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The Effect of Previous Volume History and Exercise on Closing Volume*

*Brian L. Strom***

The measurement of closing volume has been advocated as a simple and sensitive test for demonstrating early disease in small (less than 2 mm diameter) airways.[1] The concept of a volume at which small airways in the dependent portions of the lungs begin to close was introduced by Dollfuss et al[2] based upon studies of the distribution of ventilation using boluses of ^{133}xenon. Closing volume has since been measured using nonradioactive inert gases such as argon,[3] helium,[4] or nitrogen[5] as the indicators. Several studies have demonstrated that closing volume increases as a function of age in healthy subjects.[5,6] Closing volumes have been shown to be abnormally large (compared to subjects of similar age) in heavy smokers[7,8] and subjects with asymptomatic asthma.[9]

There is some difficulty in comparing results from different investigators owing to the fact that the volume history of the lungs prior to measurement of the closing volume has varied from no previous inspiration[5-7,10] to one maximal inspiration[11] to "three or four deep but not maximal breaths."[12] The purpose of this study was to examine the effects of the previous volume history and exercise on the measurement of closing volume in young healthy subjects.

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MATERIALS AND METHODS

Ten young, nonsmoking men volunteered to participate in the study. They were either professional staff employed by the Appalachian Laboratory for Occupational Respiratory Diseases or medical students and residents from the Department of Medicine West Virginia University Medical Center. The ages, heights, and weights of the subjects are shown in Table 1. None of the subjects suffered from acute or chronic respiratory symptoms as determined by responses to a modified version of the Medical Research Council questionnaire.[13]

Table 1—*Characteristics of the Study Subjects*

Subject	Age (yrs)	Height (in)	Weight (lb)
HA	25	67	156
GC	24	73	198
LD	31	74	178
BM	26	76	197
EM	36	68	144
CR	25	72	173
WR	25	72	152
JS	28	71	177
RS	27	71	164
BS	23	66	138

Each subject performed a series of maneuvers twice with an interval of at least three days separating the two series. In one series, the closing volume (CV) was measured using the single breath nitrogen method and in the other the single breath carbon monoxide diffusing capacity (DL_{CO}) was measured. Six subjects underwent the closing volume measurement series first and the diffusing capacity measurement series second, whereas four of the subjects underwent the series in the reverse order. The maneuvers preceding the determination of CV and DL_{CO} were identical in both series and were as follows: Control condition consisting of one maximal inspiration; condition I—no deep breath prior to measurement; condition II—three maximal inspirations prior to measurement; condition III—a 30-second maximal voluntary ventilation maneuver prior to measurement; condition IV—measurement at one minute post exercise; condition V—measurement at seven minutes post exercise; condition VI—measurement at 13 minutes post exercise.

Closing volume was determined by the single breath nitrogen method described by Anthonisen[5] except that: 1) there was no breath-holding period between inspiration and expiration, and 2) the flows during inspiration and expiration were voluntarily controlled to between 0.25 and 0.5 liter per second by the subject. Nitrogen concentration was plotted on the vertical axis of an X-Y plotter and exhaled volume on the horizontal axis. A typical tracing (Fig 1) illustrates the four phases as described by Dollfuss et al.[2] Phase 1 represents the washout of the anatomic and instrumentational dead spaces. Phase 2 demonstrates a rapidly rising nitrogen concentration as mixed dead space and alveolar gas are exhaled. Phase 3 shows a gradually increasing nitrogen concentration representing the alveolar plateau. Phase 4 is identified by a relatively abrupt increase in the slope of the terminal portion of the alveolar plateau that continues to the end of the exhalation. The onset of Phase 4 was determined by drawing a best-fit line through Phase 3 and noting the point at which the nitrogen concentration curve departed from this line and did not return to it. The volume from the onset of Phase 4 to the end of the exhalation was measured at the closing volume (CV). One observer (BLS) measured all of the closing volume tracings. The following indices were obtained from each curve: vital capacity, closing volume, nitrogen concentration at 1.25 liters and 2.5 liters from the beginning of the exhalation. From these measurements the ratio of closing volume to vital capacity (CV/VC) and the slope of Phase 3 (the change in nitrogen concentration between 1.25 and 2.5 liters) ($\Delta N_2/1.25L$) were calculated. Duplicate measurements were made of CV and DL_{CO} for each condition except the last three following exercise. Values reported are the means of the two tracings where they were recorded. Single breath diffusing capacity (DL_{CO}) and alveolar volume (AV) were determined using a mixture of carbon monoxide and helium by the method of Ogilvie et al.[14]

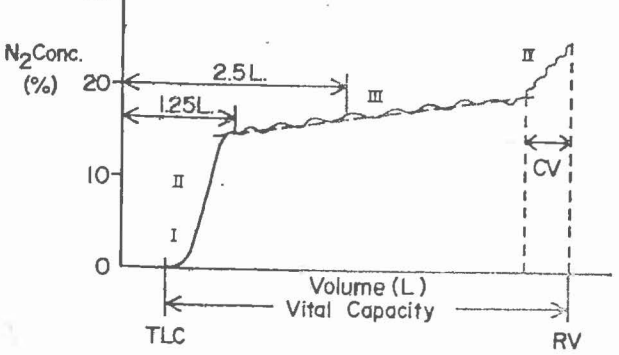

Figure 1. A typical tracing from a closing volume maneuver. Each tracing was used to determine as shown: vital capacity, closing volume (Phase 4), and nitrogen concentration at 1.25L and 2.5L from the beginning of the exhalation. See text for discussion of the significance of Phase 1–Phase 4.

The heart rate was counted by palpation of the radial pulse for 15-second intervals before each designated measurement of either the closing volume or the diffusing capacity.

Exercise was performed by each subject on an electrically-braked bicycle ergometer. The initial load was ten watts and this was increased by ten-watt increments at one-minute intervals until the subject's pulse reached 180 beats per minute or ceased to increase with increasing loads. One measurement of closing volume (or DL_{CO}) was made at 1, 7, and 13 minutes following cessation of exercise.

RESULTS

Table 1 lists the age, height, and weight of the subjects in the study. All subjects completed the exercise routine and the subsequent measurements of CV or DL_{CO}. Most had some difficulty controlling flows to the low levels required for the CV measurements at one minute after exercise but were, indeed, able to accomplish it. The duration of bicycle exercise ranged from 13 to 25 minutes. The oxygen consumption during exercise ranged from 21.7 to 52.4 with a mean of 36.8 ml/min/kg.

Table 2 lists the changes that occurred in the indices measured from the single breath nitrogen test as a result of the preliminary maneuvers or exercise prior to performance of the test. The only significant changes in any of the indices taken from the single breath nitrogen test occurred in the first minute following exercise. Both vital capacity (VC) and CV decreased significantly after exercise when compared with the control value (one single inspiratory capacity maneuver). The decreases in VC and CV were 0.23 and 0.26 liters respectively. The ratio of CV to VC increased significantly at one minute after

exercise, although the magnitude of the increase was small (mean 0.04 liters). Absolute nitrogen concentration at 1.25 and 2.5 liters exhaled and slope of Phase 3 ($\triangle N_2$/1.25L) both increased significantly at one minute post exercise as compared to the control state.

The pulse rate showed significant increases following the MVV maneuver and at all times (1, 7, and 13 minutes) post exercise.

The mean differences between measurements of the single DL_{CO} maneuver made in the control state and following the same maneuver as was performed in the closing volume series are shown in Table 3. Several changes occurred in this series. Alveolar volume was significantly larger following the MVV maneuver than in the control state although this difference was small (mean 0.06 liter). DL_{CO} increased significantly at one minute post exercise when compared to the control state, the mean difference being 7.75 ml/min/mm Hg. The only other significant differences between the control state and any of the experimental conditions were in the pulse rate which increased after the MVV maneuvers and at all times (1, 7, and 13 minutes) post exercise.

Comparison of the patterns of differences observed in the pulse rate and vital capacity (tests that were common to both protocols) appeared to confirm that the experimental conditions (I-VI) did not appreciably differ between the two protocols with the exception of the vital capacity at one minute after exercise. The significance of this change will be discussed later.

DISCUSSION

This series of measurements indicates that preceding volume history in terms of whether a subject performed no, one, or three maximal inspirations had no significant effect upon the pulse rate, vital capacity, closing volumes, or nitrogen concentrations. Further, the performance of a vigorous 30-second voluntary hyperventilation prior to measurement did not significantly affect the closing volumes or vital capacity but, as expected, did significantly increase the pulse rate. Similarly, no, one, or three maximal inspirations preceding measurement had no significant effect on the pulse, vital capacity, alveolar volume, and diffusing capacity. Performance of a vigorous 30-second hyperventilation preceding measurement of the DL_{CO} resulted in a significant increase in pulse rate, a small, but significant, increase in alveolar volume, but no change in VC or DL_{CO}.

These results are somewhat surprising since it is well-known that airway resistance (15) and dynamic compliance (16), two indicators of airway function,

Table 2—*Mean Differences from Control Single Breath Nitrogen Maneuver*

Index	Test Conditions*					
	I	II	III	IV	V	VI
Pulse (beats)	1.6 (3.0)†	−1.0 (2.9)	18.0** (11.7)	72.0** (9.9)	21.2** (10.1)	18.6** (9.0)
Vital Capacity (liters)	−0.08 (0.12)	−0.04 (0.09)	−0.04 (0.08)	−0.23** (0.29)	−0.07 (0.95)	−0.03 (0.10)
Closing Volume (liters)	−0.04 (0.15)	0.05 (0.18)	0.14 (0.27)	−0.26** (0.19)	0.05 (0.17)	0.06 (0.22)
Closing Volume / Vital Capacity	−0.01 (0.03)	0.01 (0.03)	0.03 (0.04)	0.04** (0.03)	0.01 (0.03)	0.01 (0.04)
Slope of Phase III (N_2/1.25L) (%)	0.01 (0.13)	0.01 (0.17)	0.02 (0.30)	0.28** (0.24)	0.10 (0.41)	0.05 (0.29)
Nitrogen Conc. at 1.25 liters (%)	0.01 (1.18)	−0.08 (0.96)	−0.08 (0.75)	3.54** (3.66)	0.74 (1.32)	0.69 (3.21)
Nitrogen Conc. at 2.5 liters (%)	0.00 (1.13)	−0.07 (0.88)	−0.06 (0.82)	3.86** (3.76)	0.84 (1.52)	0.74 (3.36)

*Control = One preceding inspiratory capacity maneuver
†Value in parenthesis is one standard deviation
I = No preceding inspiratory maneuver
II = Three preceding inspiratory capacity maneuvers
III = Thirty-second maximal voluntary ventilation maneuver preceding measurements
IV = Measurement at one minute post exercise
V = Measurement at seven minutes post exercise
VI = Measurement at 13 minutes post exercise
**Value significantly different from control condition, $p<0.05$

Table 3—*Mean Differences from Control Single Breath Diffusing Capacity Maneuver*

ıdex	Test Conditions*					
	I	II	III	IV	V	VI
ulse (beats)	−1.8	−0.1	19.9**	72.3**	22.3**	18.6**
	(6.1)†	(3.8)	(9.9)	(16.6)	(11.6)	(9.0)
ital	−0.02	−0.01	0.02	−0.08	0.05	0.04
apacity (liters)	(0.13)	(0.12)	(0.11)	(0.16)	(0.14)	(0.15)
.lveolar	−0.01	0.03	0.06**	0.02	0.07	0.12
olume (liters)	(0.08)	(0.13)	(0.08)	(0.24)	(0.21)	(0.16)
)iffusing	0.64	−0.57	0.23	7.75**	1.59	−0.46
apacity	(3.74)	(1.70)	(2.08)	(3.75)	(3.08)	(3.31)
ml/min/mmHg)						

Control = One preceding inspiratory maneuver
Value in parenthesis is one standard deviation
I = No preceding inspiratory maneuver
I = Three preceding inspiratory capacity maneuvers
I = Thirty-second maximal voluntary ventilation maneuver preceding measurements

IV = Measurement at one minute post exercise
V = Measurement at seven minutes post exercise
VI = Measurement at 13 minutes post exercise
**Value significant y different from control condition, $p<0.05$

re markedly influenced by the preceding volume ıistory of the lungs. Insofar as closing volumes are ıeasurements of small airway function one would ıave expected them to have also been influenced to ome extent by the lungs' previous volume history.

he pattern of response in measurements of CV and $D_{L_{CO}}$ following maximal exercise is much easier to xplain. Pulse rates were significantly increased at , 7, and 13 minutes after cessation of the exercise n both series and to approximately the same degree. hese are expected findings in non-athletic subjects vho undergo maximal exercise. Likewise, the ignificant increase in $D_{L_{CO}}$ at one minute post xercise with a return to control values by seven ninutes after exercise is an expected response.[17] he vital capacity at one minute after exercise ıeasured in the CV maneuver decreased significantly ɔut not at 7 or 13 minutes post exercise, and was ınchanged at all times in the $D_{L_{CO}}$ maneuver. A ;imple explanation for this finding can be found by ıoting that the VC performed in the CV maneuver vas done with a very slow inspiration and expiration, vhereas the VC performed during the $D_{L_{CO}}$ maneuver vas done relatively rapidly. It was difficult to maintain he low flows (0.25 to 0.50 liter per second) at one ninute following maximal exercise owing to the ıyperventilation stimulated by exertion. The ;ignificant reduction in closing volume (Phase 4) is ɔrobably accounted for by the same mechanism as ıccounted for the change in vital capacity.

he significant increases in $\Delta N_2/1.25L$ and in the ıitrogen concentrations at 1.25 and 2.5 liters from the beginning of exhalation could be related to one or more of the following factors: 1) hyperventilation, 2) back diffusion of nitrogen when the lungs are filled with a high concentration of oxygen; 3) decrease in vital capacity owing to an increase in pulmonary blood volume; 4) decrease in vital capacity owing to the difficulty performing the CV maneuver soon after maximal exercise; and 5) the large oxygen consumption achieved during and immediately following maximal exercise.

Hyperventilation *per se* seems an unlikely explanation for the increased nitrogen concentrations and $\Delta N_2/1.25L$ in that similar changes were not observed following a vigorous 30-second hyperventilation in performance of the MVV maneuver (Condition III, Table 2).

Back diffusion of nitrogen from the body stores into the lungs also seems an unlikely explanation for the findings at one minute post exercise since nitrogen is so poorly soluble in blood. The concentration of nitrogen in blood is only 0.979 ml N_2/100 ml blood.[18] If you assume a blood volume of 5 L, this would give a nitrogen content of about 49 ml of nitrogen. Even if equilibrium with the approximately 20 percent nitrogen concentration could be reached in the 30 seconds required to perform the CV maneuver, this would yield only about 39 ml of nitrogen. This would increase the nitrogen concentration of the approximately 7 L (our mean) alveolar volume by only 0.56 percent, far less than the observed 3.54 percent to 3.86 percent average increase.

If the decrease in vital capacity one minute after exercise in the CV maneuver were the result of an

increase in pulmonary blood volume, this same pattern of response should have occurred at one minute post exercise in the DL_{co} maneuver. The fact that it did not occur in the DL_{co} maneuver argues against this explanation. Also, an increase in pulmonary blood volume sufficient to cause a reduction in VC of the magnitude that occurred after exercise should have also caused a reduction in alveolar volume. In fact, no significant change in alveolar volume was observed after exercise (Table 3).

The most likely explanation for the absolute increase in nitrogen concentration at the specified lung volumes is the slight reduction in vital capacity that resulted in less dilution of the nitrogen resident within the lungs by the slightly smaller inspiration of oxygen. The mean vital capacity after exercise was 0.23 L less than in the control situation. Utilizing the following formula it should be possible to calculate the effect that a change of this magnitude should have on the nitrogen concentrations at specified lung volumes of the single breath nitrogen curve:

$$\triangle N_2 \text{ concentration} = 79.6 \left(\frac{VC_1}{AV_1 + DS_1}\right) - 79.6 \left(\frac{VC_2}{AV_2 + DS_2}\right) \quad (1)$$

where $\triangle N_2$ concentration is the change in nitrogen concentration of the alveolar plateau (in percent), VC_1 the vital capacity inhalation of oxygen during the control maneuver, AV_1 and DS_1 the alveolar volume and dead space during the control maneuver, and VC_2, AV_2, and DS_2, the vital capacity, alveolar volume and dead space following exercise. By substituting mean values for these measurements obtained during the control and post exercise states it is possible to determine that the mean change in VC post exercise would have resulted in a mean increase of 2.6 percent N_2 in the nitrogen concentration of the alveolar plateau (Phase 3). The calculated increase in nitrogen concentration agrees reasonably well with the observed value of a mean change in nitrogen concentration ranging from 3.54 percent to 3.86 percent (Table 2). This explanation is supported by the observation that the only subject to show a decrease in nitrogen concentrations after exercise also showed an increase in vital capacity. This subject was the principal author (BLS) who could be considered as more highly motivated than the rest of the subjects.

Finally, the change in slope of Phase 3 of the alveolar plateau as manifested by the significantly increased $\triangle N_2/1.25L$ (Table 2) with one-minute post exercise is most likely explained on the basis of the large oxygen consumption attained by the subjects during and immediately following exercise. Phase 3 (the alveolar plateau) normally has a slightly increasing slope as a consequence of uneven distribution of the inspired oxygen (21). Simply inspiring a smaller volume of oxygen (*ie* the smaller VC post exercise) would elevate the nitrogen concentrations at all volumes along Phase 3 but not change the slope or $\triangle N_2/1.25L$. Owing to the very slow flows utilized in the CV maneuver, the duration of the expiratory phase could allow a significant amount of oxygen consumption and thus a change in the slope of the alveolar plateau (Phase 3). If a subject were taking up oxygen from the lungs at the rate of 2.6 liters per minute (the mean in this study), and assuming a respiratory quotient of 0.8, over the course of the approximately 2.5 seconds required to exhale 1250 ml at 0.5 liter per second,* he would take up about 108 ml of oxygen and produce about 86 ml of carbon dioxide, giving a net loss of about 22 ml in volume. This would produce an increase in nitrogen concentration over the 1250 ml volume range of about 0.25 percent above that due to uneven distribution of the inspired air. This compares favorably with the observed increase of 0.28 percent nitrogen over the 1250 ml volume that the $\triangle N_2/1.25L$ was measured following cessation of exercise.

CONCLUSIONS

This study investigated the effects of previous volume history, vigorous voluntary hyperventilation, and exercise on the closing volume measurements in normal subjects. It was shown that preliminary maneuvers such as none, one, or three maximal inspirations had no significant effect on the measurements of closing volumes or nitrogen concentrations. Vigorous voluntary hyperventilation prior to measurement significantly increased the pulse rates and alveolar volume but not closing volumes or nitrogen concentrations. Maximal exercise preceding measurement significantly increased the pulse rates and nitrogen concentrations whereas it caused significant decreases in vital capacity and closing volume in the first minute post exercise. The pulse rates remained significantly elevated from the control state for as long as 13 minutes post exercise, but the vital capacities and closing volumes returned to the control values by seven minutes post exercise.

The changes in vital capacity, closing volume, and nitrogen concentrations are most likely explained by

*After exercise, most subjects maintained the maximum flow rate allowed them.

a combination of the difficulty in performing a slow, controlled expiration and the increased oxygen consumption immediately following cessation of exercise.

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