Measurement of Inspiratory Force in Anesthetized Dogs

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THE *immediate* requirement for normal blood gas exchange is adequate pulmonary ventilation. The force required to accomplish adequate minute ventilation at rest is but a small fraction of the maximum force the respiratory muscles are capable of developing; 5 per cent would be a conservative estimate. The *maintenance* of adequate ventilation probably depends to a large extent on the ability of the respiratory muscles to develop considerably greater forces than required for tidal exchange. Periodic deep breaths are most likely necessary for re-expansion of collapsed airspaces and smaller airways, as shown by Mead and Collier [1] and by Ferris and Pollard,[2] thus preventing a fall in pulmonary compliance and an increased work of breathing. Certainly efficient coughing depends on muscular strength greatly in excess of what is required for quiet breathing. It is well justified to claim that *a reserve of ventilatory effort* is necessary for the prolonged maintenance of adequate ventilation. Should the reserve remain below minimum levels, eventually, perhaps within hours, ventilation would become inadequate.

In the past, measurements of vital capacity, inspiratory capacity and expiratory reserve volume have been used to express the reserve of ventilatory effort in the conscious and cooperative individual. In the unconscious, uncooperative patient, as during or immediately after anesthesia, these measurements are not practical. In this study the possibility is explored that the reserve of ventilatory effort may be assessed in terms of pressure rather than volume. The inspiratory force (IF) is used as such an index and is expressed by the highest negative airway pressure developed during a period of complete occlusion of the airway. The early experience with this measurement has been reported.[3] The present experiments were carried out in anesthetized dogs in order to examine the various factors which can be expected to influence these pressures. These included hypoxia, hypercarbia and hypocarbia and the lung volume at the time of airway occlusion. Finally the influence of drugs commonly used during anesthesia was investigated. Clinical studies have been conducted simultaneously and are reported separately.[4]

Previously, Smith [5] has used a similar technique to show the airway pressures needed for expansion of the newborn lung; and Stead [6] has suggested that in anesthetized and curarized patients the feeble inspiratory efforts against an occluded airway serve as an index of respiratory acidosis.

Methods and Procedure

Twenty-eight healthy mongrel dogs were studied. No premedication was given; anesthesia was induced and maintained with intravenous thiopental sodium in intermittent doses sufficient to produce light general anesthesia. Ventilation was spontaneous throughout all experiments. A tracheostomy was performed, a metal tracheostomy tube (fig. 1) with Collins unidirectional valves (J-1) inserted, and the trachea tied around it for airtight fit. In five cases the vagi nerves were isolated in the neck in preparation for later high cervical vagotomy. A femoral artery was cannulated with a polyethylene catheter for sampling and continuous measurement of arterial blood pressures; the tip of the catheter was placed at the aortic bifurcation. A femoral vein was also cannulated to allow injections and infusions. In 22 experiments the isometric contraction of the gastrocnemius muscle was measured intermittently by a strain gauge arch attached to the tendon or sutured to the muscle itself. In some early experiments a

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FIG. 1. Metal endotracheal tube with unidirectional valves and spigots for gas sampling and measurement of airway pressures.

Batronic stimulator was used, in the remaining a Grass stimulator. The tibialis nerve was stimulated with a frequency of one per second, duration of stimulus 1 millisecond and voltage 3 to 20. In ten of the early experiments, end-expiratory carbon dioxide concentration was measured continuously with a Liston-Becker infrared analyzer. Sampling was by microcatheter through a spigot in the tracheostomy tube. This measurement was given up when it almost consistently failed to detect hypoventilation, unless more complete emptying of the lungs was insured by squeezing the chest. In six experiments a Benedict-Roth metabolism apparatus was incorporated in the breathing circuit to produce a spirometric record of the time during the respiratory cycle at which the airway was occluded. In these cases a closed breathing circuit with soda lime absorbtion was used; in all other cases the breathing circuit was of the non-rebreathing type. Sanborn pressure transducers were used for all pressure measurements and recording was by two Sanborn four-channel Polyvisos, model 150. Saturation of oxygen in arterial blood was determined with a Beckman Quartz Spectrophotometer, *p*H was measured by a Beckman glass electrode with a Beckman or Sanborn *p*H meter. Concentration of carbon dioxide in arterial blood was measured by the method of Van Slyke and Neill,[7] and tension of carbon dioxide was derived from the Singer-Hastings nomogram.

The measurement and continuous recording of inspiratory force, as expressed by airway pressures, were carried out during complete occlusion of the airway for 50 seconds. The occlusion was brought about at end-expiration, except in the experiments where the influence of variation in lung volume on the rate of inspiratory efforts was studied. Changes in lung volume could be brought about by injecting or withdrawing air immediately after airway occlusion using a large syringe. The most easily reproduced lung volume change was the increase resulting from occluding the airway at end-inspiration instead of end-expiration.

The blood gas changes occurring during 50 seconds of airway occlusion were determined by drawing arterial samples immediately before and after 10, 20, 30, 40 and 50 seconds of airway occlusion. The influence of dif-

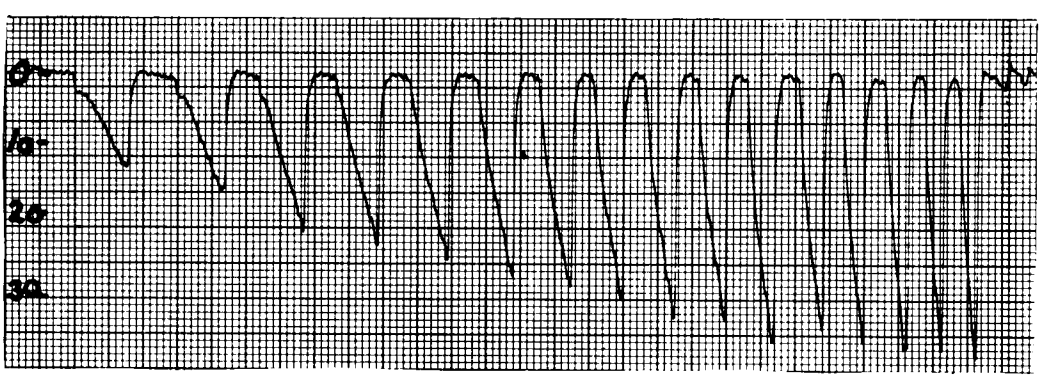

FIG. 2. An inspiratory force measurement under light thiopental anesthesia with the dog breathing room air. Note the gradual increase in rate and force during 50 seconds of airway occlusion.

TABLE 1. Inspiratory Force

Number of Cases	Inspired Mixture	Airway Occluded at	Maximum Inspiratory Force (mm./Hg Negative Pressure)	Inspiratory Force in Per Cent of Maximum					
				5	10	20	30	40	50
				Seconds of Airway Occlusion					
26	Room air	End-expiration	$\bar{X}$ 44	42	53	70	81	93	100
			SE 2.9	2.4	2.3	1.8	1.8	1.3	---
5	100% oxygen	End-expiration	$\bar{X}$ 42	48	61	68	73	93	100
			SE 9.9	6.2	3.8	6.2	5.1	3.3	---
5	5% CO_2 95% O_2	End-expiration	$\bar{X}$ 50	66	75	83	92	98	100
			SE 9.6	6.7	5.9	3.7	3.2	1.8	---
3	10% CO_2 90% O_2	End-expiration	$\bar{X}$ 42	90	91	97	97		
			SE 9.3	4.1	2.2	2.1	2.1		
4	20% CO_2 80% O_2	End-expiration	$\bar{X}$ 49	93	97	98	99		
			SE 8.3	3.1	1.4	1.5	1.5		
			After Vagotomy						
5	100% O_2	End-expiration	$\bar{X}$ 37	60	69	82	86	94	100
			SE 8.4	6.2	2.6	5.0	4.0	2.5	
3	5% CO_2 95% O_2	End-expiration	$\bar{X}$ 41	95	97	96	96	96	97
			SE 13.5	5.0	3.0	2.4	2.4	3.7	3.7
3	10% CO_2 90% O_2	End-expiration	$\bar{X}$ 59	95	96	100	99	99	
			SE 20.9	2.9	2.0	---	0.7	0.7	

ferent inspired gas mixtures was studied by measuring inspiratory force following a 5-minute period of inhalation of room air, 100 per cent oxygen and mixtures of oxygen and 5, 10 and 20 per cent carbon dioxide. In one experiment a period of hyperventilation was followed by inspiratory force measurements during an airway occlusion allowed to persist beyond 50 seconds while the negative pressures gradually reached previous levels. In three dogs the airway occlusion was continued beyond the standard 50 seconds until a maximal level of inspiratory efforts was reached.

The influence of anesthetics and pertinent drugs was studied as follows: The dog, already lightly anesthetized with thiopental and breathing spontaneously, received continuous infusion of the drug to be studied, either thiopental, *d*-tubocurarine or morphine; or it received continuous inhalation of ethyl ether or halothane vapor. Blood gases were sampled frequently, always followed by measurement of inspiratory force and contractile force of leg muscle. The infusion or inhalation was continued until hypoventilation was manifest by clinical judgment; it was then stopped and the dog allowed to recover. The objective was to determine the decrease in reserve of ventilatory effort (as expressed by inspiratory force measurement) which can be brought about without also causing immediate hypoventilation (as determined by arterial blood gases). The muscle relaxant used was *d*-tubocurarine, in a solution containing 0.1 mg./ml. Thiopental was infused as a 0.5 per cent solution in normal saline and morphine sulfate as a solution containing 1 mg./ml. Ethyl ether and halothane were administered by vaporizers in a nonrebreathing circuit.

Results and Discussion

A typical tracing of the inspiratory efforts during a 50 second airway occlusion is shown on figure 2. It may be noticed that both

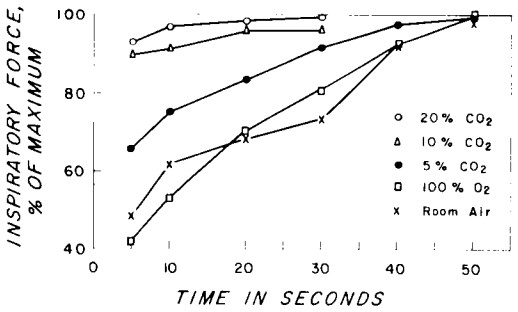

FIG. 3. Inspiratory force during 50 seconds airway occlusion. The maximal negative pressure during the 50 seconds of airway occlusion is plotted at 100 per cent. The graph demonstrates that maximal inspiratory efforts are caused to occur earlier during the period of occlusion when increasing concentrations of carbon dioxide are inspired.

rate and negative pressure increase gradually with each individual inspiratory effort, and that a maximal plateau is not reached within 50 seconds. In 26 measurements made at the start of the experiments the mean maximal negative pressure reached during 50 seconds of airway occlusion was −44 mm. of mercury (table 1). At the time of these measurements the dogs were all under very light thiopental anesthesia, and the value given (−44 mm. of mercury) should be considered a reference point, not a normal value. However, the central regulation of ventilation under very light thiopental anesthesia may be assumed to be qualitatively the same as in the normal and conscious. This is supported by the work of Moyer and Beecher,[5] who point out also that

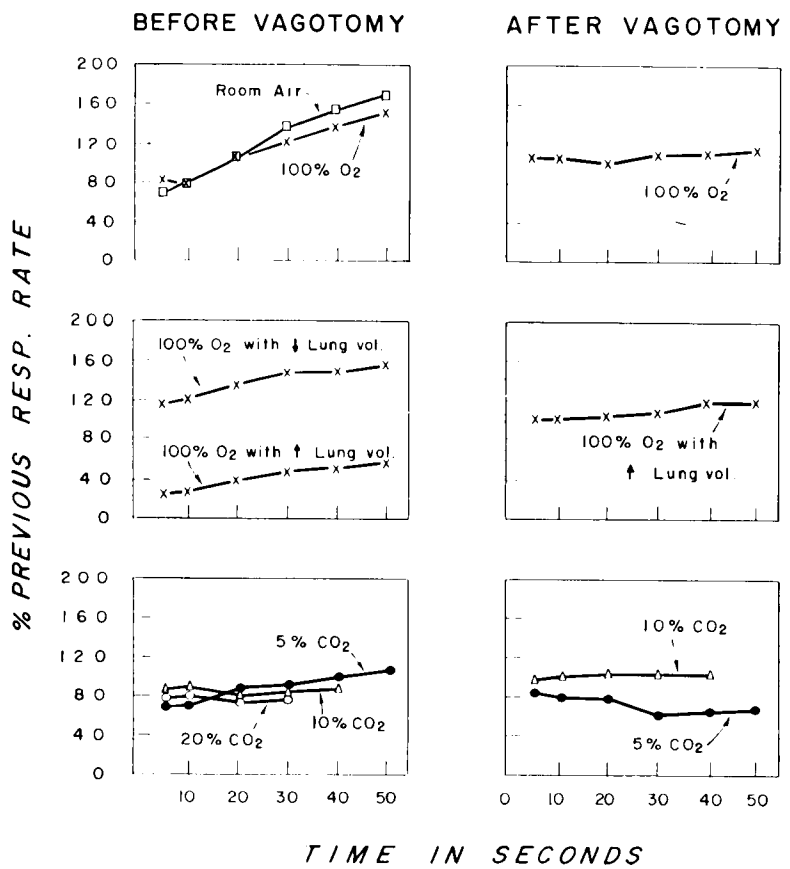

FIG. 4. Rate of inspiratory efforts during 50 seconds airway occlusion. Note the considerable difference in rate of inspiratory efforts when lung volume at the time of airway occlusion is changed; this effect is cancelled by bilateral high cervical vagotomy.

TABLE 2. Rate of Inspiratory Efforts During Airway Occlusion

Number of Cases	Inspired Mixture	Airway Occluded at	Before	Per Cent of Previous Respiratory Rate					
				5	10	20	30	40	50
				Seconds of Airway Occlusion					
23	Room air	End-expiration	$\bar{X}$ 20 SE 1.6	70 3.8	77 5.2	106 9.7	132 12.7	150 14.6	167 16.1
5	100% Oxygen	End-expiration	$\bar{X}$ 21 SE 1.8	79 2.6	77 1.3	105 6.9	115 12.0	136 11.9	149 13.9
10	100% Oxygen	End-expiration	$\bar{X}$ 25 SE 2.2	22 4.5	24 5.4	37 7.7	43 8.5	47 8.3	54 9.7
9	100% Oxygen	Lung volume decreased 100–400 sec.	$\bar{X}$ 24 SE 1.5	112 14.1	118 14.6	131 13.5	144 15.9	143 12.4	154 12.5
5	5% CO_2 95% O_2	End-expiration	$\bar{X}$ 31 SE 3.1	71 7.9	71 8.9	86 10.4	88 9.2	96 9.6	103 8.9
3	10% CO_2 90% O_2	End-expiration	$\bar{X}$ 40 SE 7.6	81 14.7	85 15.8	82 15.6	85 15.8	85 13.6	
4	20% CO_2 80% O_2	End-expiration	$\bar{X}$ 48 SE 6.3	76 10.6	75 11.0	78 12.8	78 12.8		
			After Vagotomy						
5	100% Oxygen	End-expiration	$\bar{X}$ 12 SE 3.3	103 3.44	103 3.44	99 5.54	104 2.7	106 4.8	111 4.7
3	100% Oxygen	End inspiration	$\bar{X}$ 11 SE 2.3	100 0	100 0	100 0	102 2.4	115 9.6	115 9.6
3	5% CO_2 95% O_2	End-expiration	$\bar{X}$ 20 SE 5.0	85 9.6	80 11.6	80 11.6	69 5.8	71 4.3	73 3.8
3	10% CO_2 90% O_2	End-expiration	$\bar{X}$ 19 SE 7.5	93 6.6	96 4.5	100 7.5	100 7.5	96 4.5	

the individual variation in ventilatory response is considerable, and that even small doses of a barbiturate may cause a profound change in ventilation.

The results and discussions of the experiments aiming to elucidate the various factors influencing the inspiratory force measurement and its practical application will be presented separately.

Changes in Inspired Concentrations of Carbon Dioxide and Oxygen. The influence of varying carbon dioxide and oxygen concentration in inspired air is summarized in tables 1 and 2; in figure 3 the effect on inspiratory force is shown and in figure 4 the effect on rate of inspiratory efforts. From these experiments it would appear that the gradual rise in carbon dioxide tension during the 50 seconds of airway occlusion may be largely responsible for the magnitude of the inspiratory force. Increasing concentrations of carbon dioxide in inspired air caused a plateau of maximal inspiratory efforts to be reached earlier during the airway occlusion; this is illustrated in figure 5. In one experiment, where passive hyperventilation with 100 per

TABLE 3. Inspiratory Force as Index of Reserve of Ventilatory Effort

	Number of Cases	Inspiratory Force (mm. Hg Negative Pressure)		Contractile Force of Leg Muscle		Blood Gases at Lowest Inspiratory Force	
		Before Infusion or Inhalation	Percentage of Before	Before (Per Cent)	Lowest Percentage of Before	*p*H	$Paco_2$
d-Tubocurarine infusion	4	$\bar{X}$ 50 SE 8.45	31 4.6	100	36 9.5	$\bar{X}$ 7.41 Range: 7.37–7.47	37.8 31.0–41.5
Thiopental infusion	5	$\bar{X}$ 46 SE 4.7	41 7.7	100	99 2.35	$\bar{X}$ 7.73 Range: 7.36–7.39	40.5 38–43
Ethyl ether inhalation	4	$\bar{X}$ 52 SE 4.6	34 2.9	100	81 9.7	$\bar{X}$ 7.39 Range: 7.34–7.44	40.3 39–42
Halothane inhalation	2	Inspiratory force was decreased considerably, but *no* decrease occurred without simultaneous respiratory acidosis.					
Morphine	3	*No* decrease in inspiratory force occurred in spite of severe respiratory acidosis.					

cent oxygen preceded airway occlusion, inspiratory efforts did not begin during the first 60 seconds and it took 120 seconds for the negative pressure to reach levels previously recorded in the same dog. During these 120 seconds of airway occlusion, the arterial *p*H fell from 7.55 to 7.31 units and carbon dioxide tension rose from 22 to 52 mm. of mercury. In the three experiments (with the dogs on 100 per cent oxygen and breathing spontaneously) in which airway occlusion was allowed to persist beyond 50 seconds, a maximal plateau of negative pressures was reached in 90, 105 and 120 seconds respectively.

Desaturation of oxygen in arterial blood may play some role in causing inspiratory efforts to be made, but it is most likely a minor role (at least under light anesthesia). Figure 3 shows that in our experiments there was no significant difference in rate of increase in inspiratory force between dogs breathing 100 per cent oxygen and those breathing room air. The tension of carbon dioxide thus seems to be responsible for the duration of airway occlusion required to allow a plateau of maximal inspiratory efforts to be reached.

The Influence of Anesthetic and Muscle Relaxant. The degree of fall in inspiratory force caused by *d*-tubocurarine, ethyl ether, thiopental, halothane and morphine is shown

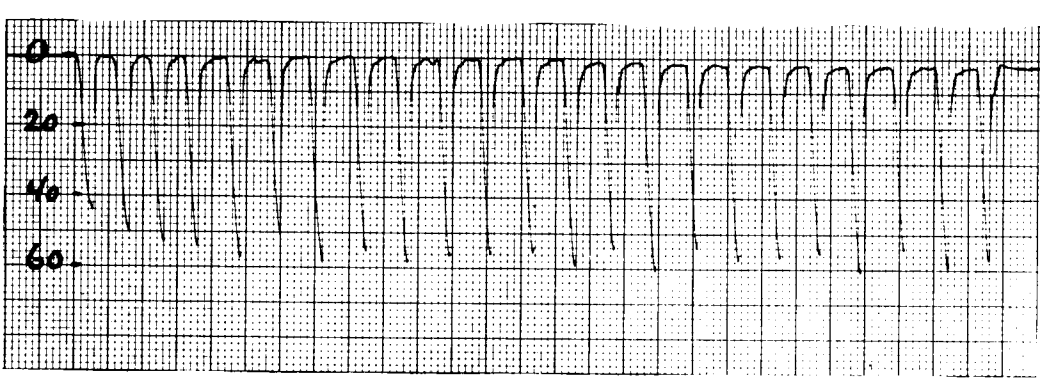

FIG. 5. Inspiratory force measurement following inhalation of 10 per cent carbon dioxide in oxygen. Note that a maximal level is reached in 10 seconds.

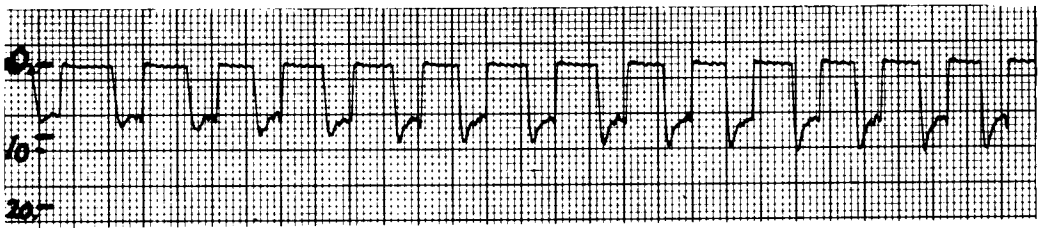

FIG. 6. This type of tracing was invariably seen during curare infusion when the respiration was predominantly diaphragmatic and the chest wall flaccid.

in table 3. The lowest values given for inspiratory force (and for contractile force of the gastrocnemius muscle) were all obtained at times when ventilation, as defined by arterial *p*H and tension of carbon dioxide, was normal. For comparison, values are given for inspiratory force before the administration of anesthetic or muscle relaxant; and mean values and the ranges of *p*H and Pa_{CO_2} are given in table 3 to illustrate what was accepted as normal.

d-Tubocurarine was effective in lowering both inspiratory force and contractile force of leg muscle about equally and to one third of baseline values. Figure 6 shows a typical tracing of inspiratory force in a partially curarized dog. Ethyl ether also lowered both forces, but while again inspiratory force decreased to one-third of the baseline value, the influence on contractile force of leg muscle was unimpressive. Thiopental caused a fall in inspiratory force comparable with changes produced by *d*-tubocurarine and ethyl ether; there was no simultaneous fall in contractile force of leg muscle with thiopental. These results compare well with the study by Cohen,[9] who followed the recovery of both minute ventilation and vital capacity in conscious human volunteers after a large dose of curare.

The effects of halothane and morphine cannot be reported in quantitative terms; with halothane it was not possible, during repeated trials in two dogs, to lower the inspiratory force without concurrent hypoventilation. It was observed in both dogs that there was a pronounced slowing in the rate of inspiratory efforts with increasing depth of halothane anesthesia (fig. 7). With morphine it was not possible in three dogs to produce any decrease in inspiratory force in spite of repeated infusions, which caused severe respiratory acidosis; and in spite of total intravenous doses ranging from 8 to 20 mg./kg. These experiments with morphine should be considered inconclusive at best.

The potential importance of the inspiratory force measurement is its possible use in patients as an index of the reserve of ventilatory effort. It must be emphasized that as a measure of reserve the inspiratory force is no more complete than the vital capacity measurement, and it should not be considered meaningful unless both elastic and nonelastic airway resistance are in a normal range. The important advantage of the inspiratory force measurement is its usefulness in the anesthetized or unconscious. The results obtained with halothane and with morphine are incon-

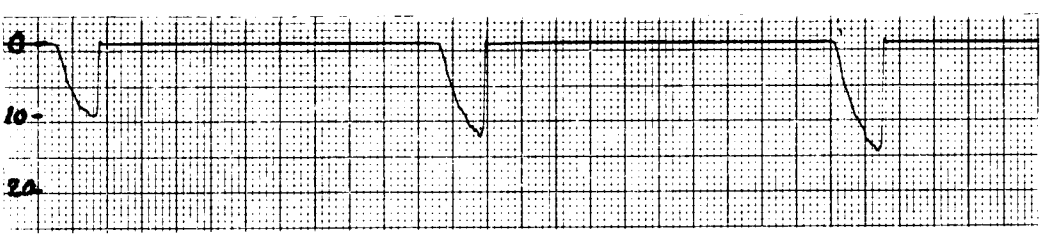

FIG. 7. In a dog breathing 2 per cent halothane, the rate of inspiratory efforts is drastically reduced. The respiratory rate before occlusion was 12 per minute.

TABLE 4. Blood Gas Changes During 50 Seconds Airway Occlusion

	Inspired Mixture	Number of Cases	Before	Seconds of Airway Occlusion: 10	20	30	40	50	Total Change	Unit
% Arterial Oxygen Saturation	Room air	4	X (−) 90 SE 0.7	83 1.0	76 0.8	67 2.5	57 5.4	58 2.8	−32 2.92	Per cent
% Arterial Oxygen Saturation	100% Oxygen	4	X 98 SE 1.2	97 1.3	96 1.3	93 1.3	92 1.0	89 2.3	−9 2.60	Per cent
Arterial *p*H	Room air or 100% oxygen	13	X 7.37 SE 0.020	7.37 0.019	7.34	7.33 0.018	7.33 0.018	7.31 0.020	−0.062 0.0190	*p*H units
Arterial concentration of Carbon Dioxide	Room air or 100% oxygen	13	X 22.5 SE 0.71	22.7 0.79	23.7 0.75	24.1 0.79	24.1 0.79	24.6 0.75	+2.1 0.68	m.Eq. l.
Arterial Tension of Carbon Dioxide	Room air or 100% oxygen	13	X 40.5 SE 2.7	40.5 2.5	45.5 2.9	47.0 3.0	48.0 3.3	50.5 3.1	+10.3 1.15	mm. Hg

clusive, but it is important that inspiratory force measurements made it possible to quantify a substantial decrease in reserve of ventilatory effort, without interference with normal minute ventilation and blood gas exchange, during the administration of a representative muscle relaxant, inhalational agent and short-acting barbiturate.

A decreased inspiratory force measurement may be caused by both central and peripheral depression of respiratory function. The fall in inspiratory force caused by *d*-tubocurarine may be assumed to be caused primarily by neuromuscular block of the respiratory muscles; thiopental, on the other hand, is most likely to exert its influence by a central depression, specifically by decreasing the sensitivity of the respiratory center to carbon dioxide; this conclusion is supported by previous findings[10] of a decreased central response to carbon dioxide with deepening anesthesia. In deep thiopental anesthesia the respiratory drive may be produced in part by hypoxia. This mechanism was not likely to be active in our experiments, with the dogs breathing 100 per cent oxygen, and with the airway occlusion limited to 50 seconds.

The Influence of Lung Volume. The effect of changes in lung volume on the rate of inspiratory efforts is shown in table 2 and figure 4. If airway occlusion is brought about at lung volumes higher than at end-expiration, the rate of inspiratory efforts is decreased; if the lung volume is lowered the rate increases. This influence of lung volume serves mostly to emphasize that, for comparable results, the airway should be occluded at end expiration, rather than at any other time during the respiratory cycle. In our fairly extensive use of the inspiratory force measurement in patients, it has not appeared to be at all critical that the airway is occluded exactly at end expiration. This impression has recently been confirmed by Widdicombe,[11] who found the Hering-Breuer deflation reflex to be weak or absent in anesthetized man, as compared with other species.

Effect of Airway Occlusion on Blood Gases. The arterial oxygen desaturation, occurring during 50 seconds of airway occlusion, was studied in four dogs. When the dogs were breathing room air prior to the period of airway occlusion, considerable desaturation occurred in 50 seconds, as shown in table 4. When 5 minutes inhalation of 100 per cent oxygen preceded the period of airway occlusion the oxygen desaturation was slight. Table 4 also shows the results of 13 experiments in which the changes in arterial *p*H and concentration and tension of carbon dioxide were followed during 50 seconds of airway occlusion.

In the evaluation of the inspiratory force measurement as a potential clinical tool its safety must be a major concern. The degree of arterial oxygen desaturation found during airway occlusion, when room air is breathed, would not be acceptable in routine clinical use. If, however, 100 per cent oxygen is administered for 5 minutes prior to airway occlusion the oxygen desaturation is negligible. Similar degrees of desaturation were found in humans during apnea by Weitzner.[12] The retention of carbon dioxide found to occur during 50 seconds of airway occlusion was

similar in magnitude to that reported during apnea by Eger.[13] Such carbon dioxide retention is probably of little importance, provided the carbon dioxide tension is in the normal range before occlusion, and provided no serious oxygen desaturation occurs.

Conclusions and Summary

No means for measuring reserve of ventilatory effort in the unconscious have been in clinical use. Experiments in 28 anesthetized dogs were designed to explore the practicality of using as an index of reserve the measurement of inspiratory force (expressed as the negative pressure developed against the completely occluded airway). The results of these experiments show that considerable falls in reserve may be produced by anesthetic or muscle relaxant drugs, without causing also immediate respiratory acidosis. These falls in reserve of ventilatory effort are uncovered by the measurement of inspiratory force, regardless of whether the limitation in reserve is caused by central depression or by neuromuscular block.

The factor most important in promoting the gradual increase in magnitude of the inspiratory effort appeared to be the retention of carbon dioxide occurring during airway occlusion. In dogs breathing room air prior to airway occlusion, degrees of arterial oxygen desaturation occurred which would be undesirable in the clinical routine use of the measurement. But if the inspiratory force measurement was preceded by inhalation of 100 per cent oxygen the arterial desaturation was negligible.

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