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Artificial Ventilation of a Canine Model of Bronchopleural Fistula

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The authors studied the abnormalities of gas exchange and lung mechanics in a canine model of bronchopleural fistula during intermittent positive pressure ventilation (IPPV) and high-frequency oscillatory ventilation (HFOV). The left lower lobe bronchus was opened to atmosphere and it was determined that end expired volume was best maintained at frequencies of 45–50 breaths/min. during IPPV. Comparing alternating periods of IPPV and HFOV in six dogs (Group 1) at matched airway opening pressure (P_{ao}), we found that Pa_{O_2} decreased significantly to 68 ± 14 mmHg and 69 ± 24 mmHg, respectively, on opening the fistula. In a second group of six dogs (Group 2), when P_{ao} was increased by additional bias flow into the ventilatory circuit during both IPPV and HFOV, Pa_{O_2} increased significantly to 89 ± 12 mmHg and 87 ± 8 mmHg, respectively. Repeating Group 2 studies after induction of oleic acid low-pressure pulmonary edema demonstrated that conventional IPPV was associated with large intrapulmonary shunts. HFOV, however, maintained gas exchange at near baseline values. For both Group 1 and Group 2, the calculated gas flow through the fistula was significantly less at all levels of airway pressure during HFOV. The authors conclude that HFOV offers advantages over conventional IPPV in the maintenance of oxygenation and in the reduction of gas leak through the fistula. (Key words: End-expiratory pressure. Hypoxia. Lung: edema. Ventilation: high frequency oscillatory; intermittent positive pressure.)

BRONCHOPLEURAL FISTULA complicates about 2% of pneumonectomies, and this complication is associated with a mortality approaching 20%.[1] As well as surgical correction, current therapy of a large, persistent bronchopleural fistula includes independent ventilation of each lung,[2] plugging the leak under bronchoscopic control,[3,4] the addition of positive end-expired pressure (PEEP) to the pleural surface,[5–7] and high-frequency ventilation.[8,¶] In order to better understand the associated abnormalities of lung mechanics and gas exchange, we studied a canine model of bronchopleural fistula during intermittent positive-pressure ventilation (IPPV) and during high-frequency oscillatory ventilation (HFOV). We postulated that the loss of volume through the fistula and the associated gas-exchange abnormalities might be improved with HFOV. We also tested the efficacy of IPPV with an additional inspiratory flow in the maintenance of gas exchange in this model. The effects of IPPV on oxygenation and leak rate through the fistula ($\dot{V}_{LEAK}$) were compared with HFOV at high and at low levels of airway opening pressure (P_{ao}). We also compared IPPV and HFOV following induction of low-pressure pulmonary edema where the gas-exchange problems would be worsened. We found that the primary determinant of oxygenation was the level of airway pressure and not ventilator mode. We also found that the $\dot{V}_{LEAK}$ was lower during HFOV for any given level of airway pressure.

Methods

Animal Preparation

Twelve mongrel dogs (21 ± 2 kg) were anesthetized (pentobarbital 30 mg/kg) and intubated with a cuffed endotracheal tube. They were mechanically ventilated at a tidal volume (V_T) of 20 ml/kg (Harvard® ventilator) with room air. A port near the endotracheal tube was connected by low-compliance tubing to an air phase transducer (Validyne DP45-28®) to measure P_{ao}. Ventilator frequency (f) was set to maintain Pa_{CO_2} between 30–35 mmHg. Throughout the remainder of the experiment anesthesia was maintained with intermittent doses of pentobarbital (50–100 mg). A large-bore catheter was inserted into the femoral artery and connected to a Statham® pressure transducer to measure blood pressure. A second catheter was inserted into the femoral vein for fluid and drug administration. Arterial blood samples were analyzed at 37° C (Corning 165-2®) for Pa_{CO_2}, Pa_{O_2}, and *p*H and were corrected for dog body temperature.[9] Heating blankets were used to maintain dog body temperature near 37° C.

Following muscle paralysis (succinylcholine 100 mg), a wide thoracotomy was performed through the left fifth intercostal space. On opening the pleural space, 3–4 cmH_2O PEEP was added to the expiratory line of the Harvard® ventilator (Emerson® PEEP valve). Using cautery, an opening was made in the lateral wall of the left

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¶ Hoff BH, Wilson E, Bennett E, Phillips W: Bronchopleural fistula during high frequency ventilation (abstract). Chest 80:381, 1981.

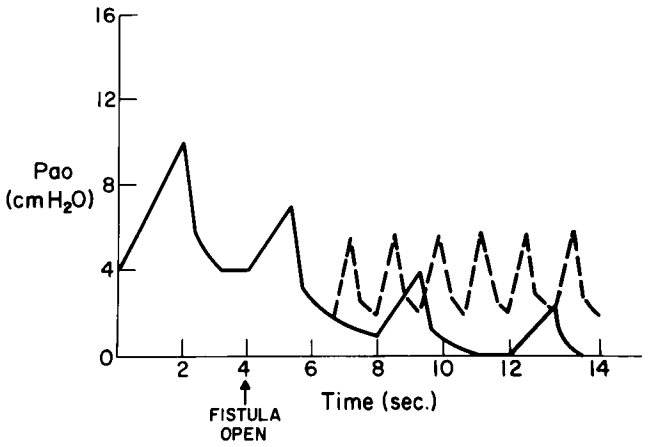

FIG. 1. Ventilatory cycles during IPPV are depicted schematically. Airway opening pressure (P_{ao}) is represented along the y-axis and time is represented along the x-axis. The solid lines represent ventilation at a frequency of 15 breaths/min. When the fistula is opened to atmosphere (*arrow*), the end expired pressure progressively decreases until it reaches atmospheric pressure. The interrupted lines depict the effect of increasing frequency to 45 breaths/min. On opening the fistula, the end expired pressure again decreases but the rapid ventilatory rate prevents it from reaching to atmospheric pressure. This formed the basis for the rapid ventilatory rates used during IPPV with the fistula open to atmosphere.

lower-lobe bronchus. A flexible tube (length 4.0 cm, ID 7 mm) was inserted through the opening in the wall of the bronchus, and the flared end of the tube was pulled against the bronchial wall. The tube was then secured with a purse-string suture with the tube at an angle of 90° to the long axis of the bronchus. The tube was clamped closed to atmosphere and the lungs were reinflated, ensuring that the left lower lobe was also inflated. A wide sternotomy was performed to ensure that pleural pressure was equal to atmosphere.

In six dogs a Swan-Ganz® catheter was positioned in the right atrium *via* the right external jugular vein. This was used for administration of oleic acid in the studies that included induction of low-pressure pulmonary edema. Following administration of the oleic acid, the catheter was then directed into a branch of the pulmonary artery and, with the balloon inflated, a pulmonary capillary wedge pressure (PCWP) could be obtained.

VENTILATOR PARAMETERS

When the fistula was opened to the atmosphere during IPPV, f was increased to 45–50 breaths/min and V_T was reduced to 10 ml/kg. Figure 1 outlines the rationale for the IPPV settings that were chosen. During HFOV, Pa_{CO_2} was set by adjustment of V_T or f on the oscillator (Metrex Instruments, Brampton, Ontario). The HFOV circuit (fig. 2) is similar to that described by Thompson *et al.*[10] Briefly, a fresh gas flow (FGF) (bias flow) enters through the line labeled FGFin, is oscillated, and exits through the line labeled FGFout. A flexible connector was interposed between FGFin and a pressure port near the endotracheal tube. During HFOV, P_{ao} was measured statically by simultaneously clamping the fistula and the flexible connector. During IPPV, mean P_{ao} was obtained by electronically meaning the pressure signal over several respiratory cycles. During HFOV, P_{ao} could be independently adjusted by altering the bias flow. In order to affect increases in P_{ao} during IPPV, we added a bias flow to the inspiratory line of the Harvard® ventilator (fig. 2). The flow rate through the bias line was controlled by a flowmeter and the fractional inspired O_2 concentration (FI_{O_2}) was controlled with a Bennett air–oxygen mixer.

MEASUREMENTS

The $\dot{V}_{LEAK}$ was calculated as the difference between inspired and expired ventilation. During HFOV, timed volumes (30–60 s) were collected at the FGFout line (fig. 2) and at the FGFin lines. The timed volumes were collected in a Latex® meteorologic balloon and measured in

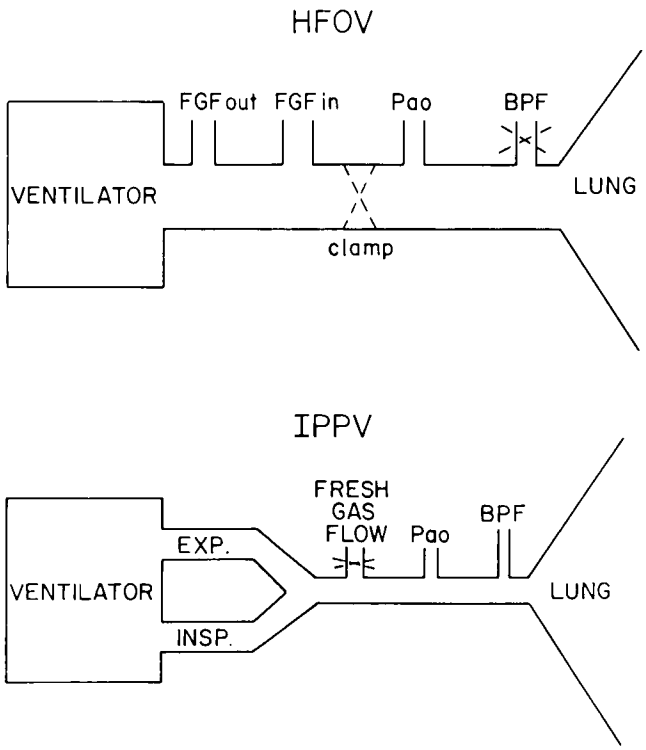

FIG. 2. Ventilator circuit and model. The upper panel shows the HFOV circuit with the fistula (BPF) at the left lower lobe bronchus. Airway pressure (P_{ao}) is measured at the pressure port after clamping the fistula and the flexible tubing (shown by X). Fresh gas enters at the inflow line (FGFin), is oscillated by the ventilator, and leaves the circuit at the outflow line (FGFout). The lower panel shows the IPPV circuit. The pressure port (P_{ao}) and fistula (BPF) are also schematically represented. During Group 2 experiments, a fresh gas flow line was connected to the circuit to allow increases in airway pressure during period $IPPV_2$ and during IPPV + FGF.

a water-sealed spirometer (Collins, Braintree, MA). Because the oscillator circuit was a closed system, the difference between flows at FGFin and FGFout was equal to the gas flow through the fistula.

During IPPV the gas flow through the fistula was calculated as the difference between the inspired flow and expired flow. Timed expired volumes were collected at the expiratory line and flows through the line were derived. Inspiratory gas flow ($\dot{V}_I$) was calculated as the product of V_T and f. Frequency was obtained from the oscillograph record and V_T from the settings of the Harvard® ventilator. The V_T settings of the ventilator, previously calibrated against the spirometer, were accurate to within 5%. In the experiments in which additional fresh gas was added to the IPPV circuit, the additional gas flow was measured as a timed-volume collection, as described for HFOV measurements. This additional gas flow was added to the calculated IPPV inspiratory flow.

Experimental Protocol

Following the sternotomy, 10–15 min were allowed for the animals to stabilize. The animals were divided into two groups of six dogs. All animals were ventilated for four 30-min periods of IPPV alternating with HFOV in the sequence $IPPV_1$, $HFOV_1$, $IPPV_2$, and $HFOV_2$ (table 1). In the first six dogs (Group 1), mean P_{ao} was low during both IPPV periods and during both HFOV periods. In the second six dogs (Group 2), mean P_{ao} was also low during $IPPV_1$ and $HFOV_1$ but was increased during $IPPV_2$ and $HFOV_2$. Between each period the fistula was closed to atmosphere and the animals received three lung inflations to total lung capacity (TLC), as defined by a transpulmonary pressure (P_{tp}) of 25–30 cmH_2O.

In Group 1, baseline measurements were made with the fistula closed (period C). These included blood pressure, rectal temperature, blood gases, and P_{ao}. The animals then received the four periods of ventilation. At the end of each 30-min period, all baseline measurements were repeated and fistula gas flow was measured as well. During $IPPV_1$ and $IPPV_2$, mean P_{ao} was a function of ventilator settings and the gas flow through the fistula. The mean P_{ao} during $HFOV_1$ and $HFOV_2$ was set to equal the mean P_{ao} of the preceding IPPV period by adjusting the bias flow.

Group 2 animals were treated similarly to Group 1 during periods C, $IPPV_1$, and $HFOV_1$. During period $IPPV_2$, the mean P_{ao} was increased by adding a bias flow to the inspiratory line of the IPPV circuit (fig. 2). The mean P_{ao} during $IPPV_2$ was set to match the mean P_{ao} of the fistula-closed period. During period $HFOV_2$ the mean P_{ao} was set equal to the mean P_{ao} of period $IPPV_2$ by adjusting the bias flow rate.

TABLE 1. Experimental Protocol

Group 1	P_{ao}*	Group 2	P_{ao}
$IPPV_1$	low	$IPPV_1$	low
$HFOV_1$	low	$HFOV_1$	low
$IPPV_2$	low	$IPPV_2$	high
$HFOV_2$	low	$HFOV_2$	high
		Oleic acid administered	
		IPPV + FGF	
		HFOV	
		IPPV	

Each period lasted 30 min. The fistula was closed and the lungs were inflated between periods. Only in Group 2 experiments was oleic acid administered following period $HFOV_2$. See text for further discussion.

* Mean airway opening pressure.

In Group 2 dogs, the experimental protocol was extended to examine the interaction of pulmonary edema with a bronchopleural fistula. Following period $HFOV_2$, oleic acid (0.05 ml/kg) was infused through a Swan-Ganz® catheter into the right atrium. The FI_{O_2} was then increased to 0.6, and for the duration of the experiment PCWP was maintained constant with volume infusion (dextran 75) as necessary. After allowing 90 min for the lesion to stabilize, all measurements were repeated with the fistula closed (period C_1). The fistula was then opened and the dogs were ventilated for an additional three periods. The first dog to follow this protocol (number 7), died during the initial IPPV period when bias flow was not added to maintain P_{ao}. For the following five experiments (dogs number 8–12), the sequence of ventilatory periods was IPPV with a bias flow (IPPV + FGF), HFOV, and then conventional IPPV (no added bias flow). Between periods the fistula was closed and the lungs were inflated to TLC. During periods IPPV + FGF and HFOV, the mean P_{ao} was prospectively set to match period C_1 by adjusting the bias flow. During IPPV without a bias flow, the mean P_{ao} was not prospectively set to a predetermined value.

Statistics

Statistical comparisons between Group 1 and Group 2 were made using an unpaired *t* test. Comparisons between periods within a group were made with an analysis of variance (ANOVA), and when applicable, Tukey's test for multiple comparisons. A *P* value less than 0.05 was considered to show a significant difference. Results are presented as mean value ± SD.

Results

Group 1. Table 2 shows the effect on mean P_{ao}, Pa_{O_2}, and Pa_{CO_2} of opening the fistula. Values of both mean P_{ao} and mean Pa_{O_2} were significantly lowered during the four

TABLE 2. Ventilatory Variables in Two Groups of Dogs with Normal Lungs

	Group	C	$IPPV_1$	$HFOV_1$	$IPPV_2$	$HFOV_2$
Pa_{CO_2} (mmHg)	1	35 ± 4	33 ± 2	34 ± 5	32 ± 7	33 ± 8
	2	34 ± 6	35 ± 5	33 ± 4	30 ± 3	29 ± 4
*p*H	1	7.30 ± 0.03	7.33 ± 0.04	7.34 ± 0.03	7.34 ± 0.03	7.32 ± 0.03
	2	7.34 ± 0.01	7.35 ± 0.10	7.38 ± 0.05	7.37 ± 0.04	7.41 ± 0.04
V_t (ml/kg)	1	19.7 ± 1.4	10.0 ± 1.0‡	2.3 ± 0.3‡	10 ± 1.0‡	2.2 ± 0.1‡
	2	20.1 ± 0.8	9.7 ± 1.3‡	1.9 ± 0.2‡	7.0 ± 2.0‡	1.9 ± 0.1‡
frequency (cycles/s)	1	0.22 ± 0.05	0.68 ± 0.07‡	10.8 ± 0.8*‡	0.69 ± 0.08‡	11 ± 2*‡
	2	0.23 ± 0.07	0.77 ± 0.06‡	15.0 ± 2.0*‡	0.78 ± 0.06‡	14 ± 2*‡
PEEP (cmH_2O)	1	4.3 ± 0.7	0.8 ± 0.4‡	—	0.7 ± 0.4‡	—
	2	4.2 ± 0.4	1.7 ± 1.3‡	—	5.1 ± 1.0†	—
$\dot{V}_{LEAK}$ (l/min)	1	0	7.72 ± 1.11	3.03 ± 1.24*	7.89 ± 1.16	2.63 ± 1.30*
	2	0	9.54 ± 1.99	8.00 ± 3.12*†	17.74 ± 2.29†	14.05 ± 1.80*†
$\dot{V}_I$ (l/min)	1	5.1 ± 0.9	8.1 ± 0.9‡	4.7 ± 1.4*	8.2 ± 1.0‡	4.4 ± 1.5*
	2	6.1 ± 1.7	9.7 ± 1.2‡	10.8 ± 3.5†‡	21.7 ± 3.4†‡	19.9 ± 2.0†‡
Pa_{O_2} (mmHg)	1	88 ± 6	70 ± 15‡	55 ± 14‡	67 ± 14‡	69 ± 24‡
	2	87 ± 7	67 ± 9‡	68 ± 16‡	89 ± 12†	87 ± 8
P_{ao} (cmH_2O)	1	6.5 ± 0.9	2.4 ± 0.4‡	2.6 ± 0.4‡	2.5 ± 0.6†	2.4 ± 0.6‡
	2	6.4 ± 1.0	3.2 ± 1.3‡	3.8 ± 0.6†‡	6.4 ± 1.0†	6.3 ± 1.0‡

During HFOV, PEEP could not be measured.
Mean results (±SD) are shown.
$\dot{V}_{LEAK}$ = gas flow through the fistula; $\dot{V}_I$ = total inspiratory flow; P_{ao} = mean airway pressure; V_T = tidal volume; PEEP = positive end-expiratory pressure.

* Significant difference from the preceeding IPPV period ($P < 0.05$).
† Difference from Group 1 to Group 2 experiments by *t* test ($P < 0.05$).
‡ Difference from control period (C) by ANOVA ($P < 0.05$).

fistula-open periods than during the fistula-closed period ($P < 0.05$). Pa_{CO_2}, however, was maintained at similar levels for all periods and did not change from period C. Also, during periods $IPPV_1$ and $IPPV_2$, PEEP decreased significantly from levels obtained during period C ($P < 0.05$). During HFOV, PEEP is not measured; therefore, no values are shown.

During periods $IPPV_1$ and $IPPV_2$, the $\dot{V}_{LEAK}$ was similar. The $\dot{V}_{LEAK}$ was not different between periods $HFOV_1$ and $HFOV_2$. During either HFOV period, however, the leak rate was lower than during either IPPV period ($P < 0.05$). The larger leak rate during IPPV necessitated a significantly greater $\dot{V}_I$ during IPPV than during HFOV.

Group 2. Table 2 also shows the mean values of P_{ao} and Pa_{O_2} for Group 2. In Group 2, during periods $IPPV_2$ and $HFOV_2$ the mean airway pressure was prospectively increased to match that during period C. Figure 3 depicts the changes in P_{ao} and Pa_{O_2} from Group 1 to Group 2 as bias flow is added ($IPPV_2$) or increased ($HFOV_2$). In Group 1, mean P_{ao} was significantly greater during period C when compared with the rest of the periods ($P < 0.05$ by ANOVA). In Group 2, mean P_{ao} was similar during $IPPV_2$ and $HFOV_2$ compared with period C, but was significantly less during periods $IPPV_1$ and $HFOV_1$. In Group 1, the mean Pa_{O_2} decreased significantly on opening the fistula and remained lower than during period C for all four subsequent ventilatory periods. In Group 2, mean Pa_{O_2} during periods $IPPV_2$ and $HFOV_2$ was similar to period C and significantly greater (by ANOVA) than either periods $IPPV_1$ or $HFOV_1$. In general the level of Pa_{O_2} paralleled the level of mean P_{ao} in both Group 1 and Group 2.

In Group 2, the leak rate through the fistula was significantly greater in periods with higher levels of P_{ao} ($IPPV_2$ and $HFOV_2$) than in periods with lower levels of P_{ao} ($IPPV_1$ and $HFOV_1$). When comparing periods with matched levels of P_{ao}, the leak rate during HFOV was significantly lower than during the matched IPPV periods. Table 2 also shows that $\dot{V}_I$ increased from period C to periods $IPPV_1$ and $HFOV_1$. $\dot{V}_I$ increased further over the preceeding periods during periods $IPPV_2$ and $HFOV_2$.

Figure 4 illustrates the mean values of minute ventilation delivered by the Harvard® ventilator and the associated mean Pa_{CO_2} for Group 2. Pa_{CO_2} was similar between the three periods but the associated minute ventilation decreased significantly from period $IPPV_1$ to period $IPPV_2$ (449 ± 74 ml · kg^{-1} · min^{-1} and 291 ± 131 ml · kg^{-1} · min^{-1}, respectively). During period C neither minute ventilation (284 ± 80 ml · kg^{-1} · min^{-1}) nor Pa_{CO_2} were significantly different from period $IPPV_2$.

Effect of Ventilator Mode on Fistula Flow

In figure 5, flow through the fistula is plotted as a function of P_{ao} for each animal. IPPV periods (*closed circles*) are examined separately from HFOV periods (*open circles*). These points yielded two distinct regression lines by ANOVA of linear regression ($F = 9.4$, $P < 0.01$). However the slopes of the lines were not different using a t statistic.

Oleic Acid

Table 3 illustrates the values of Pa_{O_2} in individual dogs following administration of oleic acid. One animal (number 10) died during period C_1 and therefore no further data are available. One animal (number 7) died while receiving conventional IPPV. A Pa_{O_2} of 40 mmHg was recorded prior to its death. In the remaining four animals (numbers 8, 9, 11, and 12), when bias flow was used to maintain P_{ao} at levels similar to period C_1, then Pa_{O_2} was similar to C_1 values. This was true for either IPPV or HFOV during which Pa_{O_2} was 93% and 90% of period C_1 values, respectively. When bias flow was not added during IPPV, the Pa_{O_2} decreased to 33% of period C_1 values and two animals became so hypoxic that we could not complete the full 30-min ventilatory period.

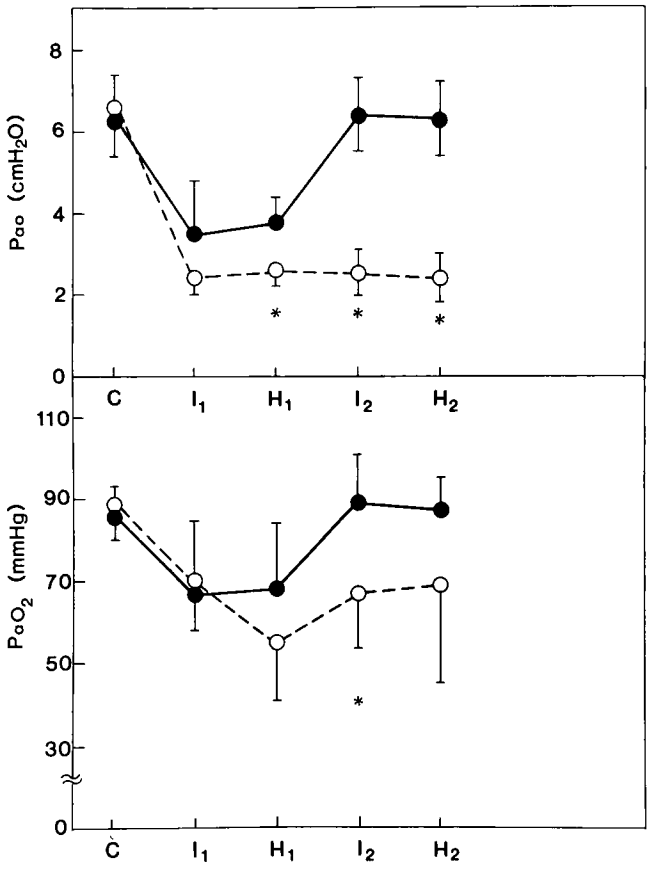

FIG. 3. Mean airway pressure (P_{ao}) is shown in the upper panel and Pa_{O_2} in the lower panel for Group 1 (*open circles* and *interrupted lines*) and Group 2 (*closed circles* and *solid lines*). The ventilatory periods are shown along the x-axis (C = fistula closed; I_1 = $IPPV_1$; H_1 = $HFOV_1$; I_2 = $IPPV_2$; and H_2 = $HFOV_2$). * represents a difference between Group 1 and Group 2 by t test ($P < 0.05$).

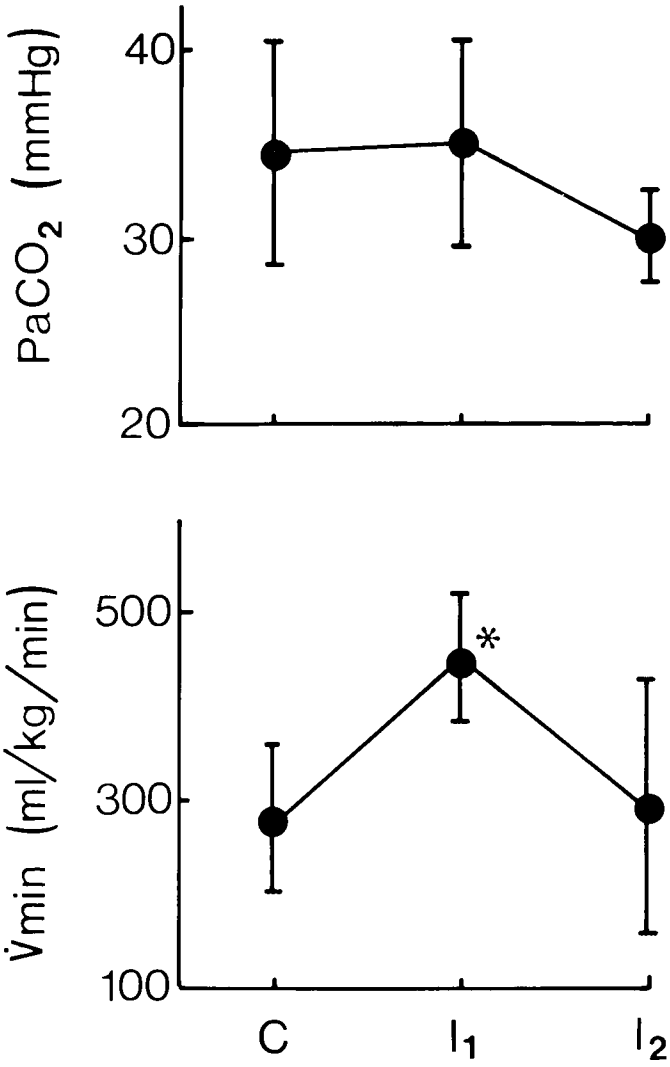

FIG. 4. The upper panel illustrates the stability of the Pa_{CO_2} in Group 2 during IPPV (C = fistula closed period; I_1 = $IPPV_1$ period; I_2 = $IPPV_2$ period). Pa_{CO_2} was similar between the three ventilatory periods. The lower panel illustrates the associated minute ventilation ($\dot{V}_{min}$) delivered by the Harvard® ventilator. There was a significant decrease in $\dot{V}_{min}$ between I_1 and I_2 ($P < 0.05$). $\dot{V}_{min}$ was similar between C and I_2.

Although the mean P_{ao} was similar during conventional IPPV and during IPPV with added bias flow (6.3 ± 1.4 cmH_2O and 6.8 ± 1.3 cmH_2O, respectively), the distribution of the airway pressures during the respiratory cycle tended to be different. Conventional IPPV had greater peak airway pressures than did IPPV with bias flow (13.8 ± 4.4 cmH_2O and 10.1 ± 3.1 cmH_2O, respectively), but

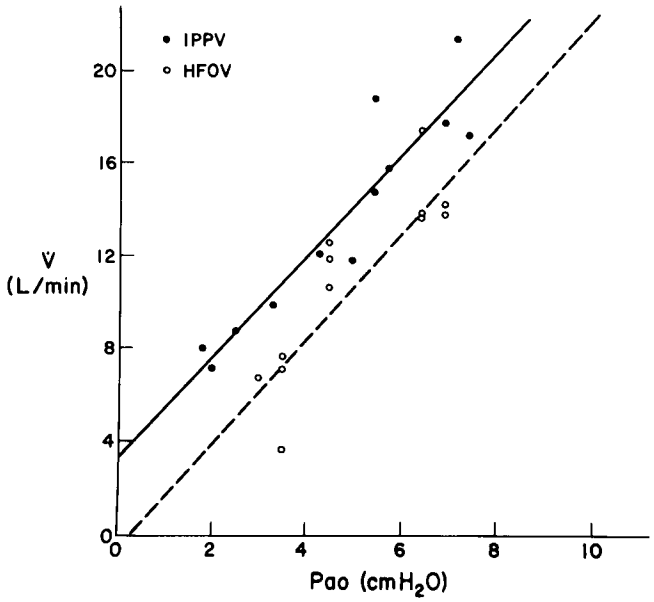

FIG. 5. The airway pressure–flow (P_{ao}-$\dot{V}$) characteristics of the fistula are illustrated. *Open circles* represent points obtained during HFOV and the *closed circles* during IPPV. The two regression lines, y = 2.13* × −3.3 (IPPV *solid line*) and y = 2.23* × +0.3 (HFOV *interrupted line*) have different intercepts ($P < 0.05$) but similar slopes.

conventional IPPV had lesser values of PEEP than did IPPV with added bias flow (1.9 ± 1.5 cmH_2O and 5.1 ± 1.2 cmH_2O, respectively). Because of the small number of animals completing all stages of the experiment, statistical tests for significance were not performed.

Discussion

Model

We believe this model of bronchopleural fistula allows useful extrapolations to be made to the clinical setting. In our model the pleural pressure was set at atmospheric pressure and, therefore, the pressure driving flow through the fistula was equal to P_{ao}. Also, P_{tp} was equal to P_{ao}. Finally, lung volumes could be inferred from values of P_{ao} because the product of compliance and P_{tp} is lung volume. In order to obtain reliable measurements of pleural pressure and of volume lost through the fistula, we elected to use an open-chest preparation. The extrapolation of our findings to the clinical setting (*i.e.*, closed chest with chest tube evacuating air) may not be exact but should yield an approximation of clinical findings. Our model, with known pressures and known size and site of fistula, allows comparisons between individual experiments and allows comparison of ventilator mode on lung mechanics and leak rate.

In preliminary experiments we found that measuring the leak rate by a volume collection of gas directly from the fistula site decreased the fistula flow rate by increasing fistula resistance. Therefore, we measured the leak indirectly, as the difference between inspiratory and expiratory flows. In this model the mean fistula leak rates were large, ranging between 81% to 98% of the $\dot{V}_I$ during IPPV periods and between 60% to 79% during HFOV periods. Also, in preliminary studies we found that IPPV at slow frequencies (10–12 breaths/min) allowed sufficient time for gas to escape through the fistula and end-expired pressure to decrease to near zero. By increasing IPPV frequency to near the maximal rate the ventilator could deliver (45–50 breaths/min), it was possible to maintain a positive, although low, value of end-expired pressure. During IPPV we could not, however, increase end-expired pressures back to control levels even with complete occlusion of the expiratory line of the ventilator. The HFOV ventilatory circuit allowed an adjustable bias flow of gas and, although increasing the bias flow increased the fistula leak rate, it also set a larger lung volume. The use of a bias flow was therefore extended to the IPPV circuit and similar results were obtained.

We elected to measure mean airway pressure as a static pressure determination. It has been demonstrated that during HFOV, static determinations better reflect alveolar pressures than do dynamic measurements obtained at the airway opening during oscillations.[11] Therefore, we elected to match airway pressures obtained dynamically during IPPV with those obtained statically during HFOV.

TABLE 3. Pa_{O_2} in Group 2 Following Oleic Acid Edema

Dog No.	C_1	IPPV + FGF	HFOV	IPPV
7	91	—	—	40*
8	74	56	59	34†
9	272	263	260	38†
10	91*	—	—	—
11	237	233	304	46
12	250	228	166	99

Each animal is represented for periods of fistula closed (C_1), positive pressure ventilations with a fresh gas flow (IPPV + FGF), oscillation (HFOV), and conventional positive pressure ventilation (IPPV).

* Represents the period during which the animal died; †represents inability to complete the full 30-min period. Dog number 7 died during IPPV prior to other periods being attempted and dog number 10 died during C_1. —represents no data available during the period.

Gas Exchange

The animals ventilated at the low airway pressures tended to be hypoxic. When the airway pressure was increased (Group 2 during $IPPV_2$ and $HFOV_2$), the hypoxia was abolished. When the level of airway pressure was matched between IPPV and HFOV, there were no significant differences in oxygenation. Therefore, we feel that in this model, the level of oxygenation is not deter-

mined by ventilator waveform (*i.e.*, IPPV *vs.* HFOV) but rather is a function of airway pressure.

We extended the study of Group 2 dogs to examine the interaction of pulmonary edema with a bronchopleural fistula. We found that despite increasing the $F_{I_{O_2}}$ to 0.6, the animals became profoundly hypoxic when ventilated by conventional IPPV. We occluded the expiratory limb of the ventilator, but we could not increase PEEP by these means. Presumably, occluding the expiratory limb increased the leak through the fistula without changing end expired lung volumes. This severe hypoxia, however, could be alleviated by ventilation at the higher levels of PEEP made possible by the use of a bias flow during IPPV. The same effect could be achieved by HFOV with increased bias flow. It has been previously demonstrated that in the presence of pulmonary edema, increasing mean P_{ao} during HFOV improves gas exchange.[10,12,13] In our model we could not increase airway pressure except by increasing bias flow. The importance of maintaining lung volumes in the setting of a bronchopleural fistula has been demonstrated clinically[14] but the methods suggested previously have included application of some fraction of airway PEEP to the pleural surface. This must result in a reduction of P_{tp}. Our data suggest that decreasing P_{tp} is associated with worsening hypoxia and cause us to question the clinical efficacy of such maneuvers, especially in the setting of associated pulmonary edema.

Alveolar Ventilation

Even in the presence of a large fistula, we were able to maintain CO_2 elimination. During IPPV in Group 1, the minute ventilation was tripled and this would tend to increase CO_2 elimination. Also, with the large flow through the fistula, there would be minimal alveolar gas in the upper airway down to the level of the fistula and, therefore, anatomic dead space would be reduced. In group 2, the addition of a bias flow to IPPV further decreased dead space. This is implied by a constant Pa_{CO_2} despite a decreased minute ventilation delivered by the ventilator from $IPPV_1$ to $IPPV_2$ (fig. 4). This may have been due to recruitment of collapsed alveoli caused by the higher airway pressures during $IPPV_2$. Alternately, the use of a bias flow may have resulted in gas exchange by constant-flow ventilation.[15] Lehnert *et al.* were able to maintain adequate O_2 and CO_2 exchange by constant flows introduced at the level of the carina. Although our model is different, it is possible that the improved gas exchange we observed was a function of constant-flow ventilation in addition to conventional IPPV.

Leak Rate

We observed a lower leak rate through the fistula during HFOV when compared with IPPV. The plot of $\dot{V}_{LEAK}$ and mean P_{ao} (fig. 5) describes the pressure–flow characteristics of the fistula. The slopes of the lines are the same. Therefore, at the frequencies we employed during IPPV and HFOV, the impedances to the flow through the fistula are the same. We believe that the decreased flow through the fistula can be explained by the Bernoulli equation.[16] This equation can be written as:

$$P_1 - P_2 = \tfrac{1}{2}\, p u_2^2 - \tfrac{1}{2}\, p u_1^2$$

where P_1 and P_2 = pressures (dynes) at location 1 and 2, respectively; p = gas density (g/cm^3); and u_1 and u_2 = gas velocity (cm/s) at location 1 and 2, respectively. (Note that 980 dyn = 1 cmH_2O). This equation implies that as gas velocity decreases, the lateral pressure exerted by the gas increases. Mean P_{ao} was measured statically during HFOV (*i.e.*, u = 0); therefore, during oscillation the lateral pressure at the left lower lobe would be less than the value of mean P_{ao}. Also, the Bernoulli equation would predict that the driving pressure for leak through a central fistula during HFOV would always be less than alveolar pressure. Using theoretical data from Fredberg[17] for gas velocity during HFOV and a value of 1.1×10^{-3} g/cm^3 for gas density yields a pressure 1 to 2 cmH_2O lower at the left lower-lobe bronchus (u_2 = 1600 cm/s) than at the alveolus ($u_1 < 0.5$ cm/s). If this explanation is true, then increasing gas velocity during HFOV by increasing oscillator frequency would further increase the Bernoulli pressure drop, and this would be associated with a further reduction in fistula gas flow.

It is not certain that a fistula occurring at a more peripheral site would behave in a similar manner, and extrapolation of these results to such a setting would not be warranted. The obvious treatment of a large bronchopleural fistula is surgical correction. When this is not possible or when an unacceptable time delay is involved, then ventilator management becomes more important. In the setting of a large, central bronchopleural fistula, the use of HFOV appears to offer advantages over conventional IPPV both in reduction of gas lost through the fistula and in the use of a bias flow system to effect increased lung volumes. In the setting where safe HFOV is not available, IPPV at relatively high frequencies in conjunction with an additional fresh gas flow line may offer a reasonable method for acute maintenance of gas exchange.

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References

1. Hankins JR, Miller JE, Attar S, Satterfield JR, McLaughlin JS: Bronchopleural fistula: Thirteen years experience with 77 cases. J Thorac Cardiovasc Surg 76:755–762, 1978
2. Brown CR: Postpneumonectomy empyema and bronchopleural fistula—Use of prolonged endobronchial intubation. A case report. Anesth Analg 52:439–441, 1973

3. Hartmann W, Rausch V: A new therapeutic application of the fiberoptic bronchoscope (letter). Chest 71:237, 1977
4. Ratliff JL, Hill JD, Tucker H, Fallat R: Endobronchial control of bronchopleural fistulae. Chest 71:98–99, 1977
5. Down JB, Chapman RL: Treatment of bronchopleural fistula during continuous positive pressure ventilation. Chest 69:363–366, 1976
6. Phillips YY, Lonigan RM, Joyner LR: A simple technique for managing a bronchopleural fistula while maintaining positive pressure ventilation. Crit Care Med 7:351–353, 1979
7. Power DJ, Grenuik A: Ventilatory management of life-threatening bronchopleural fistula. Crit Care Med 9:54–58, 1981
8. Turnbull AD, Carlon G, Howland WS, Beattie EJ: High frequency jet ventilation in major airway or pulmonary disruption. Ann Thorac Surg 32:468–474, 1981
9. Severinghaus JW: Blood gas calculator. J Appl Physiol 21:1108–1116, 1966
10. Thompson WK, Marchak BE, Froese AB, Bryan AC: High frequency oscillation compared with standard ventilation in a pulmonary injury model. J Appl Physiol 52:543–548, 1982
11. Simon B, Weinman G, Mitzner W: Mean airway pressure and alveolar pressure during high-frequency ventilation. J Appl Physiol 57:1069–1078, 1984
12. Kolton M, Cattran CB, Kent G, Froese AB, Bryan AC: Oxygenation during high-frequency ventilation compared with conventional mechanical ventilation in two models of lung injury. Anesth Analg 61:323–332, 1982
13. Sandoval J, Mayers I, Breen PH, Oppenheimer L, Ali J, Wood LDH: Relative effect of high frequency oscillatory ventilation (HFOV) and continuous positive pressure ventilation (CPPV) on hemodynamics, gas exchange and extravascular lung water (EVLW) (abstract). Am Rev Respir Dis 125:85, 1982
14. Zimmerman JE, Colgan DL, Mills M: Management of bronchopleural fistula complicating therapy with positive end expired pressure (PEEP). Chest 64:526–529, 1973
15. Lehnert BE, Oberdorster G, Slutsky AS: Constant-flow ventilation of apneic dogs. J Appl Physiol 53:483–489, 1982
16. Pedley TJ, Schroter RC, Sudlow MFD: Gas flow and mixing in the airway, Bioengineering Aspects of the Lung. Edited by West JB. New York and Basel, Marcel Deker, 1977, pp 163–265
17. Fredberg JJ: Augmented diffusion in the airways can support pulmonary gas exchange. J Appl Physiol 48:710–716, 1980