

## COMPLIANCE OF THE LUNGS AND THORAX IN DOGS UNDER THE INFLUENCE OF MUSCLE RELAXANTS

PETER SAFAR, M.D., AND LEONARD BACHMAN, M.D.

IT HAS been suggested by Fenn *et al.* (1) that the distensibility of the lungs and the thorax in dogs might be reduced by *d*-tubocurarine. Therefore, we studied the effects of the more commonly used neuro-muscular blocking agents on the elasticity of the lungs and the thorax in the dog.

The forces causing respiratory movements (the muscular forces during spontaneous respirations or the force of the respirator or of the anesthetist's hand during controlled respirations) are opposed constantly by (1) the elastic forces of tissues, (2) the nonelastic, viscous properties of tissues, and (3) the airway resistance to gas flow. The first depends on volume changes only; the second and the third on velocity (rate of gas flow).

For measuring only the elastic forces of the lungs and the thorax (that is, the compliance, the elastic recoil, or the distensibility), the lung volumes at different pressures must be measured when no air is leaving or entering the lungs (static condition). Compliance is defined as "volume change per unit pressure change" (l./cm. H<sub>2</sub>O).

If the lungs of an apneic subject are inflated with a constant pressure sufficiently long to record static conditions (no gas flow), and thereafter are permitted to empty into a spirometer until they reach their resting expiratory level at atmospheric pressure (no gas flow), 2 points at the pressure-volume diagram are obtained. From those 2 points, the compliance over that range of lung volume can be calculated.

### METHODS

Seventy successful experiments were performed on 34 mongrel dogs, weighing from 7 to 17 kg. (average, 11.29 kg.).

All dogs were unmedicated and were anesthetized with a single intravenous injection of pentobarbital sodium (25 to 30 mg./kg.). A cuffed tube was inserted rapidly into the trachea and connected immediately to the arrangement pictured in fig. 1. Apnea was produced and maintained by hyperventilation of the lungs with intermittent positive pressure breathing by means of a "spiropulsator," which was set for a peak inspiratory pressure of + 20 cm. H<sub>2</sub>O and a rate of 24 to 28 inflations per minute. The oxygen flow into the to-and-fro CO<sub>2</sub> absorption sys-

This paper was received from the Division of Anesthesiology of the Johns Hopkins University School of Medicine. It was read before the annual meeting of the American Society of Anesthesiologists in Boston, November 1, 1955, and accepted for publication December 27, 1955. Dr. Safar is now on the Staff of the Baltimore City Hospitals and Dr. Bachman is in the Division of Anesthesiology of the Childrens Hospital in Philadelphia.

tem of the spiropulsator was 5 liters per minute during the first 5 minutes (semiclosed system, for denitrogenation of the lungs), and thereafter reduced (closed system), aiming for a constant breathing pattern of the pneumotachogram tracing. This steady state of hyperventilation apnea was interrupted only by the compliance measurements described below, and otherwise maintained throughout the experiment until the dog either started moving or was sacrificed.

The first compliance test was performed in all experiments about 10 minutes after the beginning of mechanical hyperventilation and repeated at intervals of approximately 10 to 15 minutes. In 6 dogs, the compliance was measured from the onset of apnea caused by pentobarbital and hyperventilation until spontaneous breathing or movements began. In the other experiments, at least 2 control measure-

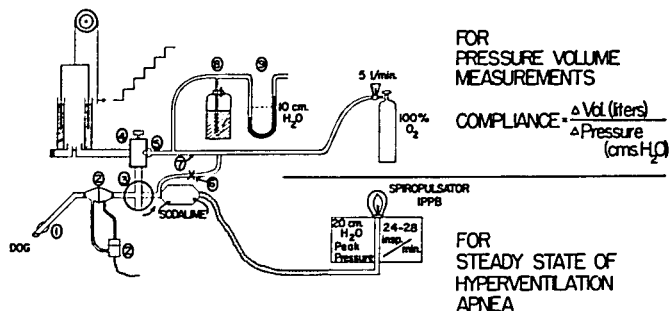


FIG. 1. Arrangement for measuring the distensibility of the lungs and the thorax under static conditions. (1) Endotracheal tube; (2) pneumotachogram for recording of gas flow; (3) stopcock for switching between spiropulsator breathing and compliance measurements; (4) stopcock for switching between inflation of the lungs from tube (5) under constant pressure, and passive expiration into the spirometer under atmospheric pressure; the clamp (x) is moved from position (6) to position (7) for interval breathing; (8) and (9) guarantee constant inflation pressure.

ments were obtained with pentobarbital alone before injection of the relaxant. The first measurement in each experiment when the animal had received only pentobarbital served as control. The drugs were injected in most experiments during spiropulsator breathing and 2 minutes after the injection a compliance test was performed, followed by others at intervals.

The following drugs were studied: succinylcholine chloride (20 mg./cc. and 50 mg./cc.), decamethonium bromide (1 mg./cc.), gallamine triethiodide (20 mg./cc.), *d*-tubocurarine chloride (3 mg./cc.), histamine (0.5 mg./cc.), Benadryl® Hydrochloride (10 mg./cc.) and combinations of the last three.

All drugs were injected intravenously at a rate of about 1 cc./3 sec. through a plastic tube and flushed with 2 to 5 cc. of saline solution.

The doses used were multiples of a "paralyzing dose" (pd). This was a rough estimate of an apneic dose obtained from the literature and personal experience in humans. One paralyzing dose (1 pd) of succinylcholine was 0.5 mg./kg.; of decamethonium 0.06 mg./kg.; of gallamine 1.5 mg./kg., and of *d*-tubocurarine 0.3 mg./kg.

Three dogs were submitted to controlled studies, under identical conditions, with pentobarbital alone and all 4 relaxants, each on a different day. The dogs served as their own controls. The sequence of the experiments was randomized. Four other dogs were studied with 2 to 3 drugs each, also under comparable conditions. The rest were subjected to only 1 or 2 experiments each.

*Measurement of the Compliance of the Lungs and the Thorax.* The technique used in this study is described in figure 1. Typical tracings are shown in figures 2 and 3.

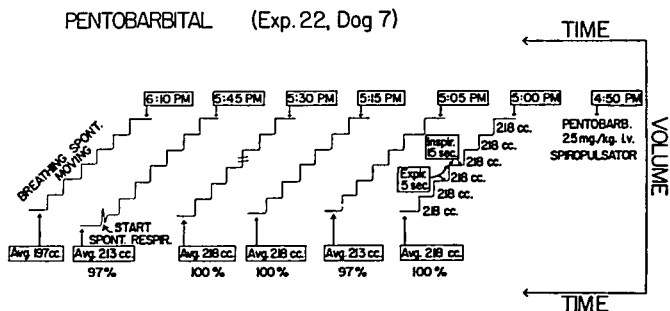


FIG. 2. Lung volumes with 10 cm. of water airway pressure during pentobarbital hyperventilation apnea, under static conditions.

The volumes of expiration were measured after inflation with one constant pressure, 10 cm.  $H_2O$  (20 cm.  $H_2O$  in the first 10 experiments) which gave only 1 point on the compliance diagram. No attempt was made to obtain complete P/V diagrams by inflating the lungs with various pressures since we wanted to keep the experiments as simple and as controlled as possible. The purpose of the authors in this study was merely to find out whether or not relaxants influence at all the distensibility of the lungs and the thorax.

During the measurements with the drugs which did not cause obvious bronchoconstriction (no flattening of the spirometer curve during expiration), there was no gas flow through the endotracheal tube 2 to 5 seconds after stopcock 4 (fig. 1) was turned to inspiration, and 1 to 2 seconds after it was turned to expiration. Therefore, inspirations of 15 seconds and expirations of 5 seconds duration during measurements

were chosen. In some experiments with *d*-tubocurarine and histamine, in which obvious bronchoconstriction could be demonstrated by the spirometer curve, inspirations and expirations of 30 and 60 seconds were used for the compliance tests in later experiments to be certain of static measurements. In these cases, the spirometer curve seemed to indicate occasionally that gas continued to leave the lungs in small amounts up to 10 to 15 seconds after the stopcock was turned, even when the pneumotachogram did not show any gas flow.

A deviation from the constant pattern of spiropulsator breathing between compliance measurements resulted in an alteration of the compliance in the subsequent measurement. Increased peak pressure

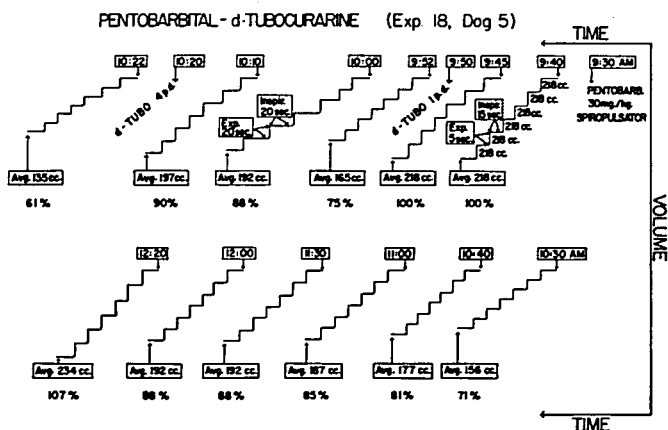


FIG. 3. Lung volumes with 10 cm. of water airway pressure during pentobarbital hyper-ventilation apnea, with *d*-tubocurarine added intravenously. (Static conditions.)

(30 to 40 cm.  $H_2O$ ) during interval breathing, even if only for a few breaths, resulted in an increase of the compliance by 7 to 20 per cent immediately thereafter (5 experiments). Lowered peak pressures (12 cm.  $H_2O$ ) or 5 minutes of apnea during interval breathing caused only a slight reduction of the compliance by 2 to 7 per cent.

Although no arterial blood samples were analyzed, we believe that hypoxia did not occur during our measurements, since the dogs were hyperoxygenated during interval breathing, spirometer and spiropulsator were filled with 100 per cent oxygen, and the dogs' tongues remained pink throughout.

In 9 experiments, we attempted to record the volumes entering and leaving the lungs by modifying our technique, in order to investigate

the question of air trapping. The spirometer (with 100 per cent oxygen, without soda lime) was connected directly to the endotracheal tube and the lungs were inflated intermittently with controlled airway pressure by manual compression of the spirometer bell.

In 15 sacrifice experiments, the arterial blood pressure was recorded. The femoral artery was dissected and cannulated with a 16-gauge needle connected via a plastic catheter to a fluid strain gauge.

In this paper we will use the term "compliance" whenever we mean "volume of expiration measured after inflation of the lungs with a constant pressure under presumably static conditions." A reduction of the volume of expiration may not indicate necessarily the total volume of the lungs inflated under a given pressure.

### RESULTS

The 6 to 8 successive respiratory volumes of each single compliance measurement were equal in all experiments except those with *d*-tubocurarine and histamine. They showed only occasional small variations, which can be explained by the manual technique of sustaining constant inflation pressure. The largest change was  $\pm 5$  per cent.

1. *Pentobarbital Control* (table 1) (fig. 2). The compliances of the lungs and the thorax in the 6 dogs studied with pentobarbital-hyperventilation apnea alone, as long as the animals remain apneic, ranged from 105 to 97 per cent of the control value. With the beginning of spontaneous respirations or moving, the compliance decreased. In 1 dog, in spite of moving during apnea, the compliance remained unchanged. Apnea with pentobarbital alone lasted from 30 to 80 min. (average 57 minutes). The first compliance tested after the initial injection of pentobarbital in the same dog on different days varied within a range of  $\pm 11$  per cent.

2. *Succinylcholine* (table 1). Six dogs received 1 pd and 4 pd of succinylcholine. None of these injections caused a change of the compliance of the lungs and the thorax greater than 10 per cent. The range was from 90 to 104 per cent of the control value.

Four other dogs received total doses of succinylcholine ranging from 100 pd to 600 pd in intermittent injections of up to 200 pd each. The greatest reduction of compliance was 91 per cent of the control value, except for 1 instance, when 200 pd was injected rapidly with 40 cc. of physiological saline solution. This caused a transient decrease of the compliance to 84 per cent of the control value.

In dog 7 (table 1), whose compliance was reduced to half because of atelectatic lung areas (complication), the compliance increased to 127 per cent of the control value after the injection of 316 pd of succinylcholine.

3. *Decamethonium* (table 1). The ranges of the compliances in the 4 dogs which received 1 pd and 4 pd was from 103 to 92 per cent of the control value.

TABLE I  
 MAXIMAL CHANGES OF EXPIRATORY VOLUMES ("COMPLIANCE" OF LUNGS AND THORAX)  
 DURING APNEA. (CONTROL: PENTOBARBITAL-HYPERVENTILATION  
 APNEA AT THE START OF EACH EXPERIMENT)

Dog	Pentobarbital Only—% of Control Expir. Volume	Pentobarbital & Tubocurarine pd	% of Control Exp. Vol.	Pentobarbital Succinylcholine pd	% of Control Exp. Vol.	Pentobarbital Decamethonium pd	% of Control Exp. Vol.	Pentobarbital Gallamine pd	% of Control Exp. Vol.
3	103	1	94	1	98	1	97	1	95
		+4	86	+4	103	+4	96	+4	93
6	97	1	92	1	96	1	96	1	95
		+4	72 B	+4	93	+4	92	+4	91
7	97	4	62 B	4	90	4		4	95
		4	56 B	316	127°	+4	93		
5	98	1	75	1	97				
		+4	61 B	+4	95				
2	105			1	100	1	103		
				+4	100	+4	103		
4	98			1	104				
				+4	99				
10				100	91				
11				40	96				
				+120	104				
				+150	100				
				+150	100				
				All over 40 min.					
20				600	97				
				All over 60 min.					
21				200	84				
				(40 cc. of saline)	92				
				+50	90				
29						32	100		
						(over 35 min.)			
						+96	91		
						(80 cc. of saline)			
27								1	100
								+4	100
								+4	100
								+24	100
								+96	
								(150 cc. of saline)	
								All over 75 min.	94

TABLE 1 (Continued)

Dog	Pentobarbital Only—% of Control Expir. Volume	Pentobarbital <i>d</i> -Tubocurarine pd	% of Control Exp. Vol.
8		4	66 (A)
16		4	50 B (A)
18		4 closed) after opened by high pressure	0 (lungs 71 B
15		4 +8	66 B (A) 77 (55) (A)
26		2 +2 +2	61 B 93 83 97 83
25		2 +4 +8	72 B 96 (A) 64 (A) 80 (A) 64 (A)
28		2 4	78 69
31		1	86
33		1	82
34		1	78
36		1	62 B
35		1	94
30		1	90
14		4 4 +8 +16	100 (A) 100 95 90
17		8 +16	86 (A) 100 (A)
24		4 +8 +Histam. 0.05 mg./kg. 100 +Histam. 0.1 mg./kg. 37 B (A) 100	100 (A) 100 (A) 39 B (A) 100 37 B (A) 100

pd: "paralyzing dose"  
 1 pd of *d*-tubocurarine: 0.3 mg./kg.  
 1 pd of succinylcholine: 0.5 mg./kg.  
 1 pd of decamethonium: 0.06 mg./kg.  
 1 pd of gallamine: 1.5 mg./kg.

Each box represents 1 experiment.

B—pronounced flattening of expiratory curve as evidence of airway obstruction (bronchoconstriction).

(A)—"Airtrapping" technique (see discussion).

\* Sick dog, with lungs partially atelectatic (autopsy).

One other dog received 32 pd of decamethonium without any change of compliance. A subsequent rapid injection of 96 pd of decamethonium with 80 cc. of physiological saline solution caused a brief reduction of the compliance to 91 per cent.

4. *Gallamine* (table 1). In 3 dogs, which received doses of gallamine from 1 pd to 6 pd and in 1 dog which received a total of 129 pd in intermittent injections, the compliances ranged from 91 to 100 per cent of the control value.

5. *d-Tubocurarine* (table 1) (fig. 3). Twenty dogs were studied with *d-tubocurarine* with single doses ranging from 1 pd to 16 pd (total doses from 1 pd to 28 pd). In 16 of these 20 dogs, the compliance fell to between 86 and 50 per cent of the control value (average 69 per cent) within two minutes after injection of *d-tubocurarine*. Four dogs were refractory (no change or less than 10 per cent reduction) with total doses of 1 pd, 1 pd, 28 pd, and 12 pd. In dog 24, which did not demonstrate any reduction in compliance with 12 pd of *d-tubocurarine*, a subsequent injection of histamine promptly caused such a reaction (table 1).

Five of the 9 dogs which received 1 pd of *d-tubocurarine* showed reductions to between 86 and 62 per cent. The 4 others showed reductions of 10 per cent or less.

All 4 dogs which were studied with various agents under exactly comparable experimental conditions on different days, whose compliance did not change more than -10 per cent + 3 per cent with succinylcholine, decamethonium, and gallamine in all instances, showed a significant stiffening of the lungs and the thorax with *d-tubocurarine* (reduction of the compliance to between 56 and 86 per cent of the control) (table 1) (fig. 4).

In 9 of the 16 dogs in which *d-tubocurarine* was followed by a reduction of the expiratory volume, an obvious flattening of the spirometer curve during expiration occurred (bronchoconstriction). In 1 animal, the lungs closed completely after 4 pd of *d-tubocurarine* and a pressure of 40 cm. of H<sub>2</sub>O was necessary to reopen them. Thereafter, the lungs remained open, but the expiratory volume measured under static conditions was 71 per cent of the control.

Dose to dose refractoriness with repeated injections of *d-tubocurarine* occurred in dogs No. 25 and No. 26 (table 1).

The reduction of the compliance after *d-tubocurarine* lasted longer than after histamine.

In 3 of 5 *d-tubocurarine* experiments and 3 of 4 histamine experiments with the airtrapping technique, there was some evidence that less gas had left the lungs than entered them with the first few inspirations after injection of the drug.

Once during experiments with the pleural cavities open, the lungs closed completely 90 seconds after the injection of 4 pd of *d-tubocurarine*, and 40 cm. of H<sub>2</sub>O pressure was necessary to reopen them.



At the time of occlusion, large lung areas were atelectatic. After re-opening of the lungs, a static measurement still revealed an expiratory volume of 50 per cent of the control value, without macroscopic atelectasis.

6. *Histamine and Benadryl.* Eight experiments were performed on 4 dogs. All injections of histamine reduced the compliance sig-

TABLE 2  
BENADRYL AND *d*-TUBOCURARINE

Dog No.	Experiment	Drug	Expiratory Volume % of Control
6	16	Pentobarbital control	100
		<i>d</i> -Tubocurarine 4 pd	72
7	36	Pentobarbital control	100
		Benadryl 4 mg./kg.	100
		<i>d</i> -Tubocurarine 4 pd	92
7	23	Pentobarbital control	100
		<i>d</i> -Tubocurarine 4 pd	62
7	32	Pentobarbital control	100
		<i>d</i> -Tubocurarine 4 pd	56
7	35	Pentobarbital control	100
		Benadryl 4 mg./kg.	100
		<i>d</i> -Tubocurarine 4 X pd	100
25	64	Pentobarbital control	100
		<i>d</i> -Tubocurarine 2 pd	72
		plus <i>d</i> -Tubocurarine 4 pd	64
		plus <i>d</i> -Tubocurarine 8 pd	64
25	61	Pentobarbital control	100
		Benadryl 6 mg./kg.	100
		<i>d</i> -Tubocurarine 2 pd	91
26	65	Pentobarbital control	100
		<i>d</i> -Tubocurarine 2 pd	61
		plus <i>d</i> -Tubocurarine 2 pd	83
		plus <i>d</i> -Tubocurarine 10 pd	83
26	62	Pentobarbital control	100
		Benadryl 6 mg./kg.	100
		<i>d</i> -Tubocurarine 2 pd	92

*d*-Tubocurarine 1 pd (paralyzing dose): 0.3 mg./kg.

nificantly: 0.01 mg./kg. of histamine reduced the expiratory volume to 85 per cent of the control value (1 experiment); 0.05 mg./kg. to 39 per cent (1 experiment); 0.1 mg./kg. to between 22 and 80 per cent (7 experiments), and 0.2 mg./kg. to 37 per cent (1 experiment). These reductions were transient and the compliances were back to normal 10 minutes after the injection. There was evidence of bronchospasm in

all instances. This phenomenon could be reproduced in the same dog without refractoriness.

In 1 dog, the lungs occluded completely 90 sec. after the injection of 0.1 mg./kg. of histamine. The lungs were reopened by prolonging the inspiration time to 30 seconds and by raising the inflation pressure. This could be reproduced in the same dog on another day. The lungs remained open thereafter but 12 minutes after the injection of histamine the expiratory volume was still only 38 per cent of the control value, under presumably static conditions.

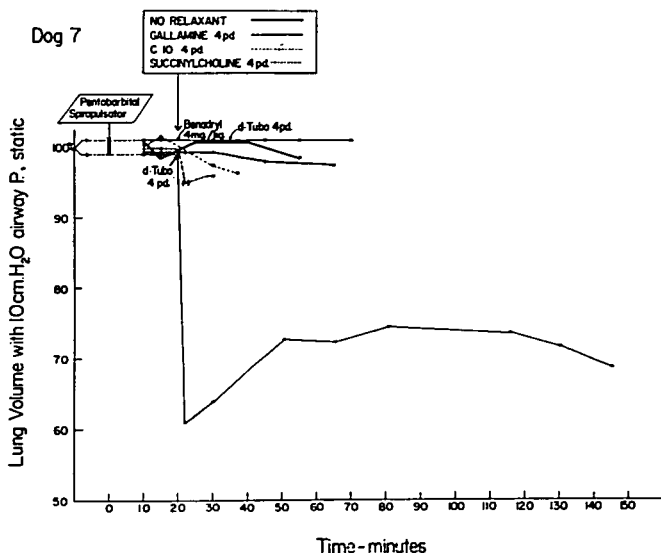


FIG. 4. Change of the compliance of the lungs and the thorax in 1 dog during 5 experiments: pentobarbital hyperventilation apnea alone; gallamine; decamethonium; succinylcholine; *d*-tubocurarine; Benadryl followed by *d*-tubocurarine.

Benadryl in doses of 1 to 5 mg./kg. did not change the compliance significantly. Histamine 0.1 mg./kg., when injected 10 to 15 min. after Benadryl, caused a reduction of the expiratory volume to an average of 84 per cent of its control value, as compared with a reduction to an average of 46 per cent after histamine without Benadryl (3 dogs).

7. *Benadryl and d-Tubocurarine* (table 2) (fig. 4). Four dogs were studied with *d*-tubocurarine and also on a different day with Benadryl,

followed by *d*-tubocurarine 15 min. later. The sequence of the experiments was randomized.

*d*-Tubocurarine caused in all 4 dogs a significant reduction of the compliance, while Benadryl protected against this phenomenon, although not entirely (table 2).

8. *Circulatory Changes* (table 3). The results obtained from the blood pressure measurements in 5 out of 8 dogs with *d*-tubocurarine caused hypotension to approximately 15 mm. of mercury mean arterial blood pressure within 90 seconds after injection (table 3). In one of these dogs, cardiac arrest occurred. In the others, the blood pressure did not return to control levels before 6 to 30 minutes. In 1 dog, the

TABLE 3  
SUMMARY OF OBSERVATIONS ON INTRA-ARTERIAL PRESSURES

Exp.	Drug	Paralyzing Dose	Circulatory Changes	C: Compliance B: Bronchoconat.
34	<i>d</i> -Tubocurarine	4	Moderate hypotension, tachycardia	C ↓
55	<i>d</i> -Tubocurarine	4	Severe hypotension, cardiac arrest	C ↓ B lungs shut
64	<i>d</i> -Tubocurarine	2, 4	Severe hypotension, tachycardia	C ↓ B
58	<i>d</i> -Tubocurarine	4	Severe hypotension, tachycardia	C ↓ B
43	<i>d</i> -Tubocurarine	4	Severe hypotension, bradycardia	C ↓ B
65	<i>d</i> -Tubocurarine	2, 2	Severe hypotension, bradycardia	C ↓ B
		2, 8	Less with repeated injections	
60	<i>d</i> -Tubocurarine	4, 8	No changes	—
	Histamine		Severe hypotension	C ↓ B
59	<i>d</i> -Tubocurarine	4, 2	No major changes	—
		2, 40		
39	Succinylch.	316	No significant changes	—
41	Succinylch.	40-150 tot. 470	Minimal hypertension and tachycardia during injection, followed by minimal hypotension	—
42	Succinylch.	100	Minimal hypertension and tachycardia during injection	—
56	Succinylch.	20-200 tot. 600	Minimal hypotension and tachycardia during injection	—
57	Succinylch.	250	Moderate hypotension	—
63	Gallamine	tot. 129	No significant changes	—
67	Decameth.	tot. 128	No significant changes	—

mean arterial blood pressure dropped from 200 to 95 mm. of mercury. In all of these instances of hypotension, side effects on the lungs also could be demonstrated (table 3).

The injections of very large doses of succinylcholine, decamethonium, and gallamine in 7 dogs caused no major changes of blood pressure and pulse rate except for 1 dog which showed a transient blood pressure drop from 115 to 40 mm. Hg mean arterial blood pressure after the rapid injection of 200 pd of succinylcholine.

#### DISCUSSION

Succinylcholine, decamethonium, and gallamine do not seem to alter the compliance of the lungs and the thorax significantly. The

compliance with *d*-tubocurarine and histamine was reduced. This decrease might be due to (1) stiffening of the tissues of lungs or chest wall, (2) airway obstruction (bronchoconstriction), or (3) increase of the resting volume of the lungs (gas trapping).

The question of whether this reduction of the compliance is due to changes in the chest wall or the lungs was not resolved completely. Presumptive evidence for the assumption that the lungs are the site of this decrease in compliance is that 3 other neuromuscular blocking agents did not cause such changes.

Airway obstruction (bronchoconstriction) being a cause of this decrease of the compliance was ruled out by the fact that no gas flow was occurring at the end of the measurements. There was evidence in the spirometer curve that bronchoconstriction did occur in the experiments with *d*-tubocurarine and histamine, as has been shown by others (2, 3).

There was some evidence of an increase in resting lung volume (gas trapping) with *d*-tubocurarine and histamine, but the amount of gas trapped cannot account for the total reduction of expiratory volume.

If the site of the reduced compliance is in the lungs themselves, what might be its cause? One may speculate on the following possibilities: (1) pulmonary edema, (2) increased pulmonary blood volume, (3) increased tone of smooth muscle fibers in pulmonary vessels.

It has been shown by others that rapid intravenous injection of large amounts of physiologic saline solution can cause a reduction of the lung and thorax compliance (4).

Spontaneous refractoriness to the "histaminic" effect of *d*-tubocurarine occurred in our study in the same incidence (20 per cent) as in Landmesser's measurements of bronchoconstriction (2). Landmesser showed that repeated doses of *d*-tubocurarine in the same animal had progressively less bronchoconstrictor or hypotensive effect, and a subsequent larger dose had a greater effect. The same phenomenon was observed in our compliance studies.

#### CLINICAL SIGNIFICANCE

The clinical significance of the results of this study is small because of the great species variation in the pharmacology of muscle relaxants. The next step would be to repeat these studies in man and follow it with detailed circulatory measurements under controlled conditions. Although bronchoconstriction and hypotension have been demonstrated clearly with *d*-tubocurarine also in man, the number of spontaneously refractory subjects is much greater in men than in dogs (2, 3). If comparative studies of the lung compliance and the circulation in men with all presently used muscle relaxants should reveal results similar to those in dogs, the clinical use of *d*-tubocurarine hardly seems justified.

## SUMMARY

1. The distensibility of the lungs and the thorax of the dog under pentobarbital anesthesia did not change significantly as long as the animal remained apneic from hyperventilation under constant conditions.

2. There was no significant change of the distensibility after succinylcholine, decamethonium, or gallamine had been added in different doses up to many times "paralyzing doses."

3. After the injection of *d*-tubocurarine, the distensibility was reduced to 50 to 86 per cent of the control value in 80 per cent of the dogs. This effect could be related to the histamine-releasing properties of curare, since it was reproducible by the injection of histamine. Previous injection of Benadryl blocked partially the effect of *d*-tubocurarine and histamine on the distensibility of the lungs and the chest. The possible explanations for the observed reduction of the compliance were discussed.

## ACKNOWLEDGMENT

The authors wish to thank Drs. D. Proctor, A. Otis, and R. Shepard for their suggestions and advice.

## REFERENCES

1. Fenn, W. O., Otis, A. B., and Suskind, M.: Accumulation of Carbon Dioxide in Apneic Dogs During Intermittent Oxygen Insufflation, *Am. J. Phys. Med.* **33**: 299 (Oct.) 1954.
2. Landmesser, C. M.: Study of Bronchoconstrictor and Hypotensive Actions of Curarizing Drugs, *Anesthesiology* **8**: 506 (Sept.) 1947.
3. Landmesser, C. M., Converse, J. P., and Harmel, M. H.: Quantitative Evaluation of Bronchoconstrictor Action of Curare in Anesthetized Patient; Preliminary Report, *Anesthesiology* **13**: 275 (May) 1952.
4. Comroe, J. H., Jr., Nisell, O. I., and Nims, R. G.: Compliance and Resistance to Breathing, *J. Appl. Physiol.* **7**: 225 (Sept.) 1954.