Factors Influencing the Measurement of Closing Volume[1-3]

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SUMMARY

The various factors influencing closing volume were studied by performing the single-breath N_2 test on 9 healthy nonsmokers. Time of day, day of the week, and preceding volume history had no effect on either closing volume or alveolar plateau. Slow inspiratory flow resulted in larger ratio of closing volume to vital capacity, ratio of closing capacity to total lung capacity, and change in N_2 concentration than fast inspiratory flow. Voluntary regulation of the expiratory flow resulted in smaller ratios of closing volume to vital capacity and closing capacity to total lung capacity than when flow was regulated by a resistance. Prolonged breath holding of the inspired O_2 led to larger ratio of closing volume to vital capacity and ratio of closing capacity to total lung capacity. To obtain uniform, comparable closing volumes, it is suggested that the subject inspire slowly, control expiratory flow (preferably voluntarily), and not pause between inspiration and expiration.

Introduction

The measurement of closing volume (CV) has recently been proposed as a simple test for detecting "small airway disease" (1). This measurement has been performed in large numbers of subjects by various investigators seeking to establish the range of normal values (1–6). Careful reading of these articles reveals variations, not only in the methods used, but also in the manner in which the subjects performed the maneuvers required for measurement of CV (table 1). Although these differences appear minor, they may contribute to the variation in the results reported by the investigators.

In this study, we systematically examined the effects of varying the manner in which the test was performed on the measurement of CV by the single-breath N_2 (SBN) resident gas method. The protocol was designed to determine whether prior lung volume history, differing methods of controlling expiratory flow, rate of inspiration, duration of breath holding at total lung capacity (TLC), time of day, and day of the week were variables that significantly altered test results.

Materials and Methods

A modified SBN, resident gas method was used to measure CV. The inspiratory line of the apparatus (figure 1) had a dead space of 200 ml that contained room air. The N_2 concentration was sampled just beyond the mouthpiece by a needle valve connected to a rapidly responding N_2 analyzer (Model 605, Med. Science Electronics, St. Louis, Mo.).[4] Expired volume was measured by an electronic spirom-

(Received in original form October 21, 1974 and in revised form January 20, 1975)

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[4] Mention of brand names or commercial concerns does not constitute endorsement by the U. S. Public Health Service.

TABLE 1
VARIOUS LABORATORY TECHNIQUES USED TO DETERMINE CLOSING VOLUME

Reference	Marker Gas	Prior Volume History	Inspiratory Flow	Expiratory Flow	Breath Holding
Dollfuss et al (2)	^{133}Xe	—*	5 – 10 sec†	10 – 15 sec†	6 – 8 sec
Anthonisen et al (3)	N_2	—	8 sec†	8 sec†	15 – 30 sec
LeBlanc et al (4)	N_2	—	"Slow"	10 – 15 sec†	Yes
McCarthy et al (1)	Argon	—	"Slow"	<0.3 liter/sec	—
Collins et al (5)	^{133}Xe	—	0.3 – 0.5 liter/sec	0.3 – 0.5 liter/sec	—
Buist and Ross (6)	N_2	"3 or 4 deep but not maximal"	0.5 liter/sec	0.5 liter/sec	None
Fowler (8)	N_2**	Normal	Maximal	Maximal	None

*Data were not specifically stated in article.
†Assuming a 4-liter VC, 5 sec is approximately equivalent to 0.8 liter per sec; 8 sec, to 0.5 liter per sec; 10 sec, to 0.4 liter per sec; 15 sec, to 0.3 liter per sec.
**Indicates resident gas technique inhaling O_2 and measuring expired N_2 concentration.

eter (Model 800, Ohio Medical Products, Madison, Wis.), and flows were monitored by a visual display meter.

Tracings of N_2 concentration versus expired volume were plotted on paper by an X-Y recorder (Model 7034A, Hewlett-Packard Co., Monroeville, Pa.). All tracings were measured by one trained technician according to the recommendations of the National Heart and Lung Institute (7). The TLC was calculated from the tracings by integrating the area under the curve and using the inspired vital capacity (VC), according to the method of Buist and Ross (6). A "best fit" line was drawn through the initial part of phase III. The slope of this line between 750 and 1,250 ml of expired volume (8) was recorded as the change in N_2 concentration (ΔN_2). Maximal expiratory flow-volume curves were obtained for each subject using previously described methods (9), from which forced vital capacity (FVC) and 1-sec forced expiratory volume (FEV_1) were calculated. The TLC was also measured in each subject by body plethysmograph, using the method of DuBois and associates (10).

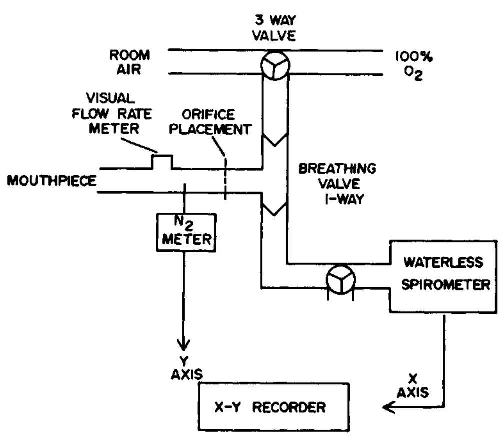

Fig. 1. Single-breath N_2 test apparatus. Expired N_2 concentration is sampled close to the mouth and is plotted on an X-Y recorder against volume.

A paired, 2-tailed t test was used to assess significance of differences between control and test conditions (i.e., to test the hypothesis that the mean of the differences was equal to zero) at the 95 per cent confidence level.

The subjects for this study were 7 male and 2 female nonsmoking, healthy volunteers of mean age 26 years.

The control SBN required the subject to take "a deep breath," exhale to residual volume (RV), and inhale 100 per cent O_2 to TLC without specific instructions to control inspiratory flow. Without breath holding, the subject then exhaled to RV while voluntarily controlling flow between 0.4 and 0.5 liter per sec. At least 2 "acceptable" (7) tracings were recorded for each variable in test performance.

Results

Prior lung volume history. No breaths, 1 maximal breath, 4 deep breaths, and 4 maximal breaths before the SBN made no significant difference in test results when compared to the control condition.

Inspiratory flow. The ΔN_2, closing capacity (CC), TLC, CC/TLC, and CV/VC were all significantly higher when inspiratory flow was controlled and slow (0.2 to 0.3 liter per sec) than when inspiratory flow was fast and uncontrolled (more than 0.7 liter per sec) (table 2).

Expiratory resistance. Expiratory flows between 0.4 and 0.5 liter per sec were achieved by 3 different methods: voluntary control, linear resistance, and alinear resistance (orifice). The use of either type of expiratory resistance resulted in larger CV, CV/VC, CC, and CC/TLC than when expiratory flow was voluntarily controlled (table 3). There were no differences in results when the 2 types of resistances were compared.

TABLE 2

EFFECT OF FAST AND SLOW INSPIRATORY FLOWS ON RESULTS OF THE SINGLE-BREATH N_2 TEST

Maneuver	Value	ΔN_2 (% N_2)	CV (liter)	VC (liter)	CV/VC (%)	CC (liter)	TLC (liter)	CC/TLC (%)
Fast inspiration (control)	Mean	0.58	0.406	4.820	8.4	1.48	5.90	25.8
Slow inspiration	Mean	0.72	0.446	4.779	9.2	1.98	6.31	32.4
	Mean of the differences (from "fast")	0.14*	0.040	−0.041	0.8†	0.50*	0.41**	6.5**

Definition of abbreviations: ΔN_2 = change in N_2 concentration between 750 and 1,250 ml exhaled; CV = closing volume, or volume of phase IV; VC = expired vital capacity; CC = closing capacity (CV + residual volume); TLC = total lung capacity determined from the tracing.

*Mean of the differences tested by 2-tailed t test was significant ($P < 0.025$).

†Significant mean of the differences ($P < 0.05$).

**Significant mean of the differences ($P < 0.005$).

Use of an expiratory resistance did not result in flatter phase III or in a sharper onset of phase IV.

Breath holding. Breath holding for longer than 15 sec (i.e., 30 and 45 sec) resulted in significantly lower VC and higher CV/VC, CC, and CC/TLC than no breath holding (table 4).

Time of day and week. No significant variations in the results of the SBN or spirometry tests were observed, whether they were performed at 8:00 A.M., noon, or 4:00 P.M., or on 3 consecutive week days.

Discussion

Ferris and Pollard (11) demonstrated a marked increase in static pulmonary compliance after 2 deep breaths. On the other hand, Sutherland and associates (12) failed to show differences in regional lung volumes after a maximal inspiration. However, both investigators studied inspiration from functional residual capacity and not from RV.

Our results indicate that prior lung volume history does not change gas distribution as measured by the SBN when inspiration is initiated from RV. In another study from our laboratory, performance of a 30-sec maximal voluntary ventilation maneuver before testing did not influence the results of the SBN (13).

The practical importance of these findings is that other pulmonary function tests (specifically, spirometry, which requires a number of maximal breaths) may be performed between SBN maneuvers while O_2 washout of the lungs is awaited.

Robertson and associates (14) demonstrated that, with faster inspiratory flows, there was a more even distribution of inspired gas throughout the vertical height of the lungs. The changes in distribution were particularly large for small changes in inspiratory flows of less than 1.0 liter per sec. The larger ΔN_2 and CV/VC with slow inspiration in this study are consistent with this observation and suggest that inspiratory flow

TABLE 3

EFFECT OF EXPIRATORY ORIFICES ON RESULTS OF THE SINGLE-BREATH N_2 TEST

Maneuver	Value	ΔN_2 (% N_2)	CV (liter)	VC (liter)	CV/VC (%)	CC (liter)	TLC (liter)	CC/TLC (%)
Voluntary control (9 subjects)	Mean	0.58	0.406	4.820	8.4	1.56	5.98	26.1
Alinear resistance	Mean	0.51	0.483	4.768	10.1	1.80	6.09	29.7
	Mean of the differences (from voluntary)	−0.07	0.078*	−0.052	1.7*	0.24*	0.11	3.6*
Voluntary control (7 subjects)	Mean	0.60	0.439	4.781	9.2	1.65	5.97	27.6
Linear resistance (7 subjects)	Mean	0.66	0.544	4.881	11.1	1.76	5.95	29.6
	Mean of the differences	0.06	0.105*	0.096	1.9*	0.11*	−0.02	2.0*

*Mean of the differences was significant ($P < 0.05$).

TABLE 4

EFFECT OF BREATH HOLD ON RESULTS OF THE SINGLE-BREATH N_2 TEST

Maneuver	Value	ΔN_2 (% N_2)	CV (liter)	VC (liter)	CV/VC (%)	CC (liter)	TLC (liter)	CC/TLC (%)
No breath hold (control)	Mean	0.58	0.406	4.820	8.4	1.56	5.98	26.1
15-sec breath hold	Mean	0.57	0.443	4.759	9.4	1.76	6.08	29.0
	Mean of the differences (from control)	−0.01	0.037	−0.061	1.0	0.20	0.10	2.9
30-sec breath hold	Mean	0.52	0.450	4.730	9.6	1.86	6.14	30.4
	Mean of the differences (from control)	−0.06	0.044	−0.090*	1.2†	0.30*	0.16	4.3†
45-sec breath hold	Mean	0.48	0.406	4.677	9.8	1.98	6.23	31.5
	Mean of the differences (from control)	−0.10	0.001	−0.144*	1.4†	0.42†	0.24*	5.4†

*Significant means of the differences ($P < 0.05$).
†Significant means of the differences ($P < 0.01$).

should be controlled to minimize variations in the results of the SBN. The choice of a specific flow is probably arbitrary. On theoretic grounds, the slower flows, which establish larger differences in vertical gas concentrations, should result in a sharper onset of phase IV, and therefore, are preferable. This must be balanced by practical experience, which indicates that flows of less than 0.2 liter per sec are difficult to maintain and that subjects perform better when given a range of flows for which to aim. For these reasons, we suggest that inspiratory flows voluntarily controlled between 0.2 and 0.3 liter per sec might be a reasonable compromise.

The values for TLC calculated from the SBN more closely approximated those measured in the body plethysmograph when inspiratory flow was slow. This is consistent with the idea that, whereas faster inspiratory flows may give more uniform gas distribution, they may exclude some areas of the lungs with long time constants from participation in the ventilatory volume. This phenomenon might be expected to be even more pronounced in subjects with obstructive airway disease. The increase in TLC and RV as measured from the SBN tracings with slower inspiratory flows account for the increase in CC and CC/TLC during the "slow" inspiration.

Martin and associates (15) studied the effect of expiratory resistances on the alveolar plateau using the xenon method. They found no difference in the alveolar plateau and also failed to demonstrate any changes in regional lung volumes with the addition of an orifice in the expiratory line.

The unchanged ΔN_2 with either a linear or a nonlinear expiratory resistance in our study confirms the observations of Martin and associates; however, we found higher CV, CC, CV/VC, and CC/TLC with the use of an expiratory resistance, whereas they found "diminished or absent terminal rises in N_2 concentration" with the use of a high resistance in the expiratory line. The higher values for CV, CC, CV/VC, and CC/TLC were not results of a change in the values given by the N_2 analyzer caused by a pressure build-up between the expiratory resistance and the mouth, as demonstrated by the following. A 1-liter plastic syringe filled with 300 ml of air and 700 ml of O_2 was attached to the system, and the mixture was pushed through the apparatus both with and without the expira-

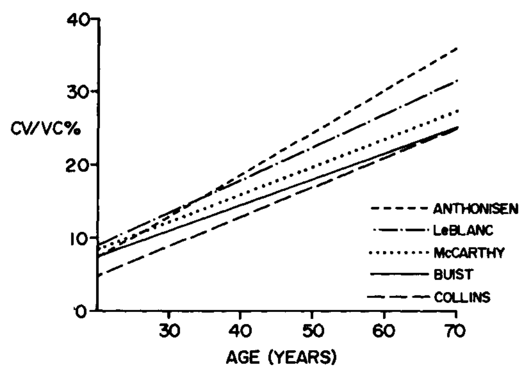

Fig. 2. Ratio of closing volume to vital capacity (CV/VC) plotted against age, as determined by various laboratories.

tory resistances. The N_2 concentrations recorded with the expiratory resistances were slightly lower than those without the expiratory resistances.

The most likely explanation for the larger CV, CC, CV/VC, and CC/TLC without an associated change in ΔN_2 during the expiration through the resistances was a change in the emptying sequence of the lungs, allowing preferential emptying of the relatively N_2-rich upper lung zones at a higher lung volume. The use of an expiratory resistance may cause a difference in the interaction of the abdominal contents, the diaphragm, and the dependent lung zones, leading to airway closure at higher lung volumes than occurs during voluntary control of expiration. Similar interaction of the diaphragm and abdomen with dependent lung zones has been speculated by Bashoff and associates (16) under conditions of rapid, forced expiration.

Expiratory VC decreased with increased breath holding (table 4). Under conditions of a high inspired O_2 concentration, an assumed respiratory quotient of 0.8 at rest, and prolonged breath holding, more O_2 would be absorbed than CO_2 produced, resulting in a smaller expired VC. It is the decrease in expired VC with breath holding, and therefore the higher calculated RV for that breath, that accounts for the higher CV/VC and higher CC and CC/TLC, rather than any increase in CV.

It is interesting to note that, of the predicted normal values for CV/VC plotted against age from various laboratories (figure 2), the 2 regression lines giving the highest values were obtained with maneuvers using breath holding (table 1). It is likely that part of this difference in CV/VC is due to breath holding.

In our small group of subjects, we found no consistent difference in FVC, FEV_1, or any parameter of the single-breath N_2 test with time of day (8:00 A.M., noon, and 4:00 P.M.) or day of the week (during 3 consecutive days). With a larger number of subjects, differences in CV might become evident.

On the basis of the data presented, it seems important to control the method of performance of tests of CV. If information from one laboratory is to be compared with that from another laboratory as new studies of the effect of various diseases on CV become available, then further standardization of the test is desirable.

The most physiologic and practical method of measuring CV is with control of the inspiratory flow between 0.2 and 0.3 liter per sec, without breath holding, and with control, preferably voluntarily, of the expiratory flow below 0.5 liter per sec.

Acknowledgment

The writers thank Sandy Amandus and Jerry Bair for performing the pulmonary function tests; Harlan Amandus, for the statistical analysis; Dr. W. K. C. Morgan, for his helpful comments; Mary Jo Powell, for typing the manuscript.

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