Ventilatory Volume and Pressure Required for Oscillatory Ventilation in Dogs

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Abstract We determined the ventilatory volume and pressure required to maintain a $P_{aCO_2}$ of 40 mmHg in dogs at between 0.5 and 16 Hz. The ventilator used was that incorporating a powerful, specially made loudspeaker to which a sine-wave signal was introduced. A windmill-type flowmeter measured the minute volume. The tidal volume, expressed per kg of body weight, was 16.1 at 0.5 Hz, decreasing linearly with $\log f$, and reaching a value of 6.1 ml/kg at 16 Hz. The minute volume increased 10 times from 0.5 to 16 Hz. The intratracheal pressure was 12 to 13 cmH$_2$O between 0.5 and 2 Hz, rising to 16 at 4 Hz and finally reaching 77.2 cmH$_2$O at 16 Hz. The $P_{aO_2}$ values were always above 500 mmHg when $F_{1O_2}$ was 1.0. The frequency-impedance data were analyzed for $R$, $I$, and $C$ values. The fitting of the data to an $R$-$I$-$C$ series model was good, but the $R$ values obtained were considerably higher than those reported using a smaller amplitude of oscillation.

Key Words: high frequency ventilation, tidal volume, intratracheal pressure, pulmonary mechanics, $R$-$I$-$C$ series model.

The aim of this investigation was to determine the ventilatory volume and pressure required to maintain a $P_{aCO_2}$ of 40 mmHg in dogs during controlled ventilation at various frequencies. It has been fairly customary to apply a respiratory rate for artificial ventilation more or less similar to that for spontaneous respiration. Recently, quite a few reports have appeared on what is called “high-frequency positive pressure ventilation (HFPPV),” or “oscillatory ventilation,” in which the positive pressure ventilation was applied using a rate considerably higher than normal. Although it was found useful in many clinical situations, its basic physiology has not been studied sufficiently. A study by Bohn et al., although quite informative, focused upon a specific frequency of 15 Hz for certain reasons (Bohn et al., 1980). In this study, we report the results of our study of the physiology, ventilatory volumes and pressure of HFPPV required to maintain a $P_{aCO_2}$ of 40 mmHg in dogs over a wider-than-normal frequency range of between 0.5 and 16 Hz.

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METHOD

**High frequency speaker ventilator.** The high frequency ventilator using a loudspeaker of our own design has been described elsewhere (SUWA, 1980; SUWA and TAGAMI, 1981a, b). In essence, it utilizes a loudspeaker as a piston, which is driven by a power-amplifier, to which, in turn, a signal is introduced from an electronic oscillator generating sine-waves at various frequencies. The respiratory circuit has no valve and is quite similar to the Jackson-Rees circuit (JACKSON REES, 1958) widely used in anesthesia and in an ICU environment, the manual compression of the bag of which was replaced by the stroke of a loudspeaker (Fig. 1). The original model, which utilized a commercially available loudspeaker (Fostex FW 200) and an old amplifier, was able to maintain the $P_{a_{CO_2}}$ of 10 kg dogs below 40 mmHg only at 3 and 5 Hz, its pressure output not exceeding 35 cmH$_2$O (SUWA, 1980). We, therefore, revised the model in two ways. First, we changed the amplifier for a more modern model using a higher power output and a direct coupling circuit (Sony, stereo-amplifier, TA-N86; 80 W per channel). Second, we changed the loudspeaker for a specially manufactured model (Fostex, special order), which incorporates a heavy, rigid and flat-surfaced cone, strong suspension, a voice-coil of large diameter and heavy line, a powerful magnet, and an efficient heat-radiating system. This system can continuously generate a pressure of up to 95 cmH$_2$O (peak to peak) against 1 liter of closed volume, and a tidal volume of more than 200 ml when open to air. Preliminary experiments showed it could ventilate dogs satisfactorily at any frequency between 0.5 and 8 Hz, and

![Diagram of speaker-ventilator arrangement](image)

Fig. 1. The arrangement of the speaker-ventilator with the approximate dimensions of the circuit is shown together with the site of sampling for $P_{SCO_2}$, $P_{it}$, and $P_{it_{CO_2}}(X)$. The point at which a windmill respirometer was inserted is also shown (W).
in many instances also up to 16 Hz.

Experiment in vivo. Nine dogs, weighing between 7.4 and 16.3 kg (mean 11.2 kg), were anesthetized with ketamine, 25 mg/kg, given intramuscularly, paralyzed with pancuronium, 4 mg, intubated with #9 cuffed endotracheal tube (internal diameter 9 mm, length 27 cm; volume 20 ml including that of the connector) and placed on the loudspeaker ventilator (Fig. 1). The initial frequency used was 0.5 Hz (30/min), and the tidal volume was adjusted so that the end-tidal $P_{CO_2}$ was between 35 and 40 mmHg. A femoral artery was canulated and the arterial pressure recorded. Anesthesia was maintained by intravenous administration of a small amount of pentobarbital and pancuronium, given intermittently. The latter was administered because the high-frequency positive pressure ventilation usually suppressed the spontaneous ventilation, but not always. When the steady state was reached, the arterial blood was sampled for blood gas analysis (Radiometer, ABL-2). If the $P_{ACO_2}$ was between 35 and 45 mmHg, the intra-tracheal $P_{CO_2}$ was recorded at the points of 5 cm ($P_{CO_2}(5)$), 10, 15, 20, 25, and 30 cm ($P_{CO_2}(30)$) down into the endotracheal tube either by a mass-spectrometer (Simadzu MASPEC R-2A) or by an infra-red analyzer (AIKA RAS-41). As shown in the figure, the sampling point for $P_{CO_2}(30)$ was just at the opening port of the endotracheal tube (Fig. 1). The $P_{co_2}$ in the ventilator chamber was also recorded ($P_{SCO_2}$; Fig. 1). A windmill respirometer was inserted between the ventilator and the endotracheal tube and the minute ventilation was measured (SUWA and TAGAMI, 1981a). If the $P_{ACO_2}$ was outside the desired range, the tidal volume was readjusted, and, after 10 to 20 min, the measurements were repeated. The intra-tracheal pressure ($P_{it}$) at the junction of the ventilator and the endotracheal tube (Fig. 1) was measured and recorded continuously using a transducer with sufficient accuracy and frequency response. After finishing measurement at 0.5 Hz, the experiment proceeded to the next step, using a different frequency. The frequencies applied were 0.5, 1, 2, 4, 8, and 16 Hz. Their order of application was randomized, except for 0.5 Hz which was always applied first. At higher frequencies, the end-tidal $P_{CO_2}$ becomes grossly different from the $P_{ACO_2}$, but its direction of change, either rising or falling, usually indicated whether the $P_{ACO_2}$ was rising or falling. Therefore, when the tidal volume was adjusted so that this new $P_{CO_2}$ neither rose nor fell, the $P_{ACO_2}$ changed little from the preceding value. After 15 min, the arterial blood was sampled and other measurements were repeated. The pattern of $P_{it}$ was judged to be of sinewave by eye. The oxygen was added to the respiratory circuit at a rate of 0.4 liters/(kg·min), and the mean $P_{it}$ was adjusted between 3 and 5 cmH$_2$O by regulating the gas outlet. The rectal temperature of the dog was maintained between 37 and 37.5°C, using a servo-controlled heat pad. With this small variation of body temperature, no temperature correction of blood gas values was necessary.

The aim of this study was to determine the ventilatory volumes and the amplitude of intratracheal pressure ($\Delta P_{it}$; peak to peak) so as to achieve the standard conditions.
$Pa_{CO_2}$ of 40 mmHg. Since the observed $Pa_{CO_2}$ values differed slightly from 40 mmHg, we derived the intended values by applying the following formula,

$$\frac{P_{\text{a}CO_2}^{\text{meas.}} - P_{CO_2}}{40 - P_{CO_2}} = \frac{VT^{40}}{VT^{\text{meas.}}} = \frac{\Delta P_{\text{it}40}}{\Delta P_{\text{it}^{\text{meas.}}}},$$

where $P_{\text{a}CO_2}^{\text{meas.}}$, $VT^{\text{meas.}}$, and $\Delta P_{\text{it}^{\text{meas.}}}$ are those respective values directly measured, while $VT^{40}$ and $\Delta P_{\text{it}40}$ are those which would have achieved a $Pa_{CO_2}$ of 40 mmHg. For the value of $P_{CO_2}$, the $P_{CO_2}$ in the respiratory circuit ($P_{SCO_2}$) was used. The pulmonary airway impedance, $Z_p$, was calculated from the $\Delta P_{\text{it}}$ and $\dot{V}_e$ while assuming the flow to be sine-wave. We applied an ordinary three-component ($R$, $I$, $C$) series model to the frequency-impedance data, and obtained the values of $R$, $I$, $C$ both for the individual animal and for the lumped data, using a curve-fitting technique.

RESULTS

In all dogs, ventilation was maintained satisfactorily and the $Pa_{CO_2}$ values were kept between 35 and 45 mmHg at frequencies between 0.5 and 8 Hz. At 16 Hz, the $Pa_{CO_2}$'s were within this range only in three dogs. Two dogs were ventilated so that their $Pa_{CO_2}$'s fell between 45 and 50 mmHg. They were included in the analysis.

The tidal volume required to maintain the $Pa_{CO_2}$ between 35 and 45 mmHg (35 and 50 mmHg at 16 Hz) was 173.8 ml at 0.5 Hz, decreasing almost linearly

Fig. 2. The tidal volumes and minute ventilation required to maintain the $Pa_{CO_2}$ between 35 and 45 mmHg (35 and 50 at 16 Hz) are shown. The mean±S.D. The abscissa is on a log-scale.

Japanese Journal of Physiology
with the logarithm of the frequency (log f), reaching the value of 53.3 ml at 16 Hz. Minute ventilation was 5.2 liters/min at 0.5 Hz, increasing gradually with the increase in frequency, reaching 51.4 liters/min at 16 Hz (Fig. 2).

The amplitudes of Pit (peak to peak: ΔPit) were almost unchanged between

![Graph showing data points for ΔPit, ΔPit raised to the 4th power, and Zp (impedance) at various frequencies. The S.D.'s for ΔPit are omitted. It is interesting that, while the absolute values of Zp are comparable between 1 and 16 Hz, the S.D. is much smaller for the latter.]

Fig. 3. ΔPit, ΔPit raised to the 4th power, and Zp (impedance) at various frequencies are shown. The S.D.’s for ΔPit are omitted. It is interesting that, while the absolute values of Zp are comparable between 1 and 16 Hz, the S.D. is much smaller for the latter.

![Graph showing recalculated tidal volumes and minute ventilation based on body weight and Paco2 values of 40 mmHg. Note that the S.D.'s are smaller.]

Fig. 4. Tidal volumes and minute ventilation are recalculated on the basis of body weight and the Paco2 values of 40 mmHg. Note that the S.D.’s are smaller.
12.1 and 13.2 cmH₂O at frequencies between 0.5 and 2 Hz, rising to a value of 17.7 cmH₂O at 4 Hz, 34.0 cmH₂O at 8 Hz, and finally 70.7 cmH₂O at 16 Hz. The pulmonary airway impedance, Zₚ, was highest of 23.4 cmH₂O/(liters·sec) at 0.5 Hz, gradually decreased as the frequency increased, reached the minimum value of 6.5 at 4 Hz, then rose again and was 12.3 at 16 Hz (Fig. 3).

The \( V_{\text{T}}^{\text{ref}}/\text{kg} \), the tidal volumes per kg of body weight which would have achieved a \( P_{\text{aco}} \), of 40 mmHg, was 16.1 ml/kg at 0.5 Hz, decreasing linearly with \( \log f \), and reaching the value of 6.1 ml/kg at 16 Hz (Fig. 4). By expressing on the basis of body weight, the variation of \( V_{\text{T}} \) and \( V_{\text{E}} \) decreased. The \( \Delta P_{\text{it}}^{\text{ref}} \) differed little from the observed \( \Delta P_{\text{it}} \) values, except that at 16 Hz it was estimated as high as 77.2 cmH₂O.

![Fig. 5](image_url)  
**Fig. 5.** \( P_{\text{co}} \) values in the ventilator and at various points down into the endotracheal tube are shown together with arterial values. Higher frequencies resulted in a generally lower \( P_{\text{itco}}(X) \), but the slope \( (\Delta P_{\text{itco}}/\Delta x) \) does not seem to differ significantly.
Table 1. Resistance ($R$), inertia ($I$), capacitance ($C$), and resonance frequency ($f_0$) values.

<table>
<thead>
<tr>
<th></th>
<th>$R$</th>
<th>$I$</th>
<th>$C$</th>
<th>$f_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Units</td>
<td>cmH$_2$O/(liters·sec)</td>
<td>cmH$_2$O/(liters·sec$^2$)</td>
<td>liters/cmH$_2$O</td>
<td>Hz</td>
</tr>
<tr>
<td>Mean 1</td>
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<td>0.105</td>
<td>0.014</td>
<td>4.14</td>
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<tr>
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<tr>
<td>Mean 3</td>
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<td>0.111</td>
<td>0.015</td>
<td>4.46</td>
</tr>
<tr>
<td>Tsai et al.</td>
<td>2.59</td>
<td>0.075</td>
<td>0.030</td>
<td>3.5</td>
</tr>
</tbody>
</table>

The mean values were calculated in three ways. Mean 1 indicates that the curve-fitting was performed for the mean $Z_p$ at each frequency, and mean 2 indicates that the curve-fitting was performed for all data lumped. Mean 3 indicates that the curve-fitting was performed for individual animals, the $R$, $I$, $C$ values determined then being averaged. For comparison, data from Tsai et al. are also included.

The $P_{aO_2}$ values were more than 500 mmHg at all frequencies, except that the mean $P_{aO_2}$ at 16 Hz was 487 mmHg. This, however, should not be interpreted as showing that ventilation at a very high frequency disturbs oxygenation (see Discussion). The $P_{lCO_2}$ values at various points down into the endotracheal tube, when averaged over a respiratory cycle, were generally higher at a lower frequency. This indicates that the CO$_2$ gradient from alveolus to carina is larger at higher frequencies. This may be contrary to what was expected (see Discussion) (Fig. 5).

The fitting of the frequency-impedance data to a series $R$-$I$-$C$ model was fairly good. The calculated values of $R$, $I$, and $C$ are presented in Table 1. The appearance of the curve and the derived values, especially those of $R$, differ somewhat from what have been reported (see Discussion).

DISCUSSION

A high-frequency ventilator using the principle of a loudspeaker succeeded in ventilating all dogs so as to achieve $P_{aCO_2}$ values of around 40 mmHg between 0.5 and 8 Hz, and with a few dogs, 16 Hz. We can predict that an adequate gas exchange can be achieved at any frequency between 0.5 and 8 Hz, and probably up to 16 Hz, if sufficiently large tidal volumes are applied.

While the CO$_2$ exchange was accomplished at these high frequencies, if should be noted that the $\dot{V}E$/kg had to increased from 0.48 liters/(kg·min) at 0.5 Hz to 5.83 liters/(kg·min) at 16 Hz, more than a ten-times increase in $\dot{V}E$ (Fig. 4). Since the $\dot{V}CO_2$ can be estimated to have remained unchanged, we can conclude that the CO$_2$ exchange at these high frequencies becomes very inefficient. We could not determine the degree of this "inefficiency," however, because it is not possible to calculate the $V_D/V_T$ ratio; accurate estimation of $PE_{CO_2}$ and $P_{lCO_2}$ was not possible.

The tidal volume achieving the $P_{aCO_2}$ of 40 mmHg at 16 Hz in our measurements and calculations, 6.1 ml/kg, was considerably larger than 2 ml/kg as has

Vol. 32, No. 3, 1982
already been reported at 15 Hz (BOHN et al., 1980). There are few factors which explain this apparent discrepancy. Firstly, Bohn et al. did not include in VT the bias flow of oxygen (FGF in their terminology). The mean of FGF (7 liters/min) divided by mean body weight of 7 kg at a frequency of 15 Hz is 1.1 ml/kg. Therefore, their tidal volume was not 2 ml/kg, but 3.1 ml/kg instead. Secondly, we had the volume of the endotracheal tube, 20 ml, loaded as a dead space, while in Bohn's study, the endotracheal tube did not function as a dead space because expiration occurred around the endotracheal tube. Thirdly, the flow of fresh gas was lower in our study (0.4 liters/(kg·min)) than in Bohn's (around 1 liters/(kg·min)), which would have contributed to an increase in $P_{tCO_2}$ in ours. It is difficult to quantitatively evaluate these factors, but it appears that, with these differences in mind, the results of the two studies may not be too far apart.

The increase in $ΔP_{t}$ at higher frequencies is very impressive. The frequency-impedance data indicate that this is influenced both by the increase in the ventilatory volume and by the increase in the effect of inertia. At higher frequency, a tidal volume which decreased only modestly had to be pushed in and pulled out against the same resistance in a very short period of time. Furthermore, the force (pressure) required to move the lung and the surrounding tissue became quite significant.

The frequency-impedance profile of our measurement differs considerably from that reported using an ordinary oscillation study (TS AI et al., 1977) (Table 1). A comparison indicates that the R values of our measurements are almost three times as high as theirs. The difference is most likely due to a grossly different flow rate ("tidal volume") applied. While the peak flow rate was 0.2 to 0.5 liters/sec in the study of Tsai et al. for dogs of 20 kg or more, we had to apply a considerably higher rate of 1.5 liters/sec (4 Hz; calculated from $\dot{V}E$ data, assuming a sine-wave) for smaller dogs (11.2 kg) in order to achieve elimination of CO₂. The discrepancies of I and C values are of much lesser magnitude and can be more easily explained by the difference in flow rate and dog size.

The $P_{aO_2}$ remained sufficiently high in all frequencies studied. A slight fall at 16 Hz is probably artificial. We could not totally control the leakage of the ventilator, and, during the expiratory phase, a high negative pressure created in the ventilator chamber sucked a small amount of air into the system and caused a slight reduction in $F_{iO_2}$.

We measured $P_{tCO_2}$ at various points in the airway with the intention of clarifying the difference in gas exchange mechanism at different frequencies. We speculated in advance that a difference in $P_{CO_2}$ between the distal end of the endotracheal tube ($P_{tCO_2}$ (30)) and the alveolus ($P_{aCO_2}$) may be less at higher frequencies, because, as the frequency increases, the ventilation may become diffusive rather than convective (BOHN et al., 1980). The measuring instrument did not have a sufficiently fast response, and we were forced to use a time-averaged $P_{CO_2}$. We could derive no significant conclusions from the data.
One may question how high a frequency can be applied in order to achieve a CO$_2$ exchange. The frequency-VT data and the frequency-$\Delta$Pit data appear to indicate that 16 Hz is not too far from the limit. Even a very powerful instrument might fail to deliver such a high pressure, the high intratracheal pressure possibly becoming harmful to the animal. Decreasing the dead space or introducing the tidal volume and the fresh gas deep into the bronchus will probably be the only way of extending the upper limit of the frequency.

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