Effects of Varying Respiratory Waveforms on Gas Exchange

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Effects of three different respiratory waveforms on magnitude of AaD_{O_2} and physiological dead space were compared during artificial ventilation of healthy anesthetized subjects. Waveforms included two intermittent positive pressure patterns with differing duration of inspiration and one positive-negative pattern. AaD_{O_2} did not vary with use of the different respiratory waveforms, with mean pressure during the respiratory cycle or with duration of inspiration. Physiological deadspace likewise did not change with the varying respiratory waveforms or mean pressure. Physiological dead space increased as duration of inspiration decreased but the change, though significant, was not dramatic. It was concluded that any respiratory pattern which provided adequate alveolar ventilation would be efficient in performing the ventilatory functions of oxygenation and carbon dioxide removal. A simple respiratory waveform should be adequate during artificial ventilation of healthy subjects and the provision for using different respiratory waveforms in apparatus seems unnecessary.

DEMONSTRATION by Frumin and his associates that variations in expiratory airway pressures during anesthesia in man caused changes in alveolar-arterial oxygen tension differences (AaD_{O_2}) suggested that under these circumstances, alterations in mean pressure and pressure profile during the respiratory cycle might also be associated with changes in pulmonary gas exchange.[1] In a subsequent study, anesthetized dogs were artificially ventilated with respiratory tidal volumes having different pressure profiles, and it was concluded that magnitude of alveolar-arterial differences for both oxygen and carbon dioxide decreased as mean pressure during the respiratory cycle became greater.[2] It therefore seemed possible that during artificial ventilation in man an optimal pattern of pulmonary inflation might exist which would provide maximum efficiency of pulmonary gas exchange. The present study was undertaken to determine the effect of artificial ventilation using different pressure profiles on magnitude of AaD_{O_2} and physiological dead space in anesthetized artificially ventilated human subjects.

Methods

Subjects of the study were eight male hospital patients whose age ranged from 32 to 71 years and whose average age was 51 years. All were free from symptomatic pulmonary or cardiac disease. Patients were premedicated and subsequently anesthetized by anesthesiologists not involved in the study. Premedication consisted of atropine, hydroxyzine (Vistaril), pentobarbital (Nembutal), meperidine (Demerol), and oxymorphone (Numorphan) in various combinations. All subjects remained supine throughout the study.

Patients were anesthetized with halothane in oxygen and artificially ventilated through a tightly fitting cuffed endotracheal tube. Concentration of halothane was adjusted according to clinical requirements and sufficient *d*-tubocurarine or gallamine triethiodide was administered to prevent spontaneous respiratory efforts. Three different pressure patterns were studied in each subject, and the order in which they were employed was varied. The first breathing pattern was intermittent positive pressure with a duration of inspiration greater than 1.5 seconds; the second was also

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intermittent positive pressure, but with duration of inspiration usually one second or less; and the third was positive-negative pressure breathing with duration of inspiration usually between one and two seconds (fig. 1). Each change in pattern of inflation was preceded by several maximum pulmonary inflations and a subsequent 15–20 minute period of equilibration occurred before measurements were made.

Artificial ventilation was performed with a Manley Ventilator.* [3] This is a time cycled, pressure controlled ventilator which incorporates a nonrebreathing circuit, so that the minute volume of the patient is equal to the total flow of gas to the ventilator. The ventilator employed was designed specially for this study and permitted quantitative collection of exhaled gas during both intermittent positive and positive-negative pressure breathing. The experimental apparatus is illustrated in figure 2. The halothane-oxygen mixture was saturated with water vapor at room temperature by bubbling through two humidifier bottles in series and then delivered to the ventilator. During periods of equilibration exhaled gas escaped to atmosphere, and during periods of measurement exhaled gas was collected in the bag of a box-bag system. A 10-liter waterless spirometer † communicated with the box and each exhalation collected in the bag displaced an identical volume of gas from the box into the spirometer permitting measurement of exhaled tidal and minute volumes. When the spirometer reached the limit of its excursion it was rapidly emptied to atmosphere by a spirometer recycling device.‡ Pressure in the airway was continuously measured with a Statham PM 5 TC pressure transducer cali-

FIG. 1. The three types of respiratory waveforms studied.

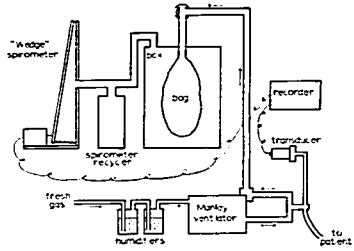

FIG. 2. Diagram of experimental apparatus. For explanation see text.

brated against a water manometer. Output of the pressure transducer and of the volume transducer of the spirometer were recorded using a Minneapolis-Honeywell Visicorder.

Arterial blood, obtained during periods of exhaled gas collection, was analyzed for oxygen and carbon dioxide tensions using an Instrumentation Laboratory System. The oxygen electrode was calibrated with oxygen-free nitrogen and with medical oxygen. The carbon dioxide electrode was calibrated with carbon dioxide-air mixtures whose exact composition had been determined by Scholander analysis. Readings were corrected for metabolic changes in blood following collection § and for differences between esophageal temperature of the patient and electrode temperature.[4] In addition, oxygen readings were corrected for the 5 per cent difference in value indicated between blood and gas of identical oxygen tension previously determined in our laboratory. Tension of carbon dioxide in mixed expired gas collected from the bag was also determined with the carbon dioxide electrode. Inspired oxygen concentration was measured using gas sampled at the point where it entered the ventilator, using a Servomex paramagnetic oxygen analyzer.¶ [5]

Alveolar oxygen tension was calculated using the formula:

$$P_{A_{O_2}} = P_{I_{O_2}} - 47 - P_{a_{CO_2}}$$

* Blease Anesthetic Equipment Company, Chesham, England.
† "Wedge" Spirometer, Med-Science Electronics, St. Louis, Missouri.
‡ Spirometer Recycling Device, Med-Science Electronics, St. Louis, Missouri.
§ Nunn and Capel, unpublished observations.
¶ Servomex Controls Ltd., Crowborough, Sussex, England.

TABLE 1. Experimental Results for Intermittent Positive Pressure Curves with Long Inspirations

Patient	Time from Induction (min.)	Rate (min.$^{-1}$)	V_T (ml. BTPS)	$\dot{V}$ (ml. BTPS)	Pa_{O_2} (mm. Hg)	AaD_{O_2} (mm. Hg)	Pa_{CO_2} (mm. Hg)	V_D/V_T (%)	Inflating Pressure (cm. H_2O)	Mean Pressure (cm. H_2O)	Duration Inspiration (sec.)
1	25	10.5	1,017	10,680	324	224	24.5	36.0	20/0	6.5	1.8
2	50	9.8	998	9,785	270	277	25.6	25.1	17/0	4.5	1.9
3	80	6.9	973	6,715	500	59	27.0	25.8	17/0	4.8	2.6
4	105	7.7	955	7,352	293	257	31.0	32.5	19/0	6.0	2.6
5	120	11.4	997	11,375	120	423	31.9	49.4	18/0	5.0	1.8
6	25	8.6	836	7,186	459	86	33.6	42.5	17/0	5.5	2.6
7	—	—	—	—	—	—	—	—	—	—	—
8	55	7.2	1,022	7,355	239	306	35.1	28.2	17/0	5.5	2.6
Mean		8.9	971	8,635	314	233	29.8	34.2	17.9	5.4	2.3
S.D.					131	126	4.1	9.1		0.7	

V_T = tidal volume, $\dot{V}$ = minute volume, Pa_{O_2} = arterial oxygen tension, AaD_{O_2} = alveolar-arterial oxygen tension difference, Pa_{CO_2} = arterial carbon dioxide tension, V_D/V_T = ratio of dead space to tidal volume.

TABLE 2. Experimental Results for Intermittent Positive Pressure Curves with Short Inspirations

Patient	Time from Induction (min.)	Rate (min.$^{-1}$)	V_T (ml. BTPS)	$\dot{V}$ (ml. BTPS)	Pa_{O_2} (mm. Hg)	AaD_{O_2} (mm. Hg)	Pa_{CO_2} (mm. Hg)	V_D/V_T (%)	Inflating Pressure (cm. H_2O)	Mean Pressure (cm. H_2O)	Duration Inspiration (sec.)
1	65	13.6	785	10,678	220	324	28.4	47.5	18/0	3.2	0.7
2	80	14.3	698	9,976	208	339	26.7	36.4	15/0	3.0	0.8
3	45	7.8	850	6,634	491	60	29.5	36.2	19/0	2.7	1.0
4	35	9.2	786	7,232	468	77	33.7	38.7	19/0	3.0	1.0
5	40	14.6	722	10,537	297	242	36.8	52.1	20/0	3.5	0.7
6	—	—	—	—	—	—	—	—	—	—	—
7	125	8.9	748	6,088	464	90	30.4	46.0	17.5/0	2.7	1.1
8	95	8.1	950	7,697	273	265	37.3	36.8	17/0	2.5	1.0
Mean		10.9	791	8,406	346	200	31.8	42.0	17.9	2.9	0.9
S.D.					124	120	4.2	6.5		0.3	

Symbols as in table 1.

TABLE 3. Experimental Results for Positive-Negative Pressure Curves

Patient	Time from Induction (min.)	Rate (min.$^{-1}$)	V_T (ml. BTPS)	$\dot{V}$ (ml. BTPS)	Pa_{O_2} (mm. Hg)	AaD_{O_2} (mm. Hg)	Pa_{CO_2} (mm. Hg)	V_D/V_T (%)	Inflating Pressure (cm. H_2O)	Mean Pressure (cm. H_2O)	Duration Inspiration (sec.)
1	105	13.3	790	10,513	198	349	27.7	44.8	12/-5	1.5	1.2
2	105	13.6	718	9,758	152	398	26.0	37.2	11/-7	0.5	1.3
3	110	7.1	943	6,692	452	108	25.4	30.5	11/-9	−0.4	2.6
4	65	11.3	649	7,330	355	189	33.7	38.1	14/-7	1.5	1.7
5	75	15.0	712	10,681	171	370	34.2	53.2	13/-5	1.5	1.1
6	60	13.3	564	7,505	456	84	36.8	47.3	13/-5	1.5	1.9
7	75	8.5	777	6,606	483	69	31.2	46.8	12/-7	1.5	1.9
8	30	9.3	811	7,540	230	305	38.9	35.9	12/-7	1.5	1.7
Mean		11.4	746	8,328	312	234	31.7	41.7	18.3	1.1	1.7
S.D.					140	137	5.0	7.5		0.7	

Symbols as in table 1.

TABLE 4. Summary of Mean Values for the Three Types of Curves Studied

	Rate (min.$^{-1}$)	V_T (ml. BTPS)	$\dot{V}$ (ml. BTPS)	P_{AO_2} (mm. Hg)	$A_aD_{O_2}$ (mm. Hg)	P_{ACO_2} (mm. Hg)	V_D/V_T (%)	Inflating Pressure (cm. H_2O)	Mean Pressure (cm. H_2O)	Duration Inspiration (sec.)
Long inspirations	8.9	971	8,635	311	233	29.8	34.2	17.9	5.4	2.3
Short inspirations	10.9	791	8,106	316	200	31.8	42.0	17.9	2.9	0.9
Positive-negative	11.4	716	8,328	312	234	31.7	41.7	18.3	1.1	1.7

$A_aD_{O_2}$ was obtained by subtraction. Minute volume and tidal volume were obtained from spirometer recordings and corrected to BTPS. Physiological dead space was calculated by substituting appropriate values for arterial and mixed exhaled carbon dioxide tensions and tidal volume in Bohrs equation.[6] Dead space of 20 ml. for the apparatus was subtracted to obtain dead space in the patient and ratio of dead space to tidal volume (V_D/V_T) was also calculated. Mean pressure during the respiratory cycle was calculated by planimetric integration of pressure curves.

Results

Experimental results are presented in tables 1–3 and summarized in table 4. Mean inflating pressure, defined as the difference between end-expiratory and end-inspiratory pressures, was identical for all three pressure curves studied. Minute volume was also similar for all three conditions, and as duration of inspiration was shortened, tidal volume tended to decrease while respiratory frequency increased. Mean arterial carbon dioxide tension for the study was 31.1 mm. of mercury and although it was less with longer inspirations, differences among the three pressure curves were not significant. Mean ratio of physiological dead space to tidal volume (V_D/V_T) was 39.3 per cent and was significantly smaller during use of curves with long inspirations than when duration of inspiration was shorter. Coefficient of correlation between V_D/V_T and duration of inspiration was −0.86 and was highly significant ($P < 0.001$) (fig. 3). There was no significant correlation between mean pressure during the respiratory cycle and V_D/V_T.

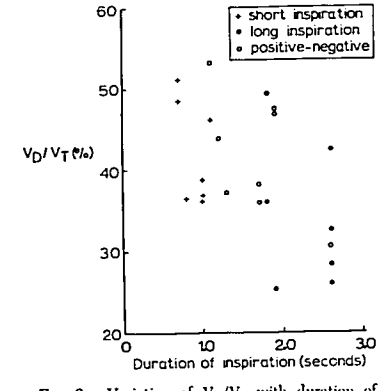

FIG. 3. Variation of V_D/V_T with duration of inspiration. The coefficient of correlation between these two variables was −0.86 and was highly significant.

Alveolar oxygen tension ranged from 535 to 560 mm. of mercury. Mean alveolar oxygen tension was 546 mm. of mercury and there was no significant difference among pressure curves. (Elevation of our laboratory is 4,780 feet above sea level and average total barometric pressure is 640 mm. of mercury.) Mean arterial oxygen tension was 324 mm. of mercury, and mean $A_aD_{O_2}$ was 222 mm. of mercury. Changes in profile of the inflating pressure curve caused no significant change in magnitude of any of these parameters.

Discussion

Mean values for $A_aD_{O_2}$ in the present study were slightly larger than but not significantly different from previously reported values.[7] Cause for the large individual variation in $A_aD_{O_2}$ among patients, which has also been observed previously, is not known. Mean values for V_D/V_T are identical with those pre-

viously measured in anesthetized man under comparable conditions.[7]

Results of the present study indicate that different breathing patterns during artificial ventilation affected V_D/V_T but had no demonstrable effect on magnitude of AaD_{O_2}. There was a highly significant negative correlation between V_D/V_T and duration of inspiration, but no clear association between V_D/V_T and waveform or mean pressure during the respiratory cycle. These findings relative to physiological dead space agree with those of Watson who demonstrated that V_D/V_T increased markedly when duration of inspiration was shortened from 1.0 second to 0.5 second during artificial ventilation, but that changes in respiratory waveform at constant duration of inspiration were not accompanied by alterations in V_D/V_T.[8] Fairley and Blenkarn have reported that during constant volume artificial ventilation in man, increasing inspiratory flow rates were associated with increasing V_D/V_T but no detectable changes in AaD_{O_2}.[9]

Although in the present study there was no discernable relationship between either AaD_{O_2} or V_D/V_T and mean pressure during the respiratory cycle, previous experiments have shown that alterations in airway pressure can be associated with changes in these parameters. AaD's for both oxygen and carbon dioxide diminished as mean pressure during the respiratory cycle increased during artificial ventilation in dogs.[2] Finley and his associates were able to produce modest decreases in shunt by imposition of 15 mm. of mercury positive pressure in the airway during exhalation in anesthetized, artificially ventilated dogs.[10] Frumin and his associates caused a significant increase in arterial oxygen saturation by changing airway pressure during exhalation from -5 to $+5$ mm. of mercury during artificial ventilation of anesthetized, paralyzed subjects, but when end-expiratory pressures of 0 and $+5$ mm. of mercury were compared, change in oxygen saturation was equivocal.[1] Also, Nunn and his associates were unable to detect any diminution in AaD_{O_2} when a 5 cm. of water threshold resistance to exhalation was imposed.[7] During artificial ventilation of conscious paralyzed human subjects Watson observed that a marked increase in V_D/V_T occurred when airway pressure during exhalation was maintained at -15 cm. of water. These reports suggest that variations in mean airway pressure much larger than those employed in the present study are required to alter AaD_{O_2} and dead space in anesthetized man during artificial ventilation. It would also seem that variations in these parameters with mean pressure are much more pronounced in dogs, which would explain failure to reproduce our previous results with animals in the present study involving human subjects.

It can be shown that magnitude of AaD_{O_2} during oxygen breathing is given by the following equation:

$$AaD_{O_2} = \frac{0.1 \times \dot{V}_{O_2} \times Q_s}{0.0031 \times CO \times (Q_t - Q_s)}$$

where $\dot{V}_{O_2}$ is oxygen consumption, CO is cardiac output, Q_s is fraction of cardiac output comprising a right to left shunt and $(Q_t - Q_s)$ is fraction of cardiac output not shunted. Findings of the present study suggest that alterations in pressure breathing patterns did not affect oxygen consumption, cardiac output, or magnitude of shunt. On the basis of known circulatory effects of positive pressure breathing,[11] however, it could alternatively be proposed that elevation of mean pressure produced a decrease in cardiac output which was accompanied by a corresponding decrease in shunt. Possibility of such "negative feedback" phenomena was recognized and discussed by Fairley and Blenkarn.[9]

In the present study, AaD_{O_2} did not change when different pressure breathing patterns were used during artificial ventilation. Although physiological dead space increased with shorter inspirations or with more rapid inspiratory flow rates,[9] changes were not dramatic and resulting decreases in alveolar ventilation could probably easily be compensated for by small increases in inflating pressure. Thus, it would appear that any pattern of pulmonary inflation which produces adequate alveolar ventilation would be quite effective in performing the functions of oxygenation and carbon dioxide removal. Results of the present study suggest that many of the controls featured by ventilators in common use

may have no obvious useful purpose, and that a simple pressure controlled ventilator which produced a square wave with a fixed duration of inspiration of 1.0 second and incorporated a respiratory rate control would be quite satisfactory for use during anesthesia. Such a device could be compact and relatively inexpensive and would permit the anesthesiologist to focus his attention on measures which are likely to more beneficial to the patient than altering his breathing pattern.

It is acknowledged that the results presented for a group of healthy subjects may not be applicable to patients with cardiac or pulmonary disease. It is possible that different respiratory waveforms, mean pressures, durations of inspiration or inspiratory flow rates might markedly increase respiratory efficiency in subjects with low compliance, high resistance, marked regional variations in resistance or other specific functional abnormalities. Search of the literature reveals a paucity of objective data supporting such a conclusion, however, and evaluation of this problem using objective measurements should be done. Similarly, claims of superiority for any specific mechanical ventilator or any feature of a ventilator must be supported by objective data collected from human subjects during use of the device. The lungs are composed, in part, of 300,000,000 alveoli together with extremely complex systems of conducting tubes for both gas and blood and are enclosed in a unique container. Their function cannot be studied by observing the inflation of two rubber bags on the end of a Y-piece.

Summary and Conclusions

Magnitude of aaD_{O_2} in anesthetized, artificially ventilated subjects did not change with alterations in duration of inspiration, respiratory waveform or mean pressure during the respiratory cycle. Physiological dead space likewise did not vary with changes in respiratory waveform and mean pressure during the respiratory cycle but became significantly greater as duration of inspiration was shortened. Changes in physiological dead space, however, were not dramatic. It is concluded that any pattern of respiration which provides adequate alveolar ventilation will be quite effective in performance of the ventilatory functions of oxygenation and carbon dioxide removal during artificial ventilation of healthy subjects.

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