Effects of Changes in Arterial Carbon Dioxide Tension on Oxygen Consumption during Cardiopulmonary Bypass*


The effects of changes in arterial carbon dioxide tension (PaCO₂) on the oxygenation of tissues in 34 patients undergoing surgery for aortocoronary bypass were studied while temperature, systemic blood flow, and the delivery of oxygen to the peripheral tissues remained constant. Mixed venous and superior vena cava oxygen tensions (PvO₂ and PSvO₂, respectively) and oxyhemoglobin saturations and the in vivo partial pressure of oxygen at which 50 percent of the hemoglobin is saturated (P50) increased with PaCO₂, while peripheral vascular resistance, in vitro P50, the level of 2,3-diphosphoglyceric acid in the red blood cells, and the level of lactate in the blood remained constant. There was a close correlation between increases in PaCO₂ and increases in PVO₂ (r = 0.912; P < 0.001) but not with increases in PSvO₂ (r = 0.364; not significant). This indicated that the total-body consumption of oxygen diminished with increases in PaCO₂ but that some regional redistribution of oxygen consumption occurred between the superior and inferior vena cava vascular beds. Since the level of lactate in the blood remained constant and since signs of metabolic acidosis did not develop, the reduced oxygen consumption due to increases in PaCO₂ did not result in detectable increases in anaerobic metabolism.

Cardiopulmonary bypass has become an essential technique for most cardiac operations. Coincident with the progress made in cardiac surgery, extracorporeal blood oxygenator systems have been developed which have characteristics of efficient transfer of oxygen and allow independent regulation of the arterial carbon dioxide tension (PaCO₂). The in vivo effects of cardiopulmonary bypass on the consumption of oxygen have been related to temperature¹ and systemic blood flow;² however, the effects of changes in PaCO₂ on oxygen consumption have not been systematically evaluated in patients undergoing cardiopulmonary bypass.

The purpose of the present investigation was to determine the effect of changes in PaCO₂ on the oxygen consumption of peripheral tissue in man

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Supported by US Army Research and Development Command contract DADA-17-73-C-3149.
Computational assistance was provided by the CLINFO project funded by the Division of Research Resources of the National Institutes of Health under contract N01-RR-5-2218.
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Manuscript received June 19; revision accepted October 27.
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arterial catheter,1 the superior vena caval catheter (svc), and
the mixed venous line (v) draining blood from separate superi-
or and inferior vena caval lines to the oxygenator. The sample
of mixed venous blood did not contain blood entering the
oxygenator from the cardiotomy reservoir, which receives
blood from the left atrial sump and the cardiotomy suctioning
system. The oxygen pressure (Po2), carbon dioxide tension
(Pco2), and the concentration of hydrogen ions in the blood
were measured in duplicate with a blood gas analyzer (In-
strumentation Laboratories 313). The concentration of hemo-
globin (Hb) and the percentage of oxyhemoglobin saturation
(\%So2) were measured in triplicate with a spectrophotometric
oximeter (Instrumentation Laboratories CO-Oximeter 182).
The oxygen content of the blood (C) was calculated by the
following standard formula:2 Hb × \%So2/100 × 1.34
+ Po2 × 0.0031. The oxygen transport index was computed
as the product of the arterial oxygen content (CaO2) and the
systemic blood flow (Q) in liters per minute per square
meter. The oxygen consumption (Vo2) was derived from
Fick's equation3 (ie, Vo2 = Q × CaO2 - Cvo2).

The in vitro partial pressure of oxygen at which 50 percent
of the hemoglobin is saturated (P50) was determined for
mixed venous blood utilizing the nomogram of Severinghaus4
and the formula described by Arturson et al.5 In vitro P50
(pH of 7.40 and 37°C) was calculated by the formula, P50
= 26.6 × PaO2/PaCO2 × 100, where PaO2 is the oxygen tension
of a venous sample corrected to standard conditions and PaCO2
is the Po2 corresponding to the measured oxygen saturation
(corrected for carboxyhemoglobin) on the standard oxygen-
hemoglobin equilibrium curve of Severinghaus.6

The design of the study is shown in Figure 1. The PaCO2
was maintained between 35 and 45 mm Hg by blending 100
percent oxygen and 95 percent oxygen with 5 percent carbon
dioxide into the oxygenating gas. In order to determine the
effects of fluctuations in PaCO2 on oxygenation of tissue,
sequential measurements of blood gas levels obtained in 25

![Figure 1. Study was designed so that systemic blood flow,
level of hemoglobin, and percent oxyhemoglobin saturation
(and, therefore, delivery of oxygen) were held stable by per-
fusion technician over ten-minute period. Either 100 percent
oxygen or mixture of 95 percent oxygen with 5 percent car-
dioxide was added to system, depending on initial PaCO2
of more than 35 mm Hg or less than 35 mm Hg, respectively.
Systemic blood pressure (BP) and results from analysis of
blood gas levels in arterial, superior vena caval (SVC), and
mixed venous blood were recorded immediately before and at
end of ten-minute normothermic period after adjustment of
oxygenating gas. SVC, Inferior vena cava.](image)

| Table 1—Absolute Gas Exchange and Hemodynamic Data |
|-----------------|-----------------|
| Data            | Low PaCO2 (35.0 mm Hg) | High PaCO2 (39.9 mm Hg) |
| Delivery of oxygen | 275.9 | 276.0 |
| Oxygen transport index, ml/min/sq m | 2.28 | 2.30 |
| Systemic blood flow, L/min/sq m | 12.1 | 12.0 |
| CaO2, volumes percent | 98.5 | 98.1 |
| SaO2, percent | 9.15 | 9.10 |
| Hemoglobin level, gm/100 ml | 26.2 | 26.4 |
| PaO2 in vitro, mm Hg | 1,232.0 | 1,283.0 |
| Peripherial vascular resistance, dyne/sec/cm² | 91.9 | 83.0 |

**Arteriovenous oxygen content difference.**

Patients were analyzed. To exclude the influence of the
delivery of oxygen and the temperature on the oxygenation of
tissue, sequential measurements were used only if the oxy-
gen transport index did not vary more than 4 percent
and if the body temperature remained normal. Twenty-two
consecutive pairs of measurements obtained from 15 of the 25
patients met these criteria. When compared to the initial
measurement, the PaCO2 decreased in seven instances and
increased in 15 instances; however, for statistical analyses
measurements of hemodynamic data and gas exchange were
grouped into periods of either low or high PaCO2 and were
compared, regardless of the time-based sequence. The relative
amount of the two gases blended into the oxygenator was
adjusted by the perfusion technologist, based on the previous
measurement of PaCO2, in order to maintain a PaCO2 as
close to 40 mm Hg as possible.

In nine additional patients, the levels of a 2,3-diphospho-
glyceric acid and lactic acid in venous blood were also
measured by enzymatic kits (Sigma 865 and 728, respec-
tively). Normal values in our laboratory were as follows:
lactate level, 0.3 to 1.3 mol/L; and 2,3-diphosphoglyceric
acid level, 4.5 to 5.9 mol/ml of red blood cells. Data were
analyzed by t-test for paired observations, and the signifi-
cance of linear regression was determined.

**RESULTS**

Measurements of hemodynamic data and gas ex-
change during periods of low and high PaCO2 are
summarized in Table 1. The determinants of the
delivery of oxygen to the peripheral tissues (includ-
ing blood flow, CaO2, and the level of hemoglobin,
as well as in vitro P50) were statistically confirmed
so be stable during the period of study. The mean
systemic blood flow as 2.3 L/min/sq m, and the
mean CaO2 was reduced due to hemodilution
Table 2—Stability of Levels of Lactate and 2,3-Diphosphoglyceric Acid during Cardiopulmonary Bypass

<table>
<thead>
<tr>
<th>Data</th>
<th>Low PaCO₂ (n=13)</th>
<th>High PaCO₂ (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen transport index, ml/min/m²</td>
<td>485</td>
<td>491</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>28*</td>
<td>41*</td>
</tr>
<tr>
<td>Level of lactate in blood, μmol/L</td>
<td>0.92</td>
<td>0.84</td>
</tr>
<tr>
<td>Level of 2,3-diphosphoglyceric acid in red blood cells, μmol/ml of red blood cells</td>
<td>4.57</td>
<td>4.64</td>
</tr>
</tbody>
</table>

*P < 0.001

(hemoglobin level, 9.1 gm/100 ml). The arterial hemoglobin saturation was maintained above 98 percent. A mean increase in the PaCO₂ of 5 mm Hg in a stable system for delivery of oxygen was associated with no changes in peripheral vascular resistance. The lower portion of Table 1 shows the measurements of oxygen in mixed venous and superior vena caval blood. Highly significant increases occurred in the measurements of oxygen in mixed venous blood in the in vitro P50. Since the components of the delivery of arterial oxygen were constant, this indicated that peripheral oxygen consumption diminished. The data in Table 2 show that the level of lactate in the blood and the level of 2,3-diphosphoglyceric acid in the red blood cells did not change when the PaCO₂ rose 13 mm Hg.

In order to assess the correlation of relative changes in these measurements, the changes in PaCO₂ were compared to the change in PV0₂, SV0₂, the concentration of hydrogen ions, SVeO₂, and VO₂. A direct positive correlation with PaCO₂ was obtained for PV0₂ (r = 0.912) and SV0₂ (r = 0.723) (Fig 2). As a result, the CV0₂ increased. For each increase of a millimeter of mercury in the PaCO₂, 1.6 percent decrease in oxygen consumption (r = 0.858) was observed (Fig 3); however, a similar close correlation was not obtained relating changes in Pco₂ to changes in PsvCO₂ (r = 0.364) or SvCO₂ (r = 0.211) (Fig 2). Finally, the concentration of hydrogen ions and PaCO₂ correlated well, so that a change of 1 mm Hg in the PaCO₂ was associated with a 0.8-nmol change in the concentration of hydrogen ions (r = 0.885).

To verify the reversibility of oxygen consumption following changes in PaCO₂ during cardiopulmonary bypass, we analyzed data from five of the 15 patients during three consecutive ten-minute periods.
during which a reduction in PaCO₂ was normalized by the addition of carbon dioxide to the oxygenating gas (Table 3). When reduction of the PaCO₂ occurred during the second period of time, the oxygen transport index remained constant; however, as noted previously in the lower portion of Table 1, there was a significant reduction in SvO₂ and SVO₂ as well as an increase in oxygen consumption. These changes were reversed when PaCO₂ was normalized during the third period of time.

Discussion

The results of this study show that normalization of a low PaCO₂ reduces the oxygen consumption of peripheral tissues. The methods used in this study have several advantages over previous investigations of the effects of carbon dioxide on the utilization of oxygen by tissue. Of prime importance is that normothermic humans were studied, contrary to numerous experiments in poikilothermic animals. Determinants of the delivery of oxygen, such as the concentration of hemoglobin, the systemic blood flow, and CaO₂, remained constant, allowing the independent effects of PaCO₂ to be assessed. The lack of change in the in vitro F50 and the level of 2,3-diphosphoglyceric acid is consistent with the previous study of cardiopulmonary bypass in non-blood-primed patients by Murphy¹⁰ and contrasts with studies by Young and Lichtenin¹¹ and by McKenna,¹² which showed a progressive decrease in the level of 2,3-diphosphoglyceric acid in blood-primed patients. This suggests that alterations in the affinity of red blood cells for oxygen, independent of the effects of changes in hydrogen ion concentration and PaCO₂, did not contribute to the observed decrease in the utilization of oxygen. Similarly, the stability of the level of lactate in the blood and the 0.8 slope of the regression line relating hydrogen ion concentration to Pco₂, which is consistent with findings of Arbus and Schwartz,¹³ suggest that the decreased oxygen consumption that was observed was due to the effects of Pco₂, independent of metabolic acid-base influences. Finally, in contrast to any previous study, sampling of the superior vena caval blood allowed analysis of the contribution of this vascular bed to the changes in Cvo₂ which were observed.

It had been previously noted that a rise in the hydrogen ion concentration depressed in vitro respiration in a tissue slice via decreased glycolytic rates.⁹ In vitro studies by Canzanelli¹⁴ confirmed this by observing that the uptake of oxygen in slices of guinea pig tissue was maximal above pH 7.4 in the incubating medium and was reduced when the pH was below 7.0. Data in intact dogs have demonstrated a positive correlation between pH and oxygen consumption, independent of the method of altering arterial pH. Increasing PaCO₂ had the same effects as infusion of acid when Pco₂ was held constant.¹⁵ All of these studies indicate that the metabolic effects of carbon dioxide are mediated, to at least some extent, by hydrogen ions.

Active hyperventilation increases the total-body consumption of oxygen in animals.¹⁶ The associated increase in the work of breathing was thought to be responsible for this change in metabolism, but Cain¹⁷ showed that oxygen consumption increased even in passively hyperventilated dogs. Diminution of oxygen consumption and lactate levels occurred as hypoxic and hypocapnic dogs were made eu-capnic. Signs of anaerobic metabolism progressively diminish in the presence of hypercapnia,¹⁷ even when hypoxemia is superimposed.¹⁸ Furthermore, 70 percent of this decrease in the lactate level has been attributed to diminished calorigenic factors.¹⁸

In the intact organism, the consumption of oxygen is independent of the delivery of oxygen until a

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Table 3—Reversibility of Changes in Oxygen Consumption by the Addition of Carbon Dioxide during Cardiopulmonary Bypass*  

<table>
<thead>
<tr>
<th>Data</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Period 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaCO₂, mm Hg</td>
<td>41.8</td>
<td>35.5**</td>
<td>41.3†</td>
</tr>
<tr>
<td>Oxygen transport index</td>
<td>494</td>
<td>486†</td>
<td>490</td>
</tr>
<tr>
<td>PVO₂, mm Hg</td>
<td>41.5</td>
<td>36.0**</td>
<td>41.0†</td>
</tr>
<tr>
<td>SVO₂, percent</td>
<td>71.5</td>
<td>65.5**</td>
<td>70.4†</td>
</tr>
<tr>
<td>Oxygen consumption,</td>
<td>142</td>
<td>163**</td>
<td>140†</td>
</tr>
</tbody>
</table>

* N = 5.  
** P < 0.001 when compared to periods 1 and 3.  
† P < 0.001 when compared to period 2.  
‡ P > .05 when compared to periods 1 and 3.
critical point, at which aerobic metabolism is limited. Beyond that level, oxygen consumption becomes directly proportional to the oxygen supply and its individual components of systemic blood flow and $\text{O}_2$. Studies in normothermic bypass have shown that oxygen consumption is independent of rates of perfusion down to 2.0 L/min/sq m, below which oxygen consumption progressively falls. Since rates of flow were held just above this level in our patients, the supply-demand relationships for oxygen were close to this critical level. This suggests that signs of anaerobic metabolism, such as metabolic acidosis or an increase in the level of lactate in the serum, might have resulted if the observed alterations in the utilization of oxygen had adverse effects on the metabolism of tissues.

Our findings indicate that a short-term increase in $\text{PaCO}_2$ has an inverse effect in vivo upon oxygen consumption of peripheral tissue. Two explanations for these changes are that $\text{PaCO}_2$ either directly reduced oxygen utilization by tissue or that regional redistribution of blood flow to areas of lower oxygen extraction occurred. The lack of correlation of $\text{CvO}_2$, in contrast to that of the $\text{CvO}_2$, with changes in $\text{PaCO}_2$ suggests that some redistribution of peripheral utilization of oxygen occurred. Whether this was due to a change in blood flow or to regional alteration of oxygen utilization by tissue is not certain; however, the lack of change in systemic vascular resistance suggests that any alteration in the superior vena caval blood flow had to have been accompanied by an opposite change in the inferior vena caval vascular bed. Since the patients did not develop an increase in the level of lactate in the serum or signs of a metabolic acidosis, the reduced oxygen utilization did not result in detectable evidence of increased anaerobic metabolism. This suggests that needs of peripheral tissue for oxygen were adequately met when oxygen utilization fell as a result of an increased $\text{PaCO}_2$. Studies in the isolated hind limb have shown that a change in pH of 0.1 alters oxygen consumption about 10 percent. Extrapolation of our data indicates that the total-body consumption of oxygen in the human is almost double this figure for a similar change in pH.

Hypothermia has been used to reduce oxygen consumption in patients undergoing cardiopulmonary bypass. The $\text{PaCO}_2$ is normally not closely monitored in cardiopulmonary bypass. Our study indicates that normalization of a low $\text{PaCO}_2$ during cardiopulmonary bypass will reduce demands for oxygen at the level of the tissues without development of evidence of increased anaerobic metabolism in the tissues.

The extension of this study to patients with respiratory failure is fraught with many problems since the basic physiology of our anesthetized patients undergoing elective surgery is different from the critically ill patient; however, therapy in respiratory failure is almost totally directed at improving oxygen supply, and little has been done clinically to decrease demands for oxygen at the level of the tissues. Normalization of the $\text{PaCO}_2$ in our study decreased demands for oxygen. Other studies have shown that normalization of the $\text{PaCO}_2$ also seems to increase the availability of oxygen by improving cardiac output and $\text{PaCO}_2$. This suggests that normalization of a low $\text{PaCO}_2$ may indeed have beneficial effects on the oxygination of tissue, from both the aspects of supply and of demand, in the critically ill patient.

References

16. Otis AB: The work of breathing. Physiol Rev 34:449-458,
Subspecialty Board Examination in Pulmonary Disease

The next examination of the American Board of Internal Medicine (Pulmonary Disease) will be on June 17, 1980. Registration for the subspecialty examination will begin August 1, 1979 and continue through November 1, 1979. For those who began their residency training in internal medicine before June 1, 1970 and who have less than two years of acceptable subspecialty training, this will be the last opportunity for admission to a subspecialty examination. Applications may be obtained from the American Board of Internal Medicine, University City Science Center, 3624 Market Street, Philadelphia 19104.

ABIM Policy Change in Training Requirements

This change will affect physicians desiring admission to a subspecialty examination who began their residency training in internal medicine before June 1, 1970. At present, these physicians are considered to have met the training requirements for admission to a subspecialty examination after completing one year of acceptable training in the subspecialty. If once informed of admission to a subspecialty examination, these physicians will continue to be considered to have fulfilled the Board's training requirements in that subspecialty. Beginning with the subspecialty examination offered in 1981, however, all physicians not previously admitted to an examination will be required to meet the same training requirements which apply to physicians beginning their residency training after June 1, 1970. These requirements currently involve two full years of acceptable training in the subspecialty. A complete description of the Board's policies and procedures may be obtained by writing the Board at the address given above.