A calibration system of O\textsubscript{2} consumption and CO\textsubscript{2} production for premature infants

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An apparatus to calibrate the system of measuring O\textsubscript{2} consumption and CO\textsubscript{2} production has been developed for premature infants. This system is based on the alcohol combustion principal. The alcohol combustion is used to test the indirect calorimetric system due to its simplicity and reliability. In the previous studies, the O\textsubscript{2} consumption rate of alcoholic combustion is too large to simulate the breath of premature infants. A new design is proposed to burn alcohol continuously at a rate as low as 0.004 ml min\textsuperscript{-1}, equivalent to an O\textsubscript{2} consumption rate of only 3.9 ml min\textsuperscript{-1}, a level in the breath range of preterms of about 660 g based on the measurement 5.9 ml kg\textsuperscript{-1} min\textsuperscript{-1}. The alcohol combuts with various steady-state rates to imitate the breath of premature infants, and it is useful for a canopy open-circuit system. The calibration tool proposed here would be helpful in the clinical study of energy expenditure for preterms. © 2001 American Institute of Physics.

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I. INTRODUCTION

In the indirect calorimeter of premature infants, the energy expenditure can be measured by the flow-through techniques that measure the amount of O\textsubscript{2} consumed and CO\textsubscript{2} produced during respiration.\textsuperscript{1} This is the frequently used method in clinical research. Frequent calibration check for the apparatus used in the determination of energy expenditure is important. The alcohol-burning method is widely used in the calibration system of indirect calorimeter because it can simulate the human respiration by consuming O\textsubscript{2} and generating CO\textsubscript{2}. The procedure, in theory, consumes known quantities of O\textsubscript{2} and produces known quantities of CO\textsubscript{2}, and therefore, the accuracy of the indirect calorimeter can be measured.

In previous studies in the indirect calorimetric system for infants, the average values of O\textsubscript{2} consumption per weight were 5.7 ml kg\textsuperscript{-1} min\textsuperscript{-1} reported by Mestyan \textit{et al.},\textsuperscript{2} 5.9 ml kg\textsuperscript{-1} min\textsuperscript{-1} by Sinclair and Silverman,\textsuperscript{3} and 5.73 ml kg\textsuperscript{-1} min\textsuperscript{-1} reported by Marks \textit{et al.}\textsuperscript{4} Marks \textit{et al.}\textsuperscript{4} obtained the minimal value of 4.6 ml min\textsuperscript{-1} consumption rate of O\textsubscript{2} by investigating 13 patients with baby weight range from 590 to 1540 g and age range from 28 to 34 days. These reports indicated that the lowest rate of O\textsubscript{2} consumption of an indirect calorimeter should reach about 4 ml min\textsuperscript{-1} or less for the studies of premature infants. Therefore, the calibration system also must achieve this level to calibrate the indirect calorimeter.

Most such studies\textsuperscript{5-7} were done at alcohol combustion rates higher than the level (4 ml min\textsuperscript{-1} or so) required to simulate the gas exchange of premature infants. The alcohol-burning apparatus was designed for neonates by Lister \textit{et al.}\textsuperscript{8} in 1970 to burn ethanol with an oxygen consumption rate over 60 ml min\textsuperscript{-1}. In 1987, Marks \textit{et al.}\textsuperscript{9} even designed an alcohol lamp that could naturally burn methanol at a very low rate, \(V_\text{O}_2 = 10.2 \text{ ml min}^{-1}\), to verify the accuracy of the indirect calorimetric system. This apparatus was proved and widely applied to calibrate indirect and direct calorimetric\textsuperscript{10} for premature infants. However, a 10.2 ml min\textsuperscript{-1} O\textsubscript{2} consumption rate is still a little further away from the level (4.6 ml min\textsuperscript{-1}) proposed by Marks \textit{et al.}\textsuperscript{4} 10.2 ml min\textsuperscript{-1} is fit for a baby weight of 1.73 kg in the system calibration based on 5.9 ml kg\textsuperscript{-1} min\textsuperscript{-1} by Sinclair and Silverman.\textsuperscript{3} This number of weight has been into the range of premature infants, but this value is quite marginal and it would be much better if the baby weight could be lower. Technically, it is difficult for the above-described apparatus to have an alcoholic burning rate low enough for babies weighing less than 1.5 kg.\textsuperscript{11,12} Furthermore, it is difficult to change the O\textsubscript{2} consumption rate in the calibration process by using the natural alcohol burner.

The purpose of this paper is to design a new apparatus to have continuous alcoholic combustion and keep the burning rate at a desirable low level to simulate the gas exchange of premature infants whose weight is less than 1.5 kg for calibrating the indirect calorimeter. In addition, the level of O\textsubscript{2} consumption rate can be changed in the calibration process.

II. METHOD

A. Combustion of ethyl alcohol

The final products of alcohol combustion are carbon dioxide, water, and heat. The combustion equation of ethanol is shown as follows:

\[\text{C}_2\text{H}_5\text{OH} + 3\text{O}_2 \rightarrow 2\text{CO}_2 + 3\text{H}_2\text{O} + \text{heat}\]
The equation indicates that each molecule of ethyl alcohol combustion consumes three molecules of oxygen and generates three molecules of carbon dioxide. In the STP (standard temperature and pressure) condition, there is a need for 1 ml of ethanol to use 1.146 l of oxygen.

In the combustion of ethanol, the theoretical total volumes of O₂ consumption and CO₂ production can be obtained by the following formulas. The molecular weight of ethanol, C₂H₅OH, is 46.069 g mol⁻¹.

The volume of oxygen consumption by one molecule of ethanol consumption is

\[
V_{O₂} = \frac{760}{p} \times \frac{273 + T}{273} \times \frac{V \times D \times M}{46.069} \times 22 414 \times 3,
\]

and the volume of carbon dioxide production is

\[
V_{CO₂} = \frac{760}{p} \times \frac{273 + T}{273} \times \frac{V \times D \times M}{46.069} \times 22 414 \times 2,
\]

where \( p \) is the atmospheric pressure in the experimental environment, 273 is 0 °C in the Kelvin temperature scale (absolute temperature), 760 is the standard pressure in mm Hg, \( T \) is the experimental air temperature, \( V \) is the total volume of burned alcohol, \( D \) is the density of alcohol, \( M \) is the anhydrous alcohol concentration, and 22 414 ml mol⁻¹ is the gas volume measured at STPD (Standard temperature and pressure dry).³⁻¹⁴

The oxygen-consuming rate and the carbon dioxide production rate are

\[
\dot{V}_{O₂} = \frac{V_{O₂}}{\text{combustion time}},
\]

\[
\dot{V}_{CO₂} = \frac{V_{CO₂}}{\text{combustion time}}.
\]

An important metabolic indicator called the respiratory quotient (RQ) is used to represent the oxidized substrate.¹⁵ RQ is determined by the ratio of \( \dot{V}_{CO₂} \) to \( \dot{V}_{O₂} \), and the theoretical respiratory quotient of ethanol combustion is obtained as

\[
RQ = \frac{\dot{V}_{CO₂}}{\dot{V}_{O₂}} = \frac{2}{3} = 0.667.
\]

B. Design of the automatic alcohol burner

The automatic alcohol burner shown in Fig. 1 consists of a microquantitative peristaltic pump (model 101U/R, Watson Marlow, England), temperature sensor, flame detector, sparking unit, electrical heater, microcontroller (AT90S8535, ATMEL, USA), and PC (personal computer).

In the pump controlling part, a microquantitative peristaltic pump controlled with a microcontroller is utilized to feed alcohol into a glass tube under a desirable flow rate ranged from 0.004 to 0.02 ml min⁻¹ with an error smaller than 1%. The microcontroller receives the order from the PC through the RS-232 interface. It can send a level of voltage to the pump with pulse width modulation signal for controlling pump speed to drive the liquid alcohol. Furthermore, it can read the pump speed and send the data to the PC. The proportional feedback control method is adopted to correct the error of pump speed.

In the heating part, a glass tube winded with a heating coil is used to receive the liquid alcohol driven from the pump and vaporize liquid into gas for ignition at the tip of the tube. The heating coil, which is winded on the glass tube and controlled with the microcontroller, is made of 0.01-mm-diam nickel—chrome wire with unit length resistance of 545 Ω m⁻¹. The microcontroller is responsible for detecting the temperature of alcohol and controlling the vaporization speed of the liquid alcohol in the glass tube by the feedback control through the heating coil.
A sparking unit put at the tip of the glass tube is applied to ignite the gas alcohol. The sparking circuit is a step-up voltage regulator to raise a level of voltage up to 1.2 kV and generate 10 sparks/s at the output electrode. The electrode is placed in front of the tip of the glass tube to ignite the gas alcohol by discharging the high voltage in air. A flame detector, thermocouple, is used to monitor the combustion of alcohol and notify the microcontroller to start or stop the ignition of the spark unit.

The apparatus of the automatic alcohol burner controls all the steps such as feeding, vaporizing, and ignition in order to control the flame burning precisely and continuously at a rate that is much lower than natural burning for mimicking the breath of premature infants.

C. Measurement of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$

$\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ are measured by the open-circuit flow-through technique. The whole system was designed by our group in 19961 to automatically analyze the neonatal O$_2$ consumption and CO$_2$ production and its block diagram is shown in Fig. 2. In Fig. 2, the automatic alcohol burner is put inside the hood, and the air flows through the hood by the suction of an aspirator. The airflow rate is determined by the flow controller. The room air flows into the hood, mixes with the respired gas due to the alcohol combustion, and flows out of the hood. Part of the output air is suctioned into gas analyzers and its water content is taken off by the driers before getting into the analyzers. To measure the O$_2$ and CO$_2$ concentrations a differential paramagnetic oxygen analyzer (Magnos 16, Hartmann & Braun) and an infrared CO$_2$ analyzer were used (Uras 14, Hartmann & Braun).

D. Calculation of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ from open-circuit apparatus

Based on the concentration differences between the air before and after the breathing space, O$_2$ consumption and CO$_2$ production can be obtained from the following formulas:

$$\dot{V}_{O_2} = \dot{V}_{S} (F_{O_2} - F_{EO_2}),$$

$$\dot{V}_{CO_2} = \dot{V}_{S} (F_{ECO_2} - F_{ICO_2}).$$

TABLE I. The alcoholic driving rate is measured by a high precision tube with a 0.05 ml resolution. Proceed with each test for 300 min and read the volume increase level of the tube per 30 minutes. Data shown are average values for six times measurement.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Driving rate (ml min$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>0.10</td>
</tr>
<tr>
<td>60</td>
<td>0.25</td>
</tr>
<tr>
<td>90</td>
<td>0.35</td>
</tr>
<tr>
<td>120</td>
<td>0.50</td>
</tr>
<tr>
<td>150</td>
<td>0.60</td>
</tr>
<tr>
<td>180</td>
<td>0.70</td>
</tr>
<tr>
<td>210</td>
<td>0.80</td>
</tr>
<tr>
<td>240</td>
<td>0.90</td>
</tr>
<tr>
<td>270</td>
<td>1.00</td>
</tr>
<tr>
<td>300</td>
<td>1.10</td>
</tr>
</tbody>
</table>

where $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ are volume rates of O$_2$ consumption and CO$_2$ production (ml min$^{-1}$); $\dot{V}_{S}$, the air flow rate (ml min$^{-1}$); $F_{IO_2}$ and $F_{ICO_2}$, the O$_2$ and CO$_2$ fractions of the inspired air (%); $F_{EO_2}$ and $F_{ECO_2}$, the O$_2$ and CO$_2$ fractions of the expired mixed air (%).

The total volumes (ml) of O$_2$ consumption and CO$_2$ production over a given period from $t_1$ to $t_2$ can be obtained by the integration of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ shown in the following:

$$V_{O_2} = \int_{t_1}^{t_2} \dot{V}_{S} (F_{IO_2} - F_{EO_2}) dt,$$

$$V_{CO_2} = \int_{t_1}^{t_2} \dot{V}_{S} (F_{ECO_2} - F_{ICO_2}) dt.$$

The experimental RQ is given as

$$RQ = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}.$$
The recovery rates of $\dot{V}_O_2$ and $\dot{V}_CO_2$ are given as

$$R_{O_2} = \frac{\dot{V}_{O_2}(\text{experimental result})}{\dot{V}_{O_2}(\text{theoretical value})} \times 100\%,$$

$$R_{CO_2} = \frac{\dot{V}_{CO_2}(\text{experimental result})}{\dot{V}_{CO_2}(\text{theoretical value})} \times 100\%.$$

### III. RESULTS

To calibrate the alcohol-driving rate of the peristaltic pump, a tube with high precision of 0.05 ml per scale was used. This high-precision tube holds the alcohol dropped from the tip of the glass tube of the alcohol burner. By reading the volume increase in the high-precision tube in a known period, we can calculate the alcohol-driving rate quantitatively. Table I shows the calibration results. Nine speeds were tested from 0.004 to 0.03 ml min$^{-1}$. Each test lasted for 300 min and the volume level in the high-precision tube was read per 30 min. As a result, shown in Table I, the pump drives the alcohol very stably and accurately in the range from 0.004 to 0.03 ml min$^{-1}$.

After the pump driving rate has been calibrated, we started to run the calibration process of the indirect calorimeter shown in Fig. 1. Table II presents the experimental data and theoretical values under different alcoholic driving rates from 0.004 to 0.03 ml min$^{-1}$. Each driving rate was measured by six experiments. The proposed system can measure a minimum $O_2$ consumption rate 3.90 ml min$^{-1}$ with good recovery rates (more than 89.49%). Such a low $O_2$ consumption rate is able to mimic the breath of premature infants with allowable accuracy of measurement.

Figure 3 shows that there is a good relation between the measured and theoretical data of oxygen consumption and carbon dioxide production over the range of the alcohol combustion from 0.004 to 0.02 ml min$^{-1}$, corresponding to 3.9–20.95 ml min$^{-1}$ $O_2$ consumption rate for baby weight ranged from 0.66 to 3.6 kg based on 5.9 ml kg$^{-1}$ min$^{-1}$ reported by Sinclair and Silverman. Line regression analysis reveals that both slopes are very close to one between measured and theoretical data.

The relationship between the recovery rate and the alcoholic burning rate under various airflow rates is shown in Fig. 4. The faster the volumetric flow rate, the higher the recovery rate under the same alcohol-burning rate. However, the recovery rate gradually reaches a plateau value over 3000 ml min$^{-1}$ flow rate. These results agree with Yeh et al. and Chang et al. Figure 4 also shows that recovery rate increases as the alcohol-burning rate increases. In conclusion, there is higher recovery rate in response to higher rate of alcohol burning and airflow.

### IV. DISCUSSION

In this paper, we have designed a new device to obtain a low rate of oxygen consumption to mimic the breath of premature infants based on alcohol combustion. In the literature, the oxygen consumption rate was too large to
simulate the gas exchange of premature infants whose weight is less than 1.5 kg, and therefore, the calibration of the indirect calorimeter becomes quite difficult for small preterm infants (~1.5 kg).

The experimental results prove that the proposed device can burn alcohol with a minimal rate down to as low as 0.004 ml min\(^{-1}\), equivalent to 3.9 ml min\(^{-1}\) oxygen consumption rate of a preterm whose weight is about 660 g based on the 5.9 ml kg\(^{-1}\) min\(^{-1}\) reported by Sinclair and Silverman.\(^2\) This value is much lower than those reported by others.\(^8,9\) The new device can maintain alcohol combustion rate precisely, accurately, and continuously over the range from 0.004 to 0.02 ml min\(^{-1}\) (Fig. 3). Alcoholic burning rate has been brought down to less than 0.004 ml min\(^{-1}\) by preheating the alcohol from liquid to gas state before it reaches the ignition tip of the glass tube. The heating temperature is feedback controlled so that the input liquid is approximately equal to the output gas ignited at the glass tip, and the liquid remaining in the glass tube reaches a steady-state level. This is the reason why the alcohol burner designed here can maintain a consumption rate much lower than the natural burning one used in literature.\(^8,9,11,12\) Furthermore, it is very easy for the device proposed here to change the level of oxygen consumption rate during the calibration process by changing the pump driving speed.

The respiratory quotient (RQ), an important growing index of preterms, is used to verify whether alcohol is burned completely. As a result shown in Table II, the experimental mean values are very close to the theoretical ones. It appears that O\(_2\) consumption and CO\(_2\) production come from the alcoholic combustion. The recovery rate is an index to show the accuracy of the indirect calorimeter. The results agree with the previous studies\(^1,6\) that a higher alcohol combustion rate leads to a higher recovery rate (Fig. 4). We got allow-

![FIG. 3](image1.png)

**FIG. 3.** Experimental results of the open-circuit system in the calibration procedure are drawing (a) oxygen consumption measurements and (b) carbon dioxide measurements. Measured \(\dot{V}_{O_2}\) and \(\dot{V}_{CO_2}\) vs theoretical ones and alcohol-burning rate for ethanol combustion. The volumetric flow rate is 5000 ± 1.5% ml min\(^{-1}\) under STPD. Solid lines represent the least-square regression lines of the equation \(Y = a + bx\). Broken lines are the theoretical ones.

![FIG. 4](image2.png)

**FIG. 4.** Recovery rate vs alcohol burning rate under various airflow rates are drawing (a) oxygen consumption measurements and (b) carbon dioxide production measurements. The results begin to reach a plateau value when flow rate exceeds 3000 ml min\(^{-1}\).
able accuracy of 89.49% of O$_2$ (Table II) for minimal oxygen consumption rate, 3.9 ml min$^{-1}$. It indicates that our device can provide valid calibration of an indirect calorimeter.

This study proves that the open-circuit indirect calorimeter can be calibrated for use in the studies of premature infants with allowable accuracy. It would greatly be helpful on the studies of the better growth environment for preterms. In future developments, we will apply the open-circuit system shown in Fig. 2 clinical research for premature babies.

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