_2$  Consumption of the Canine Lung

Authors	Method	Measured $O_2$ Consumption Reported	$O_2$ Consumption <sup>1</sup>
Evans & Starling (1913)	heart-lung preparation	1 ml/hr·g heart wt.	0.023
Stadie, Riggs, & Naugaard (1945)	Warburg	140 micromol/hr·g dry weight	0.051
Bostroem & Lochner (1955)	isolated lung lobe	0.071 ml/min·g dry weight	0.071
Aviado (1959)	Warburg	0.64 ml/min·100 g moist weight	0.032
Aviado, Daly, Lee, & Schmidt (1961)	lung in situ, perfused from A. bronchialis	0.48 ml/min·100 g moist weight	0.024
Cartwright, Lim, Luft, & Palich (1962)	Lung in situ, perfused from A. bronchialis	1.6 ml/min·whole lung	0.080
Kusachi and Piiper (1962; this article)	isolated lung lobe		0.025

<sup>1</sup>Computed by us; ml  $O_2$ /min·g dry weight.

solute values of  $O_2$  consumption between the two series of experiments -- with arterial and with venous perfusion -- may be partially accidental.

A summary of measurements of the  $O_2$  consumption of the canine lung by other authors is to be found in Table 3. The value found by us for the  $O_2$  consumption fits into the lower range of values.

Although the spread of the measurement data is usually so great that the authors' averages hardly differ from each other statistically, some interesting relationships show up in a comparison of the values. In Bostroem and Lochner's experiments on the isolated lung [4] and in the experiments of Cartwright et al. [5] on canine lungs in situ the  $O_2$  consumption of the lung was measured as the difference between the  $O_2$  absorption from the respiratory air and the  $O_2$  transport determined according to Fick's principle. The two averages are relatively high and agree well with each other. Aviado et al. determined the  $O_2$  consumption in collapsed lungs in situ by the  $O_2$  transport via the blood stream alone, or in principle the same as we did. Their average is relatively low and like our average. This relationship might be interpreted as meaning that only a part of the  $O_2$  consumption of the lung can be covered by way of the blood and that a part of the  $O_2$  consumption (of the bronchial epithelium, say?) is covered directly from the respired air. Still, it is hard to understand how the necessary substratum for  $O_2$  consumption could get into

the cells that extract  $O_2$  from the bloodstream.

In the experiments of Iviado et al. and of Cartwright et al. the lungs were perfused exclusively via the bronchial artery, but in Bostroem and Lochner's experiments and in ours, via the pulmonary artery. That the results show no relationship to this methodological difference might be viewed as an argument for a great degree of anastomosis between the pulmonary and the bronchial vascular systems.

The amount of the perfusion was naturally small in the experiments with perfusion from the bronchial artery and large in the experiments with perfusion from the pulmonary artery. Since the  $O_2$  consumption figures are very similar, no dependence of the  $O_2$  consumption upon the amount of the perfusion appeared to exist. Systematic investigation of the dependence of the  $O_2$  consumption on the perfusion in our preparations also gave a negative result (Figure 1).

The main objective of our experiments was to check the great increase in  $O_2$  consumption of the isolated lung lobe with reduction of the blood pressure of the donor dog by opening a vein, found by Bostroem and Lochner [4]. We were concerned to imitate the experimental conditions of Bostroem and Lochner's experiments as closely as possible (narcosis, perfusion with venous blood, degree of reduction of blood pressure, time relationships,  $O_2$  respiration of the donor dog). The only essential methodological difference consisted in the fact that Bostroem and Lochner inflated the lungs with  $O_2$ , while we kept them free of air and filled them with Ringer's solution.

Our result in this respect was completely negative; in none of the eight experiments could any increase in the  $O_2$  consumption of the lung lobe with lowered blood pressure of the donor dog be detected (Table 2). For the difference between our results and Bostroem and Lochner's we have no explanation.

### Summary

→ The  $O_2$  consumption of the isolated dog lung lobe perfused with blood from a donor dog was investigated. The lung lobe had been made atelectatic and filled with Ringer's solution. The arterio-venous  $O_2$  pressure difference was measured by polarography. ~~The following results were obtained:~~

1. The average  $O_2$  consumption of 11 lung lobes was 0.025 ml/min(g) of dry weight.
2. There was no significant difference in  $O_2$  consumption between lung lobes perfused with arterial blood ( $pO_2^A = 340-550$  mm Hg) and those perfused with venous blood ( $pO_2^V = 255-90$  mm Hg).
3. Variation of the perfusion rate between 350 ml/min (normal value) and 30 ml/min did not change the  $O_2$  consumption.

4. The effect of the partial pressure of the gases on the rate of the respiratory exchange and on the magnitude of the  $O_2$  consumption of the isolated lung, etc.

#### Bibliography

1. Aviado, D.M., "Changes of Experimental Pulmonary Blood in the Lung," Circulation Research, Vol 7, 1959, page 1018.
2. Aviado, D.M., Daly, M.B., Lee, C.Y., and Schmidt, C.F., "The Contribution of the Bronchial Circulation to the Venous Admixture in Pulmonary Venous Blood," Journal of Physiology (London), Vol 155, 1961, page 602.
3. Bartels, H. and Harnas, H., "Oxygen Dissociation Curves of the Blood of Mammals," Pflügers Archiv für die Gesamte Physiologie (Pflüger's Archives of General Physiology), Vol 268, 1959, page 334.
4. Bostroom, B. and Lochner, W., "The Oxygen Consumption of the Lung," Pflügers Archiv für die Gesamte Physiologie, Vol 260, 1955, page 211.
5. Cartwright, R.S., Lim, T.P., Luft, U.C., and Palich, W.E., "Pathophysiological Changes in the Lungs During Extracorporeal Circulation," Circulatory Research, Vol 10, 1962, page 131.
6. Evans, C.L. and Starling, E.H., "The Part Played by the Lungs in the Oxidative Processes of the Body," Journal of Physiology (London), Vol 46, 1913, page 413.
7. Gleichmann, U. and Lübbers, D.W., "Measurement of the Oxygen Pressure in Gases and Liquids with the Pt Electrode, with Special Attention to Measurement in the Blood," Pflügers Archiv für die Gesamte Physiologie, Vol 271, 1960, page 431.
8. Stadie, W.C., Riggs, B.C., and Haugaard, N., "Oxygen Poisoning. The Effect of High Oxygen Pressure upon the Metabolism of Liver, Kidney, Lung, and Muscle Tissue," Journal of Biological Chemistry, Vol 160, 1945, page 209.

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