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# A NEW ASSUMPTION FOR THE CHANGE IN PULMONARY VENOUS ADMIXTURE WITH VARYING INSPIRED OXYGEN

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## INDEXING WORDS

oxygen; pulmonary shunt; restrictive lung; pulmonary gas change; oxygen partial pressure in blood; lung; shunts

## SYNOPSIS

Pulmonary venous admixture was considered to be decreased by oxygen inhalation. Recent investigations, however, reveal that it may actually increase, decrease or not alter. The mechanism of producing these diversified changes is as yet controversial.

The purpose of this study is to analyze the effect of inspired oxygen on pulmonary venous admixture in the entire therapeutic range of inspired oxygen.

The investigation was performed in intact and restrictively impaired lungs of 15 anesthetized and ventilated mongrel dogs.

The results reveal that the pattern of response of pulmonary venous admixture with increasing inspired oxygen is basically biphasic, and represents a rule as a function of arterial oxygen tension rather than alveolar oxygen tension.

From the results a new assumption may be induced; the pattern is mainly decided by the shape of oxygen content curve and the scattered range of arterial oxygen tension on the curve.

## INTRODUCTION

Pulmonary venous admixture (Qsp/Qt) has been considered to be

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occurred by three major causes; namely, 1) diffusion factors, 2) ventilation-perfusion imbalance, and 3) true shunt. According to this conventional theory for pulmonary gas exchange, pure oxygen inhalation will minimize both the diffusion abnormalities and the effects of lung units with low ventilation-perfusion ratio, and the effect of true shunt remains. This indicates that Qsp/Qt at pure oxygen inhalation should be the smallest value among various inspired oxygen concentrations ($FiO_2$).[1-4]

Recent investigations,[4-10] however, reveal that Qsp/Qt actually increases or does not alter. There seems to be a tendency that the increase of it is often seen in intact or slightly impaired lungs[4-6, 9, 10] whereas the decrease is observed in moderately or severely impaired lungs.[5, 7, 8] Although several assumptions to explain the increase in Qsp/Qt have been introduced, the mechanism involved in producing these Qsp/Qt's changes is as yet controversial.[11]

The purpose of the present investigation, therefore, was to quantitate the effect of varying $FiO_2$ on Qsp/Qt in dogs with various impaired lungs, and to determine whether Qsp/Qt is directly decided by the alveolar oxygen tension.

## MATERIALS AND METHODS

Fifteen mongrel dogs weighing 7.6 ± 1.3 (mean ± s.d.)Kg were anesthetized with thiamylal (25 mg/Kg) and paralyzed with pancuronium bromide (0.1 mg/Kg) given intravenously. The dogs were placed on a heating pad to maintain a normal core temperature and ventilated with an animal volume-limited ventilator at a tidal volume of 15 to 20 ml/Kg and at a rate of about 10 cycles per minute to keep arterial carbon dioxide tension within the range of 30 to 40 mmHg. Catheters were placed in the femoral vein and artery for blood sampling and infusion. Pulmonary arterial blood sampling and pulmonary arterial pressure were obtained through a Swan-Ganz flow directed catheter.

The dogs were divided equally into three groups. The first group with intact lungs were used as control. The second and third group dogs were with restrictive lungs, in which their left chests were opened at the 4th intercostal space and about one-third and two-thirds of their chest cavities were packed firmly with gauzes in the group 2 and 3 to obtain moderately and severely impaired lung respectively.

Each dog was ventilated with gas mixtures varying oxygen in balanced $N_2$, as well as 100% $O_2$, for 15 to 20 minutes through the non-rebreathing system before blood samplings were obtained. The inspired

oxygen concentration was checked with magnetic oxygen analyzer (Model-D2, Beckman-Toshiba, Ltd.) and core temperature was measured. This procedure was repeated in various inspired oxygen concentrations; 0.2, 0.4, 0.6, 0.8 and 1.0 levels at random order. In the group 2 and 3, cardiac output was measured by the electromagnetic flow meter (MF-27, Nihon Kohden) attached to the ascending aorta.

Blood samplings from femoral and pulmonary arteries were analyzed immediately after withdrawal for blood gas tension, pH and hemoglobin concentration on micro-blood gas analyzer (ABL 2 acid-base laboratory, Radiometer, Copenhagen).

All measured data were corrected to core temperature. Alveolar oxygen tension was calculated by means of the alveolar air equation and assuming a respiratory quotient of 0.8. [12] Arterial and mixed venous oxygen contents ($CaO_2$, $C\bar{v}O_2$) were calculated using the program assuming a hemoglobin-oxygen combining capacity of 1.34 ml/g. [13] Pulmonary venous admixture was obtained using the equation:

$$Qsp/Qt = (Cc'O_2 - CaO_2) / (Cc'O_2 - C\bar{v}O_2)$$

where $Cc'O_2$ is ideal pulmonary end-capillary oxygen content.

Statistical analysis of the data was performed using Student's t tests for paired data.

## RESULTS

For each dog, arterial pH and $Pco_2$ did not significantly change in the time course throughout each investigation. The mean arterial-venous oxygen content difference in each group and the mean cardiac output in group 2 and 3, do not show any statistically significant changes (Table 1). Mean alveolar oxygen tension in all three groups are calculated to facilitate a graphical explanation. The changes of pulmonary venous admixture are greatly different between the intact lungs and the restrictive lungs (Fig. 1). The plot of Qsp/Qt as a function of mean alveolar oxygen tension in group 1 increases steadily as $FiO_2$ increases above 0.4, and when $FiO_2$ is reduced to 0.2, it increases de novo with statistical significance ($p<0.05$). In all restrictive preparations, although the plots of Qsp/Qt are changed in a somewhat similar tendency, it appears to have changed more markedly in group 3. In these groups, Qsp/Qt remarkably decreases as alveolar oxygen tension increases in the low $FiO_2$ region, but in the high $FiO_2$ region it exhibits a plateau-like curve.

On the other hand, as Qsp/Qt for each serial measurement are plotted against $PaO_2$ instead of $PAO_2$, it seems that a regular change in Qsp/Qt

Table 1 Change in cardiac output and other parameters at various $FiO_2$ values (mean ± s.d.).

| | $FiO_2$ | | 0.21 | 0.4 | 0.6 | 0.8 | 1.0 |
|---|---|---|---|---|---|---|---|
| | $PAO_2$ | (mmHg) | 116.4 ± 7.9 | 277.4 ± 16.9 | 404.1 ± 21.2 | 542.2 ± 15.6 | 676.2 ± 14.8 |
| | pHa | (unit) | 7.514 ± 0.098 | 7.519 ± 0.071 | 7.513 ± 0.067 | 7.513 ± 0.086 | 7.499 ± 0.070 |
| Group 1 | $Paco_2$ | (mmHg) | 24.3 ± 5.4 | 24.5 ± 6.3 | 23.4 ± 4.2 | 23.3 ± 4.4 | 23.6 ± 4.1 |
| | $a-\bar{v}DO_2$ | (vol%) | 5.1 ± 0.9 | 5.0 ± 1.0 | 4.9 ± 0.9 | 4.9 ± 0.6 | 5.0 ± 0.6 |
| | C.O. | (L/min.) | ———— | ———— | ———— | ———— | ———— |
| | pHa | (unit) | 7.389 ± 0.049 | 7.380 ± 0.043 | 7.388 ± 0.043 | 7.387 ± 0.045 | 7.379 ± 0.059 |
| Group 2 | $Paco_2$ | (mmHg) | 27.6 ± 3.9 | 27.6 ± 4.6 | 27.8 ± 6.7 | 27.4 ± 6.9 | 28.6 ± 6.4 |
| | $a-\bar{v}DO_2$ | (vol%) | 6.5 ± 1.4 | 6.1 ± 0.9 | 5.9 ± 0.8 | 5.8 ± 0.6 | 5.9 ± 0.6 |
| | C.O. | (L/min.) | 0.79 ± 0.13 | 0.82 ± 0.14 | 0.79 ± 0.10 | 0.75 ± 0.10 | 0.74 ± 0.11 |
| | pHa | (unit) | 7.338 ± 0.107 | 7.332 ± 0.118 | 7.338 ± 0.124 | 7.331 ± 0.126 | 7.333 ± 0.132 |
| Group 3 | $Paco_2$ | (mmHg) | 35.0 ± 7.4 | 35.4 ± 9.8 | 35.4 ± 9.2 | 36.3 ± 9.4 | 36.1 ± 10.3 |
| | $a-\bar{v}DO_2$ | (vol%) | 4.1 ± 0.9 | 4.1 ± 1.4 | 4.5 ± 1.3 | 4.7 ± 1.4 | 4.7 ± 1.2 |
| | C.O. | (L/min.) | 0.88 ± 0.28 | 0.90 ± 0.23 | 0.88 ± 0.20 | 0.80 ± 1.0 | 0.87 ± 0.1 |

Abbreviations ; $PAO_2$ : alveolar oxygen tension, pHa : arterial pH, $Paco_2$ : arterial carbon dioxide tension, $a-vDO_2$ : arterial-venous oxygen content difference, C.O. : cardiac output.

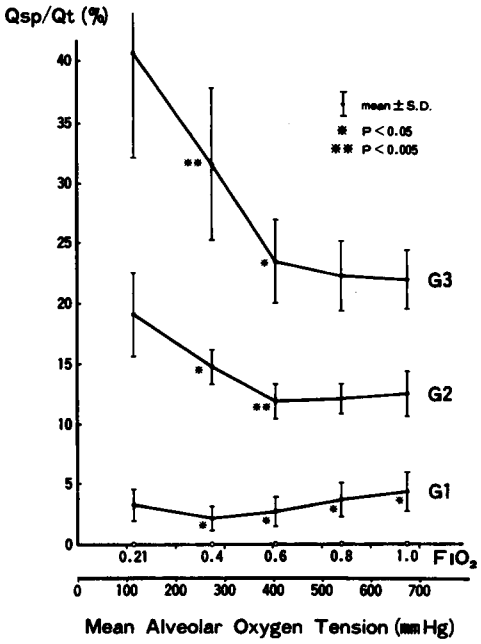


Fig. 1
Relationship between changes in mean alveolar oxygen tension and in pulmonary venous admixture produced by varying $FiO_2$ from room air to pure oxygen. Values represent mean ± sd of five observations. Asterisks indicate significant difference between two adjecent Qsp/Qt values : *p<0.05, **p<0.005.

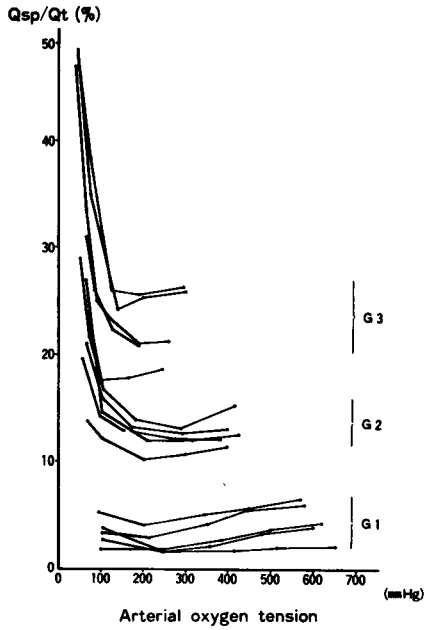


Fig. 2
Qsp/Qt for each dog is replotted as a function of arterial oxygen tension instead of alveolar oxygen tension.

is recognized (Fig. 2); the pattern of response is biphasic, and it is represented by a decreasing arm when $PaO_2$ is below 100 mmHg to 150 mmHg and an increasing arm at above 150 mmHg to 200 mmHg of $PaO_2$.

As the lung is impaired to a greater degree, the entire value of Qsp/Qt curves seems to be larger.

## DISCUSSION

According to the conventional theory of gas exchange, the significant decrease should be occurred in Qsp/Qt as $FiO_2$ increases from room air to pure oxygen.[1-4] Many diversified observations, however, have been reported. Some investigators[14-18] confirmed the propriety of the theory, and others showed the contradictory observations and introduced several

assumptions to interpret their results; absorption atelectasis and decreased functional residual capacity, [20, 21] the improvement of hypoxic pulmonary vasoconstriction in low ventilation-perfusion area, [6] the influence of low mixed venous oxygen tension on lung units, [22] the extra alveolar pulmonary shunting, [23] the releasing of a vasoactive substance [24] or the changing of $O_2$-binding capacity in the blood. [8] Some of these remain as speculated factors and others are contraversial. [7, 11] All of them, except for the last one, are based on the active bio-physiological effect of oxygen at pulmonary end-capillaries or alveoli. [25]

Recently, the serial measurements of Qsp/Qt in the same individuals in various levels of $FiO_2$ resulted in the biphasic pattern of response. [23, 24] Since the results in this study (Fig. 1) are similar to theirs, the conventional theory may be accounted for the decrease in Qsp/Qt and the active biophysiological effect of oxygen may be acceptable for the mechanism of the increasing arm in Qsp/Qt. [23]

Here is, however, a contradiction that these concepts are based on the value of $PAO_2$ but not $PaO_2$. This means these concepts are not responsible for the pattern of response in Qsp/Qt shown in Fig. 2. As a matter of fact, it is difficult to explain that the pattern of response in Qsp/Qt has a regular change against the value of $PaO_2$, that the changing range from the decreasing to the increasing arm should be at around 150 mmHg of $PaO_2$, and that the decreasing arm is steeper than the increasing arm.

We suggest an assumption that the biphasic pattern of response in Qsp/Qt as varying $FiO_2$ may be induced by the shape of oxygen content curve and the scattered range of $PaO_2$ on the oxygen content curve, but not by the lung units.

This assumption is based on the following concepts: it may be assumed on the shunt equation that the pattern of response in Qsp/Qt is contributed to the pattern of response in pulmonary capillary-arterial oxygen content difference ($Cc'O_2 - CaO_2$), since if arterial-mixted venous oxygen content difference ($a\text{-}vDO_2$) do not change, the relationship between Qsp/Qt and $Cc'O_2 - CaO_2$ is a inversed parabolic curve but it seems to be linear within the narrow range of the $Cc'O_2 - CaO_2$. The value of $PAO_2$, on the other hand, is generally included within the flat portion of oxygen content curve, even if $FiO_2$ will be varied from room air to pure oxygen. This means the change of $Cc'O_2$ may be within small range in parallel with the value of $PAO_2$. On the contrary, the value of $PaO_2$ may be scattered widely from the flat to the steeper portion of oxygen content curve depending on the lung function of gas exchange, then the value of $CaO_2$ may

be varied more widely than $Cc'O_2$. The value of $Cc'O_2 - CaO_2$ may be changed mainly depending on the value of $CaO_2$.

These characteristics of the shunt equation and the oxygen content curve indicate that the change in Qsp/Qt as varying $FiO_2$ may be attributed to the varying $PaO_2$, and thus resulting in a characteristic biphasic shape.

This assumption can be acceptable for the diversified observations of the change in Qsp/Qt obtained at two $FiO_2$ levels, which have been previously reported (Table 2).

In the group of the decreased Qsp/Qt at high inspired oxygen concentration, $PaO_2$ obtained at room air is below 100 mmHg and the Qsp/Qt represents larger value on the decreasing arm than the Qsp/Qt, $PaO_2$ at room air is usually over 100 mmHg, and the Qsp/Qt may situate around the bottom of the biphasic curve or on the increasing arm and has smaller value than the Qsp/Qt at high oxygen inhalation. It is reasonable that there may be very few chances to obtain the same value on each arm.[5]

These facts seem to coincide with the tendency that the increase of Qsp/Qt is induced in intact or slightly impaired lungs whereas the decrease in moderately or severely impaired lungs.

According to this assumption, it may be suggested that the intrapulmonary factors i.e. diffusion, ventilation-perfusion imbalance and true shunt, and also speculating factors induced by the effect of oxygen at alveoli, may not influence directly on the pattern of response in Qsp/Qt as $FiO_2$ is varied, but are the deciding factors for the entire level of a Qsp/Qt curve and contribute to the scattered range of $PaO_2$ on the oxygen content curve.

Mashiko[8] suggested that in both dogs and artificial lungs the change in Qsp/Qt as varying $FiO_2$ may be the phenomena independent of the intrapulmonary factors and may be caused by the change of oxygen binding capacity in the blood. His assumption is partly similar to ours in this respect.

Although a possibility may be considered that the restrictive lung model has a pathognomonic pattern of response in Qsp/Qt, the similar observation in this study can be represented by replotting data which were obtained from patients with non-restrictive lung deseases,[24] and was illustrated partly in other report.[9] Therefore, the pattern may be irrespective of the patho-physiological causes.

In conclusion, although Qsp/Qt has been used widely to assess the lung function of gas exchange, it is very questionable that the change

Table 2 Representative studies from the literature illustrating changes of Qsp/Qt and $PaO_2$ at two different levels of $FiO_2$.

| Study and Reference | Low $FiO_2$ | | High $FiO_2$ | | Remarks |
|---|---|---|---|---|---|
| | $PaO_2$ | Qsp/Qt | $PaO_2$ | Qsp/Qt | |
| | | Increased Data | | | |
| Nunn, Bergman and Coleman (1965) 9 | 102 ± 24.7 | 9.3 ± 6.5 | 517 ± 65.7 | 10.8 ± 4.1 | Controlled ventilation |
| Bergman (1967) 19 | 81 ± 20 | 10.4 ± 6.4 | 347 ± 84 | 11.0 ± 4.5 | Controlled ventilation |
| Suter, Fairley and Scholbohm | 103 ± 7.0 | 15.5 ± 1.8 | 369 ± 26 | 21.7 ± 2.1 | Controlled ventilation |
| (1975) 6 | 112 ± 7.0 | 14.1 ± 1.7 | 398 ± 20 | 19.7 ± 1.9 | Controlled vent. with PEEP |
| Kerr * (1975) 26 | 170 | 6.7 | 422 | 12.3 | Controlled vent. (Patiat No. 12) |
| Drummond, Wildsmith and Masson * (1978) 7 | 143 ± 31.3 | 5.4 ± 3.3 | 333 ± 43 | 8.4 ± 2.4 | Controlled vent. (Group H.) |
| | | Decreased Data | | | |
| Said and Banerjee (1963) 16 | 93 ± 3 | 3.3 ± 1.8 | 630 ± 15 | 1.6 ± 0.7 | Spont Resp. (Normal) |
| | 70 ± 11 | 20.7 ± 12 | 521 ± 70 | 7.4 ± 4 | " (Emphysema) |
| Aryers, Criscitiello and Grabovsky (1964) 14 | 87 ± 6.1 | 6.2 ± 4.0 | 654 ± 86.4 | 3.0 ± 1.9 | Spont Resp. (Normal) |
| Nunn (1964) 18 | 70 ± 13.6 | 21.0 ± 11.7 | 476 ± 76 | 14 ± 4.4 | Spont Resp. (Normal) |
| Hedley-Whyte, et al. | 65 ± 3.9 | 15.5 ± 0.7 | 319 ± 43.9 | 14.2 ± 1.7 | Controlled Vent. (Post AVR) |
| (1965) 15 | 67 ± 3.6 | 15.1 ± 1.7 | 356 ± 65.0 | 11.8 ± 0.8 | " (Post CMC) |
| | 53 ± 3.1 | 26.2 ± 1.7 | 324 ± 54.4 | 13.7 ± 2.1 | " (Post OMC) |
| Colgan and Fanning (1970) 17 | 71 ± 3.1 | 22 ± 2.6 | 451 ± 18.6 | 13 ± 1.0 | Spont Resp. (before Atelectasis) |
| | 58 ± 2.7 | 46 ± 5.1 | 189 ± 19.4 | 13 ± 3.9 | " (after Atelectasis) |
| Kerr * (1975) 26 | 66 | 33.1 | 190 | 21.1 | Controlled Vent. (Pat. No. 19) |
| Drummond, Wildsmith and Masson * (1978) 7 | 75.8 ± 3.0 | 17.1 ± 2.1 | 272.3 ± 7.5 | 11.5 ± 0.1 | Controlled Vent. (Pat No. 1 and 10 in Group T.) |

* Qsp/Qt is calculated by assuming $a\text{-}\bar{v}DO_2$ of 5.0 Vol%

in Qsp/Qt is always the indicator for the lung function of oxygen transport. Our assumption does not concern with the mechanism of oxygen transfer in the lung, nor does it deny the concepts of the conventional theory and the active bio-physiological effect of oxygen in the lung. It is intended only to explain the pattern of response in Qsp/Qt with varying $FiO_2$.

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