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VENTILATORY FUNCTION TESTS. III. RESTING VENTILATION, METABOLISM, AND DERIVED MEASURES

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One important phase of respiratory function is the ventilation of the lungs with an alternating flow of respired air. The rate at which this process is carried on, expressed in terms of the volume of air, either inspired or expired, per minute, is the *pulmonary ventilation*. The maximum rate which this process can attain is the *ventilation capacity*. The difference between the two, commonly expressed as a percentage of the capacity, is appropriately called the *ventilation reserve* (1). It represents that portion of the capacity which is not in use and therefore available as a reserve to be called upon when the necessity arises.

The common denominator of most disturbances in the ventilatory function of the pulmonary bellows is a loss of ventilation reserve. This may occur in two ways. First, the reserve may be reduced because the ventilation capacity is impaired. In the preceding two reports of this series (2, 3), procedures for measuring the degree of impairment of ventilation capacity and for analyzing its causes were considered. Second, the reserve may be reduced by an increase in pulmonary ventilation. The present report is concerned principally with procedures for measuring this type of disturbance and differentiating some of its causes.

Any kind of increase in pulmonary ventilation may be called a hyperpnea since this term is non-committal with respect to the type or cause. However, hyperpneas in general may be divided into two types, depending upon whether they are normal responses to increased metabolic demands or are compensatory responses to disturbances in internal or external environment.

In *metabolic hyperpneas*, the increase in pulmonary ventilation is in direct proportion to the increase in metabolism as measured by O_2 consumption. The ratio of ventilation to O_2 consumption, therefore, does not change. This ratio, expressed as the liters of air respired per 100 cc. of O_2 consumed, is known as the *ventilation equivalent for O_2* (4-7). In thyroid disease as well as

in moderate physical exercise the ventilatory responses are so adjusted to the metabolism that the ventilation equivalent for O_2 remains essentially unchanged (8).

By contrast, in *compensatory hyperventilation*, the increase in pulmonary ventilation is out of proportion to the metabolism. As a result, the ventilation equivalent for O_2 is materially increased. This is true of simple anoxia, of CO_2 inhalation, of metabolic acidosis, of fever, and of various types of reflex hyperpneas (8).

Simultaneous determination of the pulmonary ventilation and O_2 consumption and calculation of the ventilation equivalent for O_2 , therefore, permits a quantitative evaluation of the degree of disturbance in pulmonary ventilation, and should aid in the identification of possible causes. It was the purpose of the present study to determine the reliability of such determinations and to establish normal values.

METHODS

A sample of 100 healthy young male medical students served as subjects for this study. Their age and physical characteristics are summarized in Table I. The plan of the experiment was to make duplicate determinations of the various tests at one sitting, and then to repeat this procedure approximately one week later. The voluntary ventilation capacity and the vital capacity were determined according to the previously standardized techniques already described (2, 3). These determinations were made on a separate occasion from the others, since resting conditions are neither required nor possible.

The pulmonary ventilation and O_2 consumption were determined simultaneously under *resting conditions*. This

TABLE I
Characteristics of sample of 100 male medical students

	Mean	St. d.	C. var.
Age, years	23.3	3.4	14.6
Height, inches	70.5	2.2	3.1
Weight, pounds	158.0	18.9	11.9
Surface area, sq. m.	1.88	0.13	6.9

TABLE II
Results of tests applied to 100 normal subjects

	First day			Second day		
	Mean	St. d.	C. var.	Mean	St. d.	C. var.
Voluntary ventilation capacity, V.V.C.	160.9	19.5	12.1	168.6	19.2	11.4
Vital capacity, V.C.	5.18	0.68	13.2	—	—	—
Resting ventilation, R.V.	7.56	1.23	16.2	6.87	0.97	14.1
Resting metabolic rate, R.M.R.	274	32.4	11.8	275	32.9	11.9
Resting ventilation reserve, R.V.R.	95.3	0.88	0.92	95.9	0.72	0.75
Resting ventilation equiv., R.V.E.	2.78	0.45	16.2	2.51	0.30	11.9
Respiratory rate, R.R.	10.5	3.0	28.5	10.1	3.1	30.7
Tidal volume, T.V.	770	220	28.5	730	190	25.9

involved a period of resting in a chair for at least 10 minutes, followed by an additional five-minute period of reclining on a cot with the back rest elevated at a 30 degree angle. No precautions were taken with respect to previous fasting, since true basal conditions are an inconvenient limitation on routine clinical use. The results revealed that the preliminary rest was somewhat too short; a 20-minute period in the semi-reclining position would have been superior, as shown by Soley and Shock (9).

The Benedict-Roth basal metabolism spirometer was used with the soda-lime absorber in position (in contrast to ventilation capacity and vital capacity tests), and with the spirometer filled with O₂. Several minutes were allowed for the respiratory excursions to stabilize. A six-minute run was used, at the end of which the mechanical ventilometer, thermometer, and barometer were read and the subject's mouthpiece removed. After a short interval to refill the spirometer and adjust the instruments, the procedure was repeated.

The O₂ consumption was obtained in the usual fashion from the slope of the tracing and expressed in cc. per minute, STPD (760 mm. Hg 0° C.); the pulmonary ventilation was determined from the ventilometer and expressed in liters per minute, BTPS (Body Temperature, Pressure and Saturated), taking into account the effect of the soda-lime on water vapor tension. The respiratory rate, or frequency, was also read from the tracing and the mean tidal volume calculated.

The following formulae were used to calculate the two derived measures, resting ventilatory reserve (RVR) and the resting ventilation equivalent for O₂ (RVE_{O₂}):

$$\text{RVR in per cent} = \frac{\text{Voluntary Ventilation Capacity} - \text{Resting Ventilation}}{\text{Voluntary Ventilation Capacity}} \times 100$$

$$\text{RVE}_{O_2} \text{ in L./100 cc.} = \frac{\text{Resting Ventilation in L./min., BTPS}}{\text{Resting O}_2 \text{ Consumption in cc./min., STPD}} \times 100$$

RESULTS

The repeated application of the various test procedures to 100 healthy adult male subjects yielded the results summarized in Tables II and III. The means, standard deviations, and coefficients of variation for each type of test and for the mean of two trials on each of two days are included in Table II; the reliability coefficients based upon test repetition, both within and between days, are included in Table III. The last columns of Table II, which represent the means of duplicate trials on the second day, are preferred as a source of norms.

The resting pulmonary ventilation showed a tendency to fall during successive trials (from 7.89 to 7.24 on the first day and from 7.03 to 6.71 on the second). In part this reflects the inadequate preliminary rest period, and the growing familiarity with the test and its procedures. The normal mean is taken at 6.87 L./min. (BTPS) with a coefficient of variation of 14.1 per cent; 95 per cent of the healthy young adult population, therefore, should lie within the limits of 5.90 and

TABLE III
Reliability coefficients

	Reliability coefficients		
	Within one day		Between days
	1st day	2nd day	
Voluntary ventilation capacity	.728	.825	.754
Resting pulmonary ventilation	.753	.917	.628
Resting ventilation reserve	—	—	.404
Resting metabolic rate	.868	.904	.583
Resting ventilation equivalent for O ₂	.646	.749	.556
Vital capacity	.975	—	—
Resting respiratory rate	.879	.953	.886
Resting tidal volume	.754	.924	.782

7.84 L./min. The reliability of the determination improved considerably on the second day, reaching a coefficient of 0.917.

The *resting metabolic rate*, or O_2 consumption also showed a tendency to fall slightly during successive trials within one day (from 280 to 268 on the first day and from 281 to 270 on the second). The normal mean is taken as 275 cc. of O_2 (STPD) consumed per minute, with a coefficient of variation of 11.9 per cent. The reliability coefficients within days are consistently high, but that between days fell to 0.583. This is presumably due to the fact that resting, rather than resting and fasting, conditions were observed.

The *voluntary ventilation capacity* yielded a normal mean of 168.6 L./min. (BTPS) with a coefficient of variation of 11.4 per cent. Thus, these three primary measurements show variability of nearly the same degree.

The *respiratory rate* and *tidal volume* averaged 10.1 per minute, and 730 cc. (BTPS) respectively. Their variability was considerably higher, however, for the respective coefficients of variation were 30.7 and 25.9 per cent. Their distributions are skewed, as revealed by a mean tidal volume of 730 cc. as compared with the ratio of the mean resting ventilation to the mean respiratory rate of only 680 cc. The reliability coefficients, however, are quite good.

The *resting ventilation reserve*, a derived measurement, is the difference between the resting ventilation and the ventilation capacity, expressed as a percentage of the latter. Inasmuch as the ventilation capacity was determined at a different time than the resting ventilation, the reserve has been calculated only from the means obtained on the different days. Even this, however, should affect the reliability coefficient adversely. The normal mean is taken as 95.9 per cent, with a standard deviation of 0.72 per cent, and a coefficient of variation of only 0.75 per cent. The extremely low variability is, of course, due to the fact that the resting reserve expressed in liters per minute is so large in comparison with the variability of the resting ventilation.

The second derived measure is the *ventilation equivalent for O_2* , which expresses the volume of air breathed for each 100 cc. of O_2 absorbed. The normal mean is 2.51, with a coefficient of variation of 11.9 per cent, which is nearly identi-

cal with those of the elements of the ratio. Its reliability is less than that of its elements, however.

The correlation coefficient for the relationship between the resting ventilation and resting metabolic rate was found to be 0.592. The statistically fitted regression equation was

$$RV = 0.0175 RMR + 2.01$$

This equation implies that the ventilation equivalent for O_2 is not constant, but a hyperbolic function of the resting metabolic rate. However, because the metabolic rate, which is the independent variable in the above regression, is subject to error, the resulting regression equation is biased in the direction of departure from the simple direct proportion required for a constant ventilation equivalent for O_2 . This bias can be overcome by extending the range of metabolic rate. This extension occurs in hyperthyroid states and may be produced experimentally by moderate physical exercise, in neither of which is the ventilation equivalent appreciably altered (8). It is concluded, therefore, that in health the resting ventilation equivalent for O_2 remains constant within the range established by its standard deviation as shown in Table II.

DISCUSSION

Comparison of the present normal values for the various ventilatory function tests with values previously reported in the literature is difficult because of the diversity of procedures used. In many instances coefficients of variation of 25 to 50 per cent are evident in the reported results, indicating a failure to standardize methods. Furthermore, corrections for temperature, pressure, and water vapor are commonly either not made or not disclosed. Inasmuch as gas volumes of BTPS are about 25 per cent greater than at STPD, this item alone can produce a consistent error which is beyond the range of normal individual variation.

In the case of metabolic rate, or O_2 consumption, the present resting values may be compared with basal metabolism standards. According to the Boothby and Sandiford standards, the basal O_2 consumption for male subjects averaging 23 years old and 1.88 sq. m. in surface area should be 266 cc. per minute. This is only slightly less

than the present resting values of 275 cc. per minute.

The present norms apply only to the male sex. Preceding reports of this series have demonstrated an appreciable sex difference in voluntary ventilation capacity and vital capacity (2, 3). Both average in women only 70 per cent of the value for men, leaving the ventilation capacity per liter of vital capacity (the capacity ratio) the same in both sexes. Both resting ventilation and metabolism are likewise lower in women than in man. No significant sex difference has been reported for their ratio as calculated in the ventilation equivalent for O_2 , implying that both are reduced proportionately in females. Judging from the data of Shock and Soley (10) and the basal metabolism standards, the reduction is less than that for ventilation and vital capacities. Thus the resting ventilation reserve should be slightly lower in women.

The various ventilatory function tests investigated in this and preceding reports are for the most part long known tests. The object of re-examining them has been twofold: *first*, to provide normal values based on a healthy young population and employing better standardized procedures, and *second*, to elaborate a rationale for their combined use in the clinical examination of disturbances of ventilatory function. In the past the tests have been used more or less in isolation with disappointing results, since none of them provides all the desired information (11). When used systematically and in combination, however, they should be rather effective in *a*) identifying the nature of a ventilatory disturbance, *b*) evaluating the degree of such disturbance, and *c*) differentiating possible causes.

A common form of ventilatory disturbance is a reduction in ventilatory reserve, the accompanying subjective symptom of which is dyspnea. This may be identified and its severity measured by the present tests. Furthermore, many possible causes may be differentiated. In the first place, the ventilatory reserve can be reduced by either of two major causes, namely, a reduction in ventilation capacity, or an excessive ventilation. These possibilities can be readily differentiated and the contribution of each evaluated by the present tests. Furthermore, each of these major possibilities can be further analyzed by means of the remaining tests of the series. A reduced ventilation capacity,

for example, may be due to excessive pulmonary resistance, to muscular weakness, or to a small vital capacity. In the latter case the capacity ratio (3) remains unaltered; in the former cases the capacity ratio will be reduced. Also muscular weakness can be identified by means of the maximum expiratory pressure (3). The other major possibility, namely, excessive ventilation, can be identified as a metabolic hyperpnea, if the ventilation equivalent for O_2 is unchanged, or as a compensatory hyperventilation, if the ventilation equivalent is elevated. The former is a normal response to an excessive metabolism; the latter is an adjustment of ventilation designed to compensate for some abnormality in the inspired air, blood pH, body temperature, altered blood pressure (both venous and arterial), etc.

This scheme may be presented in the form of a classification of impaired ventilatory reserve, as follows:

- I. Reduction in *resting ventilatory reserve*.
 - A. Due to impaired *ventilation capacity*.
 1. With normal *capacity ratio*.
 - a. Due to reduced vital capacity.
 2. With reduced *capacity ratio*.
 - a. Due to increased pulmonary resistance or
 - b. Reduced muscular force, as shown by the *maximum expiratory pressure*.
 - B. Due to excessive *pulmonary ventilation*.
 1. With normal *ventilation equivalent for O_2* .
 - a. Metabolic hyperpnea, due to increased *metabolism*.
 2. With elevated *ventilation equivalent for O_2* .
 - a. Compensatory hyperventilation, due to ventilatory adjustment to some other disturbance.

This analysis, it should be clear, is made in terms of physiological function and not in terms of disease entities. Diseases which produce different patterns of physiological disturbance in ventilatory function should be differentiable on the basis of this analysis. In any case the type of disturbance, its degree, and to a considerable extent, its causes can be evaluated.

SUMMARY AND CONCLUSIONS

1. Procedures, reliabilities, and normal values based upon 100 healthy medical students are presented for the four primary measurements of voluntary ventilation capacity, vital capacity, resting pulmonary ventilation, and resting O₂ consumption; and the three derived measurements of resting ventilatory reserve, the capacity ratio, and the ventilation equivalent for O₂.

2. A scheme is presented for the systematic use of these ventilatory function tests in the analysis of clinical ventilatory disturbances in terms of their nature, degree, and causes.

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