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Lung volumes, mechanics, and single-breath diffusing capacity in anesthetized cats

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WATANABE, SUETARO, AND ROBERT FRANK. *Lung volumes, mechanics, and single-breath diffusing capacity in anesthetized cats.* J. Appl. Physiol. 38(6): 1148–1152. 1975.—We measured lung weight, lung volumes, pulmonary mechanics, and carbon monoxide transfer (D_{LCO}, single-breath method) in healthy cats (3.3 ± 0.4 kg) that were anesthetized, paralyzed, and mechanically ventilated through a tracheal cannula. Compared with Stahl's predicted values which were based on regression analyses of data collected from several species, our cats had larger and more compliant lungs in relation to body weight, higher D_{LCO} per unit body weight, and similar D_{LCO}/TLC (size independent constant). Compared with Robinson et al.'s values derived entirely from studies on dogs, our cats had significantly smaller lung volumes and D_{LCO} per unit body weight, D_{LCO}/TLC and similar ratios of C_L/FRC. Several factors appear to contribute to the functional variations among mammalian species: differences in the relation of lung to body weight, differences in the relation of chest wall compliance to lung compliance, and differences in the fundamental structure and design of the respiratory systems. Differences in methodology are acknowledged to be an additional factor.

cat pulmonary function; lung weight; dynamic compliance; pulmonary flow resistance; quasi-static pressure-volume curve; CO diffusing capacity

THE ACCOMPANYING CONTROL DATA were collected during the control period of experiments designed to measure the functional effects of ozone on the lungs of cats (21). They include values for lung weight, lung volumes, pulmonary mechanics, and carbon monoxide transfer (D_{LCO}, single-breath method).

Stahl (17) analyzed a number of respiratory variables in mammals in relation to body weight. Robinson et al. (16) developed prediction formula for similar variables from studies on dogs of varying weights. Where possible, we have included for comparison their scalings in our tabulated results.

METHODS

We studied 37 cats of both sexes weighing 2.4–3.9 kg that were anesthetized with intraperitoneal injection of chloralose (50 mg/kg) and urethane (500 mg/kg). The level of anesthesia was assessed by continuous monitoring of the pulse rate and femoral artery pressure and by periodic examination of pupillary size. After an artificial pneumothorax (50 ml) was created using a blunt needle that was intended to prevent injury to the lung, a rubber mushroom catheter (Bardex 10, Bard Hospital Division, C. R. Bard Inc., Murray Hill, N.J.) was inserted in the right anteriomedical fourth or fifth intercostal space for measuring intrapleural pressure. Approximately 10 ml of air in the intrapleural space were maintained throughout the experiment to prevent occlusion of catheter opening by the lung tissue. The animals were paralyzed with intravenous gallamine hydrochloride (initial dose: 30 mg; maintenance dose: 10–15 mg/h) and were ventilated through a steel tracheal cannula with a respiratory pump (Harvard model 661). Tidal volume was adjusted on the basis of body weight and breathing frequency (25 breaths/min) according to the nomogram of Kleinman and Radford. The range of V_T was 27–38 ml. An infusion of 5% glucose in saline was maintained by continuous infusion pump (Harvard Series 940) at a rate of 0.05 ml/min throughout the experiments.

Deep breaths (volume of 3 × V_T) were given every 15 min to prevent atelectasis.

The experimental preparation is outlined in Fig. 1. The animals were placed supine inside a Lucite plexiglass volume displacement plethysmograph.

Volume was measured with a Krogh spirometer fitted with a linear transducer. Transpulmonary, airway, and airway-plethysmographic pressures were measured with differential inductance transducers. Flow was obtained by electrical differentiation of the volume signal. Differentiated flow was used to compute pulmonary flow resistance (R_L). All signals were amplified and recorded on a direct-writing thermal oscillograph. A cathoderay "memory" oscilloscope was used for continuous monitoring of the pressure-volume loops.

Arterial blood pressure was monitored with a differential inductance transducer.

The frequency response of the plethysmograph-spirometer system was tested with the ventilatory pump set at a fixed tidal volume operating at frequencies from 10 to 60 cycles/min. Over this range the response of the system in terms of changes in the recorded stroke volume did not exceed more than 2%.

The R_L was calculated as an average value for inspiration and expiration at isovolumes in the range of midtidal breathing as follows

$$R_L = \frac{[Pao - Ppl\ (insp)] - [Pao - Ppl\ (exp)],\ cmH_2O}{\dot{V}\ (insp) + \dot{V}\ (exp),\ l/s}$$

where Pao = pressure at the tracheal cannula; Ppl = pleural pressure on inspiration (insp) or expiration (exp); $\dot{V}$ = instantaneous flow during inspiration (insp) and expiration (exp) at the isovolumes.

Dynamic compliance (Cdyn) was calculated as the ratio of V_T to the changes in transpulmonary pressure at the instant of zero flow (11)

$$Cdyn = \frac{V_T,\ ml}{Pao - Ppl,\ cmH_2O}$$

The measurements were made at frequencies of 10, 25, and 50 breaths/min. The resistance of the expiratory tubing was adjusted to minimize the shift in expiratory lung volume within this range of breathing frequency.

Cdyn and R_L were obtained 3 min after the application of two deep inspirations and were based on averages of three consecutive breaths. With this standardized procedure, there was no significant decrease in Cdyn up to a period of 6 h.

The functional residual capacity (FRC), defined here as the lung volume of the unconscious paralyzed cat in the passive expiratory supine position was measured with the gas compression method of Laver and associates (7), originally described by Nisell and DuBois (13). The plethysmograph was first converted to an airtight pressure chamber by disconnecting the Krogh spirometer. The animal was disconnected from the pump at end expiration and the connecting tube between the tracheal cannula and the pump was occluded. Airway pressure and the difference between plethysmographic and airway pressure (Pplethysmograph-Pairway) were recorded simultaneously. A bolus of 3–4 ml of air was injected into the airways through the tracheal cannula and the chamber was rapidly pressurized by compressed air until Pplethysmograph-Pairway pressure was zero. The lung volume at passive end expiration (FRC_{PV}) was calculated according to Boyle's law as follows

$$P_1 V_1 = P_2 V_2$$

Let V_L = the volume of air in the lung at passive expiration; ΔV = the volume of air injected into the airway; ΔP = increase in Pairway above atmospheric pressure required to compress the volume ($V_L + \Delta V_L$) back to V_L (Pplethysmograph-Pairway = 0); P_B = atmospheric pressure. Then

$$(P_B - 47) \times (V_L + \Delta V) = [(P_B - 47) + \Delta P] \times V_L$$

Solving for V_L

$$V_{L,\,BTPS}\ (ml) = \frac{\Delta V_{BTPS}}{\Delta P} \times (P_B - 47)$$

Corrections were made for the volume of the tracheal cannula and external tubing. The procedure took less than 5 s. The value used was based on an average of five consecutive measurements. Each measurement was made 1 min after application of two deep inspirations.

The FRC was also measured by the single-breath neon gas dilution method as a byproduct of the single-breath diffusing capacity determinations (to be described).

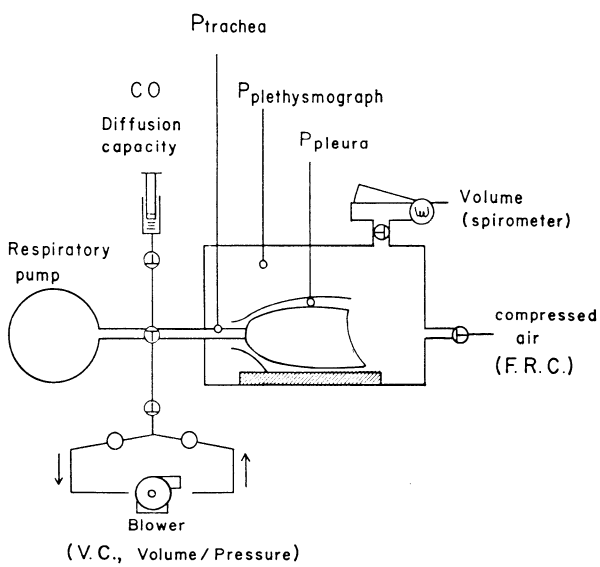

FIG. 1. Schema of method for measuring pulmonary mechanics, lung volumes, and diffusing capacity. See text for details.

TABLE 1. *Body and lung weights* ($n = 9$)

	BW, kg	TLW, g	(RL/TLW) × 100, %	Wet/Dry Wt Ratio	
				RL	LL
Mean	3.3	20.68	57.3	4.60	4.70
± SD	±0.4	±3.75	±2.4	±0.42	±0.43
Range	2.4–3.8	15.32–25.24	55.7–58.6	3.93–5.24	4.10–5.49
Predicted*					
Mean		36.8			
Range		18.4–55.2			

BW = body wt; TLW = total lung wt; RL = right lung; LL = left lung. * From Stahl's regression formula (17).

A slow vital capacity (VC) was measured together with changes in transpulmonary pressure. The VC was defined as the volume of gas emitted from the lungs as the distending pressure was decreased from a peak of 20 cmH_2O to a subatomspheric level of -5 to -7 cmH_2O: at the latter pressure, no additional gas could be suctioned from the lungs. The peak distending pressure was maintained for 7–8 s before deflation was begun. The volume changes were produced with a commercial vacuum cleaner controlled by a voltage regulator and operated through electrically driven solenoid valves (Fig. 1). The sequence of slow volume changes was as follows

FRC → total lung capacity (TLC) → residual volume (RV) → TLC → FRC

The entire procedure required approximately 30–40 s. Before each measurement the animal was hyperventilated at 50 breaths/min for 15 s. The measurement was repeated 3 min after the first measurement.

The slow volume-pressure curves were constructed by plotting volumes as percentage of VC on the ordinate and the pressure on the abscissa. For this purpose only a part of the volume sequence (TLC → RV → TLC) was used.

Carbon monoxide diffusing capacity (D_{LCO}) was measured 1 minute after application of two deep inspirations with the single-breath method (14) as follows: 100 ml of a gas mixture containing 0.32% CO, 0.625% neon (Ne), 21.0% oxygen (O_2), and the balance nitrogen (N_2) were delivered from a syringe into the lungs through the tracheal cannula at FRC. After 10 s, 15 ml were withdrawn and discarded (dead space volume), and the next 110 ml were quickly withdrawn for analysis. Neon was used to estimate the lung volume in communication with the trachea. The concentrations of CO and Ne were measured with a gas chromatograph. D_{LCO} was calculated as follows

$$D_{LCO} = \frac{V_A\ (STPD) \times 60}{(P_B - 47) \times t,\ s} \times \ln \frac{F_{ACO}}{F_{ECO}},\ ml/min\ per\ mmHg$$

$$F_{ACO} = F_{ICO} \times \frac{F_{ENe}}{F_{INe}}$$

$$FRC_{Ne(ATPD)} = 100 \times \left[\frac{F_{INe}}{F_{ENe}} - 1\right] - V\ tracheal\ cannula$$

$$V_{A(STPD)} = (FRC_{Ne+100}) \times \text{factor for ATPD to STPD, ml}$$

where V_A = alveolar volume; F_{ACO} = concentration of CO in the alveoli after injection; F_{ECO} = CO concentration in the expiratory sample; F_{ICO} = CO concentration in injected test gas; F_{ENe} = Ne concentration in the expired gas; F_{INe} = Ne concentration in the inspired gas. The volume of the tracheal cannula was 6 ml.

TABLE 2. *Lung volumes*

	VC		IC		FRC				TLC		RV	
					Compression		Dilution					
	ml	ml/kg	ml	ml/kg	method ml	(P/V) ml/kg	method ml	(Ne) ml/kg	(FRC_{Ne} + IC) ml	ml/kg	ml	ml/kg
Mean	240.4	74.3	203.4	62.8	93.7	29.4	83.7	26.1	287.3	87.9	47.2	14.5
±SD	±33.8	±11.5	±23.7	±8.1	±16.1	±5.5	±14.6	±4.9	±34.6	±10.3	±12.3	±3.9
Range	180.0–322.0	54.8–103.1	157.5–278.0	47.7–81.7	69.1–134.5	20.9–44.1	63.7–127.8	20.8–38.7	251.7–394.8	70.4–106.7	20.3–72.8	7.0–20.2
BW, kg	3.3 ± 0.3		3.3 ± 0.3		3.2 ± 0.3		3.2 ± 0.3		3.3 ± 0.4		3.3 ± 0.4	
No. of animals	22		22		25		22		19		19	
Predicted												
Mean	191.5*	56.7*					90.7* (154.1)‡	24.1* (17.8)†	188.5* (374.5)‡			
Range	155.0–228.0*						50.0–132.0*		113.0–263.0*			

IC = inspiratory capacity; Ne = neon used in single-breath dilution method; RV = residual volume. A pneumothorax of about 10 ml was maintained to ensure patency of the mushroom catheter used to measure pleural pressure. * From Stahl's regression formulas and Table 3 (17). † Crosfill and Widdicombe (3), mean of 4 cats weighing 2.3–5.7 kg BW. ‡ Robinson et al. (16), calculated from regression formulas in dogs.

TABLE 3. *Pulmonary mechanics (n = 28)*

	BW, kg	C_L, ml/cmH_2O	C_L/FRC_{PV} + 1/2 V_T, ml/cmH_2O/ml	C_L/BW, kg	R_L, cmH_2O/l per s	Cond, l/s per cmH_2O	Cond/FRC_{PV}, (l/s)/(cmH_2O/l)	Cond/BW, kg
Mean	3.1	16.3	0.152	5.2	7.6	0.140	1.511	0.045
± SD	±0.3	±2.6	±0.020	±0.7	±1.7	±0.035	±0.396	±0.011
Range	2.4–3.8	10.7–21.7	0.105–0.202	3.9–6.4	4.5–11.3	0.089–0.222	0.723–2.410	0.027–0.074
Predicted								
Mean		7.1* (14.4)‡	(0.140)‡	(3.6)†	11.0*			(0.024)†
Range		4.8–9.4*			6.8–13.1*			

C_L was measured at a frequency of 25 breaths/min; Cond = pulmonary conductance = $1/R_L$. * From Stahl's regression formulas (17). † Crosfill and Widdicombe (3). ‡ Robinson et al. (16).

Values of D_{LCO} were based on duplicate analyses of the gas sample.

At least two complete sets of functional measurements were made during the control period that lasted 60–90 min.

Nine pairs of lungs from cats that had not been exposed to ozone were excised and weighed wet (main stem bronchi included). The lungs were inflated and dried with compressed air for 24 h, then placed in an incubator another 24 h at 40°C for further drying. The ratio of wet/dry lung weight was obtained for each lung.

RESULTS AND COMMENTS

The data were summarized in Tables 1–5 and Fig. 2. They are shown as mean and SD which were calculated using average value from each animal.

Lung weight and wet/dry weight ratio (W/D). The mean total lung weight was considerably less than that predicted by Stahl's power law formula (Table 1), but close to the value reported by Crosfill and Widdicombe (3). The average difference in W/D ratio between the left and right lungs was not significant. Earlier, Frank et al. (5) reported values of 4.98 (right) and 5.10 (left) for rabbits' lungs. Staub (18) reported an average W/D ratio of 5.2 for 13 pairs of normal human lungs.

Lung volumes (Table 2). FRC_{PV} was significantly higher than FRC measured with the gas dilution method (FRC_{Ne}); each measurement was made 1 min after two deep breaths. The difference was about equal to the volume of the artificial pneumothorax. Mead and Collier (9) reported a similar trend in studies comparing the two measurements in dogs.

The FRC relative to body weight (FRC_{Ne}/kg) agreed closely with Stahl's predicted value. Crosfill and Widdicome (3) reported

TABLE 4. *Cdyn (f = 10, 25, and 50 breaths/min; n = 11)*

	BW, kg	V_T,* ml	f_{10}, ml/cmH_2O	f_{25}		f_{50}	
				ml/cmH_2O	% of f_{10}	ml/cmH_2O	% of f_{10}
Mean	3.1	34	16.9	16.1	96	15.7	94
± SD	±0.5	±3.7	±2.9	±2.5	±7.1	±2.3	±2.2
Range	2.7–3.8	31–39	12.6–24.0	12.6–19.9	83–101	12.5–19.8	83–100

* Dead space of tracheal cannula included.

TABLE 5. *D_{LCO} (single-breath method; n = 23)*

	BW, kg	D_{LCO}, ml/min per mmHg	D_{LCO}/BW, kg	D_{LCO}/TLC
Mean	3.2	1.31	0.41	0.0045
± SD	±0.3	±0.29	±0.08	±0.0010
Range	2.7–3.8	0.84–2.01	0.28–0.61	0.0029–0.0063
Predicted				
Mean		0.88* (4.18)‡		(0.0111)§
Range		0.50–1.30*		0.0041†

* From Stahl (17); Fig. 3. † From Stahl (17); Table 3. ‡ Robinson et al. (16), calculated from regression formula in dogs. § Robinson et al. (16), calculated as D_{LCO}/TLC for 3.2 kg BW.

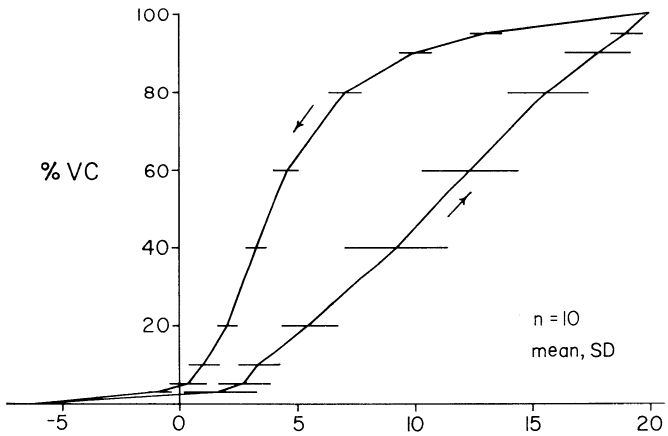

FIG. 2. Procedure was begun at FRC and had the following sequence: FRC → TLC → RV → TLC → FRC. For simplicity, only TLC → RV → TLC are shown. VC = 258.7 ± 26.4 ml. Horizontal bar represents 1 SD. Pao-Ppl is difference in pressure of airway opening and pleural pressure. We have found that the inflation curve may shift to the right as a result of alveolar inflammation or intense airway constriction (due to ozone), with only minor or no changes in the deflation-curve.

smaller FRC in cats of similar body weight. Volume in their study was measured by immersing the lungs in saline; the lungs were removed from the chest immediately after clamping the trachea in end expiration.

The total lung capacity (TLC_{Ne}/kg) and vital capacity (VC/kg) were larger than predicted by Stahl. (According to his formula, VC should equal TLC at a body weight of 6.934 kg, and exceed TLC at small weights.) The TLC at 20 cmH_2O in our in vivo lungs compare very closely with earlier data on excised lungs measured at the same transpulmonary pressure (4). Tenney and Remmers (19) described lung volumes/body weight relations in cats only slightly higher than the values reported in the present study. They inflated and dried excised lungs with air at 20 cmH_2O and obtained volumes equivalent to TLC by a displacement method.

From measurements on dogs, Robinson et al. (16) developed similar power law equations for the subdivisions of lung volume in relation to body weight. Their values for TLC and FRC measured with closed-circuit nitrogen equilibration technique exceeded those predicted by Stahl. Robinson et al. attributed the differences largely to the deep inspirations they imposed on the animals prior to the measurements and to the fact that most of their animals were not paralyzed. Their formulas yield predictions for TLC and FRC that, if applied to cats, are higher than those we found empirically. Our animals were paralyzed although they were subjected to deep inflations before the measurements. Westbrook et al. (22) reported the effect of anesthesia and muscle paralysis on FRC in healthy men in the supine position. They found that the ratio of FRC to control TLC decreased significantly with anesthesia, following paralysis this ratio fell further and approached the control RV/TLC ratio. The procedure of paralyzing the respiratory muscles does appear to decrease FRC. Therefore, FRC in a conscious animal in the same position would be expected to be larger.

Values recorded for other mammalian species have also differed from ours and those predicted by Stahl: for example, FRC/body weight ratios in rats (6), and several ratios of lung volume to body weight in rabbits (1), fall below the general predictions of Stahl, while the lung volumes of rabbits (1) are lower than those of our cats despite similar body weights. It would appear that biological as well as methodological factors contribute to these functional variations among mammalian species. Differences in the relations between lung and body weights, between chest wall compliance (Ccw) and C_L, as well as fundamental differences in the structure and design of the respiratory systems (8, 20) are probably contributory factors. Crosfill and Widdicombe (3) reported that small mammals (mouse, rat, guinea pig, rabbit) have a greater Ccw per unit lung volume than do larger mammals (cat, dog, man), and that there is an inverse relation between C_{cw}/C_L and body weight. They showed that as C_{cw}/C_L increased, FRC/g of lung decreased.

Mechanics. Cdyn at a frequency of 25 breaths/min was almost double the predicted value of Stahl (17) and considerably higher than the value reported by Crosfill and Widdicombe (3) (Table 3). Consequently, C_L/FRC was also higher than predicted by Stahl (being close to that measured in dogs (16)). Our convention of applying deep breaths 3 min prior to measuring Cdyn probably contributed to this discrepancy, since Cdyn decreases with time in supine animals that are mechanically ventilated in the tidal range (9). These changes may be considerable but are immediately reversed following forced inflation of the lung. We found no frequency-dependence of Cdyn within the range of 10–50 breaths/min (Table 4). Among the laboratory animals commonly studied, the rabbit's lung is the most compliant when related to lung weight or volume; its C_L/FRC ratio is approximately 0.30 (1, 3).

A slow (quasi-static) volume-pressure curve is shown in Fig. 2. There was considerably more interanimal variability on inflation than on deflation. The shape and magnitude of hysteresis are similar to those of in vivo studies in anesthetized cats (15) and dogs (23) in which pressure was measured by the esophageal baloon method. R_L was lower than predicted by Stahl (17) and the values of Crosfill and Widdicombe (3), but slightly higher than reported by Colebatch et al. (2) for vagotomized cats. The lower values in the present study could have been due to the deep breaths given prior to the measurements (12).

The technique and validity of measuring pleural pressure with a mushroom catheter has been well established in human subjects (10) and dogs (9, 23). To what extent this volume of pneumothorax altered pulmonary mechanics at FRC is uncertain. Occasionally we encountered sudden changes in pleural pressure at lung volumes below FRC (i.e., if pneumothrax is small) measuring only a few milliliters. Wohl et al. (23) reported a similar finding in dogs. This artifact was uncommon when pneumothorax of 10 ml was used. Our values for C_L related to body weight are slightly higher than those reported by Colebatch et al. (2) for vagotomized cats in which a no. 10 Malecot pleural catheter was used combined with a 6–10 ml pneumothorax. We found no artifacts in pressure recordings such as a shift in the end-expiratory pressure, distortion of wave forms, or phase lag between flow and pressure tracings within the range of breathing frequency studied. The catheter system appeared adequate for Cdyn measurements. Close agreement between our values for TLC at 20 cmH_2O and the data from excised cat lungs at the same transpulmonary pressure (4) suggests that the measurement of pressure with the mushroom catheter was valid at high lung volumes.

DL_{CO} (single-breath method). When related to body weight, the average value for D_{LCO} was higher than predicted by Stahl (Table 5), and smaller by the same method than in dogs (16). D_{LCO} per unit lung volume (i.e., independent of size) approximated the values reported by Stahl but was smaller than in dogs (16). Dogs appear to have larger alveolar surface area and/or pulmonary capillary blood volume than cats (16).

We repeated the measurements of D_{LCO} every 25–30 min for 3–4 h without finding a significant decline in value.

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