OXYGEN CONSUMPTION AND CARBON DIOXIDE ELIMINATION IN INFANTS AND CHILDREN DURING ANAESTHESIA AND SURGERY

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Oxygen consumption (\(\dot{V}O_2\)) and carbon dioxide elimination (\(\dot{V}CO_2\)), expressed on a weight basis, are greater in younger than in older, awake children [1-3]. However, during halothane anaesthesia, \(\dot{V}CO_2\) correlates poorly with weight in young, spontaneously breathing infants of less than 10 kg [4, 5]. This discrepancy was found also by Nightingale and Lambert during mechanical ventilation in children, and they stated that \(\dot{V}CO_2\) was unpredictable in infants weighing less than 10 kg [6]. These studies [4-6] showed an unpredictable \(\dot{V}CO_2\) in spite of different measurement and anaesthetic techniques and mode of ventilation. It seems unlikely, therefore, that such factors are responsible for the changeable \(\dot{V}CO_2\) observed in anaesthetized infants. However, it does suggest that metabolic variations may occur in anaesthetized infants.

The aim of the present study was to measure \(\dot{V}CO_2\) and \(\dot{V}O_2\) simultaneously in infants and children anaesthetized with halothane and to determine normal values for \(\dot{V}O_2\) and respiratory quotient (RQ) both before and during surgery.

PATIENTS AND METHODS

We studied 38 children aged between 1 day and 7 yr, with body weights in the range 3.6-25 kg. All patients were fasted for at least 4 h before induction of anaesthesia. Four children weighing 4.9, 3.8, 3.7 and 3.6 kg had congenital heart disease (ASA Classes II, III) and their lungs were ventilated mechanically before and during surgery. These patients were scheduled to undergo repair of total anomalous pulmonary venous drainage, truncus arteriosus, Type I, large ventricular septal defect or transposition of the great arteries. The remaining 34 patients (age range 20 days to 7 yr, weight range 3.6-25 kg) were scheduled to undergo elective, general, urological or orthopaedic surgical procedures and had no signs of cardiorespiratory disease (ASA class I).

SUMMARY

Oxygen consumption (\(\dot{V}O_2\), ml min\(^{-1}\)) and carbon dioxide elimination (\(\dot{V}CO_2\), ml min\(^{-1}\)), minute ventilation (\(\dot{VE}\)), tidal volume (\(VT\)), rate of ventilation (\(1\)) and end-tidal carbon dioxide concentration (\(\varepsilon_{CO_2}\%\)) were measured in 38 infants and children (body weights 3.6-25 kg). Four children (body weight < 5 kg) had congenital heart malformations and were studied during controlled mechanical ventilation, whereas the remainder (n = 34) who were healthy, breathed spontaneously. Anaesthesia was maintained with oxygen in air (\(F_{O_2}\) 0.45) and halothane through a non-rebreathing circuit. Minute ventilation was measured by pneumotachography, \(\dot{V}CO_2\) with an in-line infra-red carbon dioxide meter and gas concentrations with a mass spectrometer. There were no differences in \(\dot{V}O_2\) and \(\dot{V}CO_2\) between children with and without heart disease. \(\dot{V}O_2\) was related to body weight by the equation: \(\dot{V}O_2 = 5.0 \times kg + 19.8\) (\(r = 0.94\)) and \(\dot{V}CO_2\) to body weight by the equation: \(\dot{V}CO_2 = 4.8 \times kg + 6.4\) (\(r = 0.94\)). There were no differences between \(\dot{V}O_2\) or \(\dot{V}CO_2\) before and after the start of surgery. In 11 of 21 patients weighing less than 10 kg, a reduced \(\dot{V}CO_2\) was noted, giving respiratory quotients of less than 0.7. It is speculated that this age-dependent variation of \(\dot{V}CO_2\) may result from partial inhibition of lipolysis in brown adipose tissue produced by halothane.

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The study was approved by the Institutional Review Board at the Mayo Clinic and parental consent to the study was given in each case.

Anaesthesia

Premedication was not used. Anaesthesia was induced with halothane and nitrous oxide in oxygen (FiO₂ 0.5). In non-cardiac patients, the trachea was intubated without the use of neuromuscular blockade. In cardiac patients, pancuronium bromide 0.1 mg kg⁻¹ was used to facilitate tracheal intubation. Cuffed tracheal tubes (Mallinckrodt) were used to ensure an airtight connection. Anaesthesia in cardiac patients involved a Servo-ventilator 900 B with a rate of 30 cycles min⁻¹ and ventilation volumes adjusted to produce an arterial carbon dioxide tension of approximately 4 kPa. Anaesthesia was maintained with fentanyl up to 40 μg kg⁻¹ with a mean (SD) end-tidal halothane concentration of 0.26 (0.10)% in oxygen and air (FiO₂ 0.5). Non-cardiac patients were allowed to breathe spontaneously halothane 0.82 (0.17)% (mean value of end-tidal halothane concentration before surgery) in oxygen and air (FiO₂ 0.45) through a non-rebreathing anaesthesia circuit (Hans-Rudolph valve 2210B, deadspace 2.3 ml). MAC values for non-cardiac children were corrected for age according to Gregory, Eger and Munson [7] in children older than 6 months of age and according to Lerman and colleagues [8] in the younger. A heated humidifier was positioned in the inspiratory limb.

An infusion of 5.0% dextrose 3.6 ml kg⁻¹ h⁻¹ was given during the procedure, up to the time of measurements. In all patients, heart rate was recorded with an ECG, pulse rate and oxygen saturation with a pulse oximeter (Nellcor or Ohmeda) and systemic arterial pressure with a non-invasive oscillometric technique (Dinamap). Invasive arterial pressures were recorded in cardiac patients.

Measuring apparatus

An in-line infra-red capnometer (Hewlett-Packard 14360A) and a pneumotachograph (Fleisch Nos 00 and 0) were placed in the apparatus deadspace in order to confirm that ventilation was steady at the time of measurements. The deadspace of the system was 5 ml with Fleisch No. 00 and 8 ml with Fleisch No. 0, measured by water displacement. The inspiratory and expiratory resistances of the measuring apparatus were 14 cm H₂O litre⁻¹ s⁻¹ for Fleisch No. 0 and 18 cm H₂O litre⁻¹ s⁻¹ for Fleisch No. 00 at a flow of 6 litre min⁻¹. Minute ventilation (Ve) was measured by electrical integration of the flow signal from the heated pneumotachograph and a differential manometer (Microswitch, Honeywell, 170PC). The Fleisch No. 00, used in patients weighing less than 6 kg, was linear for flows up to 8 litre min⁻¹ and the Fleisch No. 0, used for heavier patients, was linear up to 18 litre min⁻¹. The capnometer, which was positioned between the pneumotachograph and the valve, had a response time of 190 ms and an end-tidal plateau was identified in all patients. The capnometer confirmed also that rebreathing did not occur in any of the children.

Air flow, Ve and end-tidal carbon dioxide concentrations were recorded on a six-channel recorder (General Scanning, R S6-5P) together with oesophageal, axillary, gas and room temperatures.

Vo₂ and Ve were measured over a 4-min period.Expired gas was collected in a Douglas bag (Neoprene). The bags used kept the gas concentration inside the bag constant for at least 10 min and no carbon dioxide diffusion was detected. Inspired gas concentrations were determined in duplicate (only variations in the second decimal place were accepted) by a mass spectrometer (Perkin-Elmer, Medical Gas Analyzer, MGA 1103). Mean expired concentrations of oxygen (FEo₂), nitrogen (FEn₂) and carbon dioxide (FECO₂) were measured immediately by the same mass spectrometer at the end of the collection. The volume of gas in the bag (gas collection Ve) was measured by a calibrated 3-litre syringe.

Calculations

Deadspace ventilation (VD), deadspace ratio (VD/VT), alveolar ventilation (VA), VCO₂, VO₂ and RQ were calculated according to the following formulae:

\[
\dot{V}_{\text{CO}_2} = \left(\text{gas collection } \dot{V}_e\right) \times \left(\text{FE}_{\text{CO}_2} - \text{Fi}_{\text{CO}_2}\right)
\]

\[
\dot{V}_{\text{O}_2} = \left(\frac{\text{FE}_{\text{O}_2} \times \text{Fi}_{\text{O}_2}}{\text{Fi}_{\text{N}_2}} \times \text{Fi}_{\text{O}_2} - \text{FE}_{\text{O}_2}\right) \times \left(\text{gas collection } \dot{V}_e\right)
\]

\[
RQ = \frac{\dot{V}_{\text{CO}_2}}{\dot{V}_{\text{O}_2}}
\]

\[
\dot{V}_{D'} = \dot{V}_e - \dot{V}_{A'} - \dot{V}_{D''}
\]

\[
\dot{V}_{D'/\text{VT}} = \frac{\dot{V}_{D'}}{\dot{V}_e}
\]
\[ V_A' = \frac{V_{CO_2} \cdot P_B}{P_{CO_2}} \]

where \( P_{CO_2} \) = end-tidal carbon dioxide tension, \( P_B \) = atmospheric pressure, \( F_{IN_2} \) = inspired nitrogen fraction, \( F_{IO_2} \) = inspired oxygen fraction. \( V_{B\text{app}} \) = apparatus deadspace. The superscript ' indicates that \( V_A, V_B \) and \( V_D \) were calculated non-invasively from \( P_{CO_2} \) [9]. All gas volumes were corrected to standard temperature and pressure dry (STPD).

**Calibrations**

Flow and volume were calibrated with an accurate pump at flows of 50 and 100 ml s\(^{-1}\) delivering a volume of 100 ml. The flow from the pump was checked against a precision rotameter and the volume with a spirometer and found to be reproducible within \( \pm 0.25\% \). Flow and volume calibrations were performed before each measurement with the gas composition, temperature and humidification used during the measurements. The Hewlett-Packard capnometer was calibrated before each measurement with gas mixtures with carbon dioxide concentrations between 1 and 7.5\% (prepared gravimetrically after actual weight and percentage were determined by gas chromatography) and found to be linear within this range. The mass spectrometer was calibrated daily and before each measurement with certified gases containing 1.31\% carbon dioxide, 35.04\% oxygen, 63.65\% nitrogen and 3.98\% carbon dioxide, 49.99\% oxygen and 46.03\% nitrogen. The reproducibility of the mass spectrometer was investigated by 10 repeated measurements with the same certified gas concentrations. The largest deviation between these repeated measurements was 0.015\%.

**Procedure**

The anaesthetic management was standardized as far as possible. The circuit connections were checked for leaks up to an airway pressure of 15 cm H\(_2\)O for children who were breathing spontaneously and up to 25 cm H\(_2\)O in those whose lungs were mechanically ventilated. Immediately after intubation of the trachea, nitrous oxide was discontinued and air substituted. No measurements were performed until 30 min after induction of anaesthesia. A 4-min gas collection period was started, samples and measurements being taken as described above. Immediately after termination of the gas collection, mean fractions of oxygen, carbon dioxide and nitrogen were recorded by the mass spectrometer and expired volumes measured. Anaesthesia was deepened and surgery commenced. The same measurements were repeated approximately 10 min after the start of surgery during a stable state of anaesthesia and surgery in 24 of the 34 children without cardiac disease, and in the four patients with cardiac disease. In the 10 non-cardiac children not studied during operation, the type of surgery did not permit spontaneous breathing.

**Statistical analysis**

Mean values and standard deviations (SD) were calculated. Linear regressions were performed and standard error of the estimates calculated. Comparisons were carried out with paired two-tailed t-tests and probability values < 0.05 were considered to indicate statistical significance.

**RESULTS**

Mean (SD) values of systolic arterial pressure, heart rate and oxygen saturation before and during surgery are presented in table I. Ventilation was stable during collection periods as indicated by mean (SD) values of tidal volume (\( VT \)), rate of ventilation (\( f \)), and end-tidal carbon dioxide concentration (\( E_{CO_2} \)) measured at the beginning, middle and end of the 4-min gas collection period, both before and during surgery (table II). Mean (SD) values of \( V_B'/VT \) ratios were 0.18 (0.10) for infants weighing less than 10 kg and 0.15 (0.07) in children weighing more than 10 kg. Corresponding ventilation rates were 45 (14) and 38 (9) b.p.m. The mean concentrations of halothane expressed as age-adapted multiples of MAC were 0.75 (0.9) before and 1.36 (0.32) during surgery in children weighing less than 10 kg and 0.89 (0.17) before and 1.53 (0.31) during surgery in children weighing more than 10 kg. Values of \( VO_2 \) and \( VO_2 \) were similar in the four children with congenital heart disease when compared with the non-cardiac children.

**Table I. Mean (SD) values of mean arterial pressure (MAP), heart rate (HR) and oxygen saturation (SO_2) before and during surgery in patients without congenital heart malformations**

<table>
<thead>
<tr>
<th></th>
<th>Before surgery (n = 34)</th>
<th>During surgery (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>81.8 (19.9)</td>
<td>87.0 (18.1)</td>
</tr>
<tr>
<td>HR (beat min(^{-1}))</td>
<td>131.8 (26.3)</td>
<td>131.3 (23.3)</td>
</tr>
<tr>
<td>SO_2 (%)</td>
<td>97.4 (2.3)</td>
<td>97.4 (2.4)</td>
</tr>
</tbody>
</table>
TABLE II. Mean (SD) values of tidal volume (VT), rate of ventilation (f) and end-tidal carbon dioxide concentration (E'CO₂) at the beginning (B), middle (M) and end (E) of the collection period both before and during surgery in patients with a normal cardiopulmonary function (n = 34 before and n = 24 during surgery)

<table>
<thead>
<tr>
<th></th>
<th>VT (ml kg⁻¹) (STPD)</th>
<th>f (b.p.m.)</th>
<th>E'CO₂ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>M</td>
<td>E</td>
</tr>
<tr>
<td>Before surgery</td>
<td>3.58 (0.79)</td>
<td>3.60 (0.78)</td>
<td>3.50 (0.69)</td>
</tr>
<tr>
<td>During surgery</td>
<td>2.78 (0.90)</td>
<td>2.75 (0.81)</td>
<td>2.75 (0.68)</td>
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</tbody>
</table>

Temperature effects

The coefficient of correlation between body temperature and V̇O₂ was 0.14 before and 0 during surgery. The corresponding coefficients for V̇CO₂ and body temperature were 0.30 and 0.32, respectively. Similarly, the correlation before surgery was poor both between V̇O₂ and the difference between skin and room temperatures (ΔS - R, °C) and between V̇CO₂ and ΔS - R with coefficients of correlation of 0.33 and 0, respectively.

Oxygen consumption

There was a linear relationship between V̇O₂ (ml min⁻¹) and weight which was described before surgery by the regression equation: V̇O₂ = 5.0 × kg + 19.8; r = 0.94 (fig. 1). The relatively high intercept of 19.8 showed that there was no direct proportionality between V̇O₂ and weight for this age group. Consequently, no single mean value could be used for the calculation of V̇O₂ and the best estimate of V̇O₂ is reached if the regression equation is used as a formula. For children weighing less than 10 kg (n = 21), the regression equation between V̇O₂ and weight was: V̇O₂ = 6.8 × kg + 8.0; r = 0.78, and for those weighing more (n = 17): V̇O₂ = 4.0 × kg + 35.8; r = 0.89.

Oxygen consumption was similar before and during surgery with mean (SD) values of 72.0 (32.0) ml min⁻¹ and 69.2 (32.3) ml min⁻¹, respectively. V̇O₂ and V̇A' were related linearly to each other and, before surgery, followed the regression equation: V̇O₂ = 0.07 × V̇A' + 6.9; r = 0.93 (fig. 2).

![Fig. 1](https://academic.oup.com/bja/article-abstract/62/1/70/262068/fig1)

**Fig. 1.** The relationship between V̇O₂ (ml min⁻¹) and body weight (kg). The area between the dashed lines indicates the standard error of the estimate. Open circles denote patients with congenital heart malformations.

![Fig. 2](https://academic.oup.com/bja/article-abstract/62/1/70/262068/fig2)

**Fig. 2.** The relationship between V̇O₂ (ml min⁻¹) and alveolar ventilation (V̇A' ml min⁻¹). The area between the dashed lines indicates standard error of the estimate. Open circles denote patients with congenital heart malformation.
Carbon dioxide elimination

The relationship, before surgery, between $V_{\text{CO}_2}$ (ml min$^{-1}$) and weight was described by the regression equation: $V_{\text{CO}_2} = 4.8 \times \text{kg} + 6.4; r = 0.94$ (fig. 3). Fourteen of the 21 children who weighed less than 10 kg had a $V_{\text{CO}_2}$ that was below the regression line (fig. 3) and this resulted in a low intercept. If regression analysis of $V_{\text{CO}_2}$ vs. weight was used for infants weighing less than 10 kg ($n = 21$), the regression equation for this group was: $V_{\text{CO}_2} = 7.2 \times \text{kg} - 8.9; r = 0.90$, whereas those weighing more ($n = 17$) followed the regression equation: $V_{\text{CO}_2} = 3.7 \times \text{kg} + 25.4; r = 0.84$. There were no differences in $V_{\text{CO}_2}$ before and during surgery.

Respiratory quotient

When individual results of $V_{\text{O}_2}$ and $V_{\text{CO}_2}$ were related, a discrepancy between the two was found in the youngest patients (fig. 4). This was caused by a relatively lesser $V_{\text{CO}_2}$ than $V_{\text{O}_2}$ in infants weighing less than 10 kg, resulting in a reduced RQ. None of the children who weighed more than 10 kg had a RQ less than 0.7.

Discussion

An RQ less than 0.7 justifies a careful scrutiny of measurement techniques. The apparatus was checked for audible leaks and cuffed tracheal tubes were used. However, leaks may occur and pass undetected. Expired gas is mixed homogeneously in the distal trachea, shown by the high correlation between $P_{\text{et}}\text{CO}_2$ sampled in the distal trachea, $P_{\text{a}}\text{CO}_2$, in both infants and children [10]. Therefore, leaks of expired gas should not affect RQ measurements. Similarly, a reduction of $V_{\text{E}}$ produced by leaks does not affect the RQ, as the same volume is used for the calculation both of $V_{\text{CO}_2}$ and of $V_{\text{O}_2}$. Leaks can occur also across the type of non-rebreathing valve used in this study [11]. However, this does not affect the calculation of either $V_{\text{CO}_2}$ or $V_{\text{O}_2}$. Methodological errors did not appear to cause the lower than expected RQ in infants weighing less than 10 kg.

This study has confirmed earlier findings [4–6] that $V_{\text{CO}_2}$ varies in anaesthetized infants with markedly low values in some. This variability in $V_{\text{CO}_2}$ has been found not only with different measurement techniques, but also during various anaesthetic techniques. When the present data were pooled with previous studies [4, 5] the same variability in $V_{\text{CO}_2}$ was shown clearly (fig. 5). It may be concluded that this variability is independent of differences in measurement technique or type of anaesthesia and that metabolic causes could be responsible.

Environmental temperature is an important
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Fig. 5. \( \dot{\text{V}}_\text{CO}_2 \) per unit body weight (ml min\(^{-1}\) kg\(^{-1}\)) related to body weight (kg) for patients weighing less than 10 kg. Closed circles — values from Lindahl, Olsson and Thomson [4]; open circles — from Olsson and Lindahl [5]; crosses — present study. The regression equation for the relationship was: \( \dot{\text{V}}_\text{CO}_2 = 0.33 \times \text{kg} + 3.3 \); and the coefficient of correlation 0.44.

factor for metabolic requirements in awake neonates [12, 13], and there is a high correlation for the difference between skin and room temperatures (\( \Delta S - R \)) and \( \dot{\text{V}}_\text{O}_2 \). In contrast to awake infants and children, there was no correlation between \( \Delta S - R \) and \( \dot{\text{V}}_\text{O}_2 \) in these children anaesthetized with halothane. This is in conformity with the findings of Holdcroft [14] who stated that anaesthetic agents reduced heat production and other responses to cold environments. The lack of correlation between \( \Delta S - R \) and \( \dot{\text{V}}_\text{O}_2 \) found in this series was seen in all children and showed no age dependency. Temperature-dependent changes in metabolism should have an equal effect on \( \dot{\text{V}}_\text{CO}_2 \) and \( \dot{\text{V}}_\text{O}_2 \) and leave RQ within normal limits.

\( \dot{\text{V}}_\text{O}_2 \) was more predictable than \( \dot{\text{V}}_\text{CO}_2 \), and the expected increase in \( \dot{\text{V}}_\text{O}_2 \) was found in the youngest patients when expressed on a weight basis. If the regression equation was used as a formula for the estimation of \( \dot{\text{V}}_\text{O}_2 \), a 5-kg child consumed 9.0 ml min\(^{-1}\) kg\(^{-1}\) of oxygen, whereas a 10-kg child had a \( \dot{\text{V}}_\text{O}_2 \) of 7.0 ml min\(^{-1}\) kg\(^{-1}\). These values are somewhat greater than in non-anaesthetized, healthy, spontaneously breathing neonates [15]. They are greater also than \( \dot{\text{V}}_\text{O}_2 \) calculated from the Brody equation (\( \dot{\text{V}}_\text{O}_2 = 10 \times \text{kg}^{3/4} \), where \( \text{kg}^{3/4} \) represents the lean body mass) [16]. The increase was 35% for infants weighing less than 5 kg and between 20 and 30% for children that weighed more. This suggests that the constant used by Brody should be adjusted for the age of the infant.

In most patients, respiratory quotient varied between 0.7 and 1.0. However, an unexpectedly low RQ was found in some of the youngest patients weighing less than 10 kg. If the age-weight-dependent reduction of \( \dot{\text{V}}_\text{CO}_2 \) was caused by generalized metabolic changes, a proportional decrease of \( \dot{\text{V}}_\text{O}_2 \) and a normal RQ would have been expected. However, as illustrated in figure 4, this did not occur. The low RQ was caused instead by reduced \( \dot{\text{V}}_\text{CO}_2 \). This discrepancy between carbon dioxide output and oxygen consumption may have been caused by hyperventilation and an increased carbon dioxide storage in the body. On the other hand, this was most unlikely, as end-tidal carbon dioxide concentration, tidal volume and rate of ventilation were the same throughout the gas collection period, indicating a ventilatory steady-state during measurements before surgery. Another factor that has to be taken into account is the quantity of glucose infused. In the present study, this was standardized to 3 mg kg\(^{-1}\) min\(^{-1}\) in order to attain normoglycaemia. It was shown by Nilsson and colleagues [17], that hypoglycaemia did not occur in infants older than a few weeks of age, even if a balanced Ringer acetate solution only was used. It is believed, therefore, that hypoglycaemia was not a cause of the reduced \( \dot{\text{V}}_\text{CO}_2 \). Since low RQ values are known to occur in awake neonates [18], the decreased \( \dot{\text{V}}_\text{CO}_2 \) seems to result from an age-specific alternate metabolic pathway.

There is one distinct metabolic difference between infants and children: the presence of brown adipose tissue (BAT). This tissue is located mainly in the interscapular region, in the neck and around upper mediastinal blood vessels [19, 20]. The amount of BAT is greater in younger than in older infants. The exact time when it disappears during the first year of life is not known. BAT acts as a thermogenic source in the newborn and young infant and is important for non-shivering heat production in small infants with less well developed muscle tissue. It is rich in blood vessels and has an oxygen consumption higher than normal fat tissue and most other tissues [21]. BAT has an abundant sympathetic innervation [10] and noradrenaline released from nerve endings stimulates lipolysis, which produces carbon dioxide. It has been shown that halothane inhibits lipolysis stimulated by isoproterenol [22]. Sympathetic nerves may be involved with the metabolism of
lipids, as denervated rabbit muscle has been shown to accumulate fat [23]. Denervated fat tissue does not participate in fat mobilization, even during starvation and, if nerves to adipose tissue in hibernating mice are damaged, fat mobilization does not occur and the animal dies during a cold stress [24]. Thermogenesis from brown fat is known also to be blocked if local anaesthetic is applied to BAT [25]. These observations suggest that lipolysis and fat mobilization are related to neuronal activity. It may be postulated that halothane inhibited lipolysis in active BAT by "pharmacological denervation" and could lead to the unusually low $\dot{V}_{CO_2}$ seen in this study in small infants. Intermediate lipid metabolites could have accumulated in the body or been excreted through the liver or kidneys, thereby decreasing carbon dioxide production by oxidation, and thus $\dot{V}_{CO_2}$.

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REFERENCES