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Research Article

VARIABILITY OF RESPIRATORY AND CIRCULATORY PERFORMANCE DURING STANDARDIZED EXERCISE [1]

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In the preceding report (1) the complementary adaptations of respiration and circulation to the stress of exercise in normal subjects were described. Various isolated measurements, obtained by a method of continuous observation, were found to be in accord with those reported by earlier investigators employing the established Tissot-Haldane techniques of respiratory gas analysis. Because of the continuity of observation, various rates of change in adapting from a state of rest to a standardized stress of exercise (treadmill walking) as well as rates of recovery could be observed in relation to each other as loops of cardio-respiratory responses. These respiratory and circulatory pathways portray the representative responses in normal subjects, but a survey of the *range of variability* in normals and patients is needed before these pathways can be utilized properly for the study of impaired functions in patients with cardiorespiratory diseases. Pelnar (2) has critically reviewed the existing methods of functional appraisal of the causes of dyspnea in patients and expressed the opinion that his new method based upon the continuous study of the R.Q. curve during rest, exercise and recovery provides a more satisfactory appraisal of function in relation to dyspnea than any other method previously available. If these observations can be confirmed, then continuous observation of standardized exercise may provide the means of rating disability in relation to functional impairment of respiration and circulation and possibly differentiating between the two chief types of dyspnea in patients: pulmonary insufficiency and circulatory insufficiency.

It is the purpose of this paper to analyze statistically the data obtained from the same 35 normal adults previously reported (1) to determine the range of normal variation for the several measurements. By this means the minimum and maximum value for each factor during rest, exercise or recovery can be determined. Secondly, the magnitudes of change in the several factors in normal subjects performing at this standardized workload are assessed in both normal subjects and patients with various diseases causing clinical symptoms and signs of functional impairment. Hence the necessary percentage change in the various exercise measurements for a significant difference in the same individual on repeated examinations was estimated. Thus the comparative value of the various measurements made can be estimated to ascertain those which are more reliable for discriminating functional impairment and rating physiological disability.

METHODS

Statistical analyses consisted of determination of the standard deviation, standard error and coefficient of variation for each of the observations in the same 20 normal males and 15 normal females previously reported in terms of mean values. The standard deviation of the mean values was calculated according to the formula $\sigma_m = \sqrt{\frac{\Sigma d^2}{N-1}}$,[4] assuming, of course, that our sample was truly a representative group. Standard error was calculated according to the formula $SE_m = \frac{\sigma_m}{\sqrt{N-1}}$, and the coefficient of variability was calculated as $\frac{\sigma_m}{\text{mean}}$ multiplied by 100 to express all values in per cent. Because two standard deviations above and below the mean include approximately 95% of the range that can be expected on the basis of random sampling, the limits of normality are tabulated as plus or minus two standard deviations from the mean values for the periods of rest, exercise and recovery.

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[4] σ_m = standard deviation of mean; d = difference of observation from the mean; Σ = summation; N = degrees of freedom.

TABLE I

Statistical analysis of all measurements (20 males—15 females)

Factors analyzed	Units	Mean		Standard deviation		Standard error		Coefficient of variability (*per cent*)	
		M	F	M	F	M	F	M	F
Age	*years*	30.2	32.2	5.3	10.2	1.21	2.73	17.5	31.7
Arterial oxygen saturation (oximeter)	*per cent*								
Rest		95	96	1	3	.24	.83	1.1	3.1
Exercise		95	97	2	4	.48	1.11	2.1	4.5
Recovery		95	98	2	4	.48	1.11	2.1	4.5
Breath-holding time	*seconds*	37	38	17	8.3	4.8	2.3	46.0	21.8
Cardiovascular data									
Circulation time (lungs to ear)	*seconds*	5.6	5.2	1.	1.1	.23	.30	17.8	21.2
Heart rate									
Rest	*beats min.*	80	81	11.0	7.7	2.67	2.06	13.7	9.5
Exercise		102	107	11.0	3.0	2.67	2.43	10.8	8.5
Recovery		82	85	12.0	7.9	2.91	2.11	14.6	9.3
Systolic pressure									
Rest	*mm. Hg*	124	118	10.0	11.0	2.36	2.94	8.1	9.3
Exercise		139	136	14.0	18.0	3.30	4.82	10.1	13.2
Recovery		128	121	10.0	13.0	2.36	3.42	7.8	14.9
Diastolic pressure									
Rest	*mm. Hg*	80	78	11.0	6.0	2.6	1.60	13.7	7.7
Exercise		82	78	10.0	7.0	2.36	1.87	12.2	9.0
Recovery		82	79	9.0	7.0	2.12	1.87	11.0	8.8
Pulse pressure									
Rest	*mm. Hg*	44	40	10.0	8.0	2.36	2.14	22.7	20.0
Exercise		55	58	13.0	16.0	3.07	4.28	23.6	27.6
Recovery		46	42	7.0	11.0	1.65	2.94	15.2	26.2
Metabolic demands									
Calories									
Rest	*cal. min.*	1.28	1.02	.22	.15	.051	.041	17.5	15.0
Exercise*		2.56	2.26	.41	.66	.95	1.71	16.1	29.2
Ratio of $\frac{\text{Exercise cal.}}{\text{Resting cal.}}$		2.02	2.22	.11	.16	.025	.044	5.4	7.5
Oxygen consumption									
Rest	*ml./sq.m./min.*	137	125	21.0	16.0	4.8	4.3	15.3	12.8
Exercise	STPD	393	379	47.0	55.0	10.8	14.7	11.9	14.5
Recovery		160	153	22.0	14.0	5.1	3.7	13.8	9.1
Oxygen debt	*per cent*	8	10	3.0	3.0	.69	.81	37.5	30.0
Half-time recovery	*min.*	.8	1.1	0.2	0.3	.046	.08	25.0	27.2
Oxygen transport									
Rest	*ml./sq.m./min.*	1.72	1.54	.26	.19	.059	.058	15.1	12.3
Exercise	STPD	3.83	3.44	.24	.28	.055	.075	6.3	8.1
Recovery		1.96	1.82	.32	.21	.074	.056	16.3	11.5
Respiratory gases									
Oxygen absorbed (expired air)									
Rest	*vol. %*	4.18	3.86	.39	.34	.089	.091	9.3	8.8
Exercise		5.17	4.86	.39	.45	.089	.12	7.5	9.3
Recovery		4.14	3.86	.39	.34	.089	.09	9.4	8.8
Carbon dioxide excreted (expired air)									
Rest	*vol. %*	3.91	3.43	.50	.44	.11	.12	12.8	12.8
Exercise		4.64	4.14	.53	.44	.12	.12	11.4	10.6
Recovery		4.23	3.82	.55	.44	.13	.12	13.0	11.5
Respiratory quotient (expired air)	*ratio*								
Rest		.94	.88	.03	.08	.007	.021	3.4	9.4
Exercise		.89	.85	.03	.08	.007	.021	3.4	9.4
Recovery		1.02	.99	.04	.09	.009	.024	3.8	9.1
Oxygen absorbed from mid-capacity air	*vol. %*								
Rest		5.33	4.89	.48	.37	.11	.09	9.0	7.6
Exercise		6.41	6.01	.28	.48	.066	.128	4.4	8.0
Recovery		5.39	4.99	.30	.36	.071	.096	5.5	7.2

TABLE I—*Continued*

Factors analyzed	Units	Mean		Standard deviation		Standard error		Coefficient of variability (*per cent*)	
		M	F	M	F	M	F	M	F
Surface area	*sq.m.*	1.88	1.66	.13	.14	.029	.037	6.9	8.4
Ventilation	(STPD)								
Maximum mask breathing capacity	*L/sq.m./min.*	30.3	29.3	6.0	5.2	1.4	1.4	19.8	17.7
Minute ventilation									
Rest	*L/sq.m./min.*	3.28	3.25	.54	.50	.124	.134	16.5	15.3
Exercise		7.57	7.86	.93	1.19	.213	.318	12.3	15.1
Recovery		3.84	3.91	.55	.49	.126	.131	14.3	12.5
Respiratory rate									
Rest	*breaths/min.*	14	15	2.76	2.6	.63	.69	19.7	17.3
Exercise		18	22	3.03	3.5	.69	.93	16.8	15.9
Recovery		14	16	3.21	2.5	.73	.67	22.9	15.6
Tidal air									
Rest	*ml./sq.m./min.*	252	226	67	38	15.	10.	26.5	17.0
Exercise		434	367	81	66	18.6	17.6	18.7	18.0
Recovery		285	251	72	33	16.5	8.8	25.2	13.1
Ventilation equivalents for oxygen	*L/min.*								
Rest		2.42	2.63	.22	.24	.05	.06	9.1	9.1
Exercise		1.96	2.11	.12	.21	.027	.056	6.1	9.9
Recovery		2.46	2.66	.24	.24	.055	.064	9.7	9.0
Ventilation index	*ratio*	5.4	7.1	1.0	2.3	.23	.61	18.5	32.0
Vital capacity (STPD)	*L/sq.m.*	2.1	1.8	.3	.4	.068	.107	14.3	22.0
Average vital rate	*L/sec.*	1.7	1.4	.5	.7	.11	.20	29.4	50.0

* Corrected for R.Q. and Oxygen Debt

Variations within each of the three periods of observation were studied similarly for the basic primary measurements of heart rate, ventilation volume, and respiratory efficiency (volumes per cent oxygen absorbed). Each item was measured at one minute intervals consecutively, and the standard deviation of the mean values was calculated for all 35 normal subjects. By this method, one thus obtains a measure of the variability of minute-to-minute analysis in any one period.

The magnitude of change from one period to another in the various factors was expressed as percentage change from the resting values during exercise and recovery.

The reproducibility of exercise performance was determined by analysis of the standard deviation of the mean value for repeated tests on the same individual. This analysis also includes seven abnormal patients upon whom repeated tests were made. Coefficients of variability were determined in this group as described above for the average heart rate, ventilation volume and respiratory efficiency, oxygen consumption, volumes per cent of carbon dioxide excreted in expired air, estimated R.Q., duration of walking in minutes, oxygen transport per heart beat and oxygen debt. All gas volumes were expressed in terms of STPD, corrected for surface area. The patients utilized for this purpose had the following clinical diagnoses: chronic pulmonary granulomatosis associated with beryllium compounds (two), bronchostenosis following organizing pneumococcal pneumonia (one), pericardiectomy for relief of constrictive pericarditis (one), coronary insufficiency following healed coronary occlusions (two), and congenital heart disease due to pulmonary stenosis and auricular septal defect (one). The period of time for these observations ranged from one month to 12 months.

RESULTS

1. *Statistical variations between normal subjects to the standardized exercise test (2.6 mph level walking for 10 minutes)*

The observations on 35 normal adults are summarized in Table I in terms of mean values, standard deviations, standard errors, and coefficients of variability according to sex. There is no significant difference [5] between sexes,[6] and accordingly the averages for men and women for the several

[5] A difference is considered significant when there is less than one possibility in 369 of being due to chance selection, or there is a three-fold difference between the standard errors.

[6] The apparent difference in resting oxygen saturation is an artefact since the calibration of the oximeter is arbitrary. The ventilation index is almost significantly higher in men than women, largely because the vital capacity (used in the denominator of the formula) is slightly smaller in women. Ventilation index equals the sum of the average exercise and recovery minute ventilation values divided by the vital capacity, all expressed in volumes corrected for STPD and body surface area.

TABLE II

Normal limits plus or minus two standard deviations from combined mean value (male and female)

		Mean	Min.	Max.
Breath-holding	*seconds*	37.5	12	63
Circulation time	*seconds*	5.4	3.2	7.6
Heart rate				
Rest	*beats/min.*	81	62	99
Exercise		104	90	118
Recovery		84	61	107
Systolic pressure				
Rest	*mm. Hg*	121	101	142
Exercise		138	106	170
Recovery		125	102	148
Diastolic pressure				
Rest	*mm. Hg*	79	62	96
Exercise		80	63	97
Recovery		81	65	97
Pulse pressure				
Rest	*mm. Hg*	42	24	60
Exercise		56	27	85
Recovery		44	26	62
Calories				
Rest	*cal./min.*	1.16	.79	1.53
Exercise		2.43	1.36	3.50
Ratio $\frac{\text{Exercise}}{\text{Rest}}$		2.09	1.82	2.36
Oxygen consumption				
Rest	*ml./sq.m./min.*	132	95	169
Exercise	STPD	381	279	483
Recovery		156	120	192
Oxygen debt	*per cent*	9	3	15
Half-time recovery of oxygen consumption	*min.*	.94	0.5	1.4
Oxygen transport				
Rest	*ml./sq.m./heart beat*	1.64	1.16	2.12
Exercise	STPD	3.65	3.13	4.17
Recovery		1.89	1.35	2.43
Respiratory efficiency (expired air)	*vol. %*			
Rest		4.04	3.31	4.77
Exercise		5.03	4.19	5.87
Recovery		4.02	3.29	4.75
Carbon dioxide excreted (expired air)	*vol. %*			
Rest		3.70	2.76	4.64
Exercise		4.42	3.45	5.39
Recovery		4.05	3.06	5.04
R. Q. (respiratory ratio)				
Rest		.91	.80	1.02
Exercise		.87	.76	.98
Recovery		1.01	.88	1.14
Mid-capacity respiratory efficiency	*vol. %*			
Rest		5.14	4.29	5.99
Exercise		6.23	5.47	6.99
Recovery		5.21	4.55	5.87
Ventilation:				
Maximum mask breathing capacity	*L/sq.m./min.*	29.8	18.6	41.0
Minute Ventilation	STPD			
Rest		3.27	2.23	4.31
Exercise		7.69	5.57	9.81
Recovery		3.87	2.83	4.91
Respiratory rate				
Rest	*breaths/min.*	14	9	19
Exercise		20	14	26
Recovery		15	9	21
Tidal air				
Rest	*ml./sq.m./min.*	240	135	345
Exercise		405	258	552
Recovery		270	165	375
Ventilation equivalents for oxygen				
Rest	*L/min.*	2.51	2.05	2.97
Exercise		2.02	1.69	2.35
Recovery		2.56	2.06	3.04
Vital capacity	*L/sq.m.*	1.97	1.27	2.67

measurements are combined for purposes of all subsequent discussion. Allowing for differences in temperature and basal state of activity, the observed mean values for resting ventilation and oxygen consumption show satisfactory agreement with those reported by others using the Tissot-Haldane method of gas analysis (3). The volume per cent of oxygen absorbed (or ml. per liter of air) is in exact agreement with previously reported values (2, 3). The measurements with coefficients of variability of *less than 10%* are the estimations of the arterial oxygen saturation, respiratory quotients, volumes per cent of oxygen absorbed from either expired air or mid-capacity air, and the ventilation equivalents for oxygen. In contrast the heart rate, blood pressure, pulse pressure, ventilation volume, oxygen consumption, calories of heat production, ventilation index and vital capacity all exhibit greater variability. Many of these factors reflect changes due to emotional stimuli, and some may be slightly affected by differences in environmental temperature [7] as well as the type and amount of clothing worn—factors which are not controlled in this study. The overall variability for all the measurements throughout the three periods of observation is about 12%.

The *consecutive one minute variations* in the heart rate, ventilation volume and expired air analysis for oxygen concentration, expressed in terms of standard deviations, are shown in Figure 1. The last of the three listed is the least variable. The standard deviations are of the same order of magnitude throughout the three periods of observation.

The *limits of normality* for the several factors studied are shown in Table II. These minimal and maximal values have been determined arbitrarily as plus or minus two standard deviations from the combined mean values for both males and females. All volume measurements are expressed at STPD values corrected for surface area per unit time of one minute. This is to facilitate estimation of the oxygen consumption by the short-cut method previously described. The respiratory gas concentrations are expressed in terms of volumes per cent to eliminate minor differences related to daily fluctuations in barometric pressure which would be reflected in partial pressure values for oxygen. (Alveolar pCO_2 appears to be homeostatically regulated by ventilation and is less dependent upon barometric fluctuations.) The maximal blood pressure values are above the conventional range of 140/90 mm. Hg in part perhaps because of the erect posture, but more likely because of vasomotor responses to apprehension about the testing procedure. Since these individuals often show lower pressure values when relaxed in the recumbent position, a more liberal interpretation of significant blood pressure increments may be necessary. Similar comments apply to measurements of heart rate, ventilation volume and oxygen consumption—all of which reflect responses to anxiety. It is apparent from these considerations that much of the spread of normal variation is dependent upon psychoneurogenic stimuli which of course may operate in either normal individuals or those with functional impairment from cardio-respiratory diseases. Since there is less variation in concentrations of the respiratory gases, and rates of CO_2 excreted to O_2 absorbed per unit volume of ventilation may be a direct measure of neuropsychogenic hyperventilation, Pelnar's opinion that these measurements afford a more reliable appraisal of performance in patients with dyspnea is strengthened (2).

2. Magnitude of changes in normal subjects to the standardized exercise test

The amount of work done by this type of exercise is moderate since the average working caloric expenditures is only 2.1 times above the resting value.[8] The magnitudes of changes caused by this amount of work are summarized in Table III as percentage differences from the corresponding resting measurements. Whereas the ventilatory reserve, respiratory quotient and ventilation equivalents for oxygen diminish somewhat during exercise, the remainder of the factors observed increase. The increments range from 1.5% for diastolic blood pressure to 193% for oxygen consumption. There is an average increase of 108% in calories of heat production, 135.5% in ventilation volume, 29.5% in heart rate, and 124.0% in oxygen

[7] Statistical evaluation of the environment showed barometric pressure to be 747.3 ± 1.13 mm. Hg (0.15% coefficient of variability) and room temperature to be $24.9 \pm 1.9°$ C (7.9% coefficient of variability).

[8] Hard work is not performed until the metabolic rate is at least three times greater than the basal metabolic rate expressed in calories.

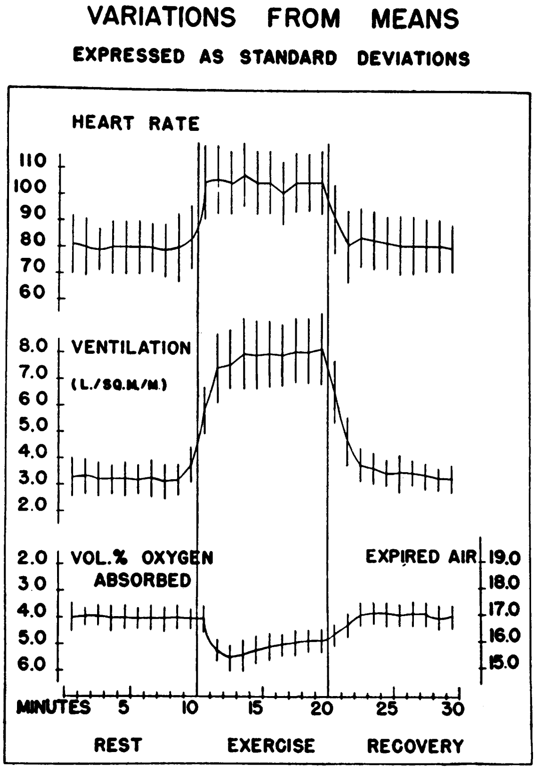

FIG. 1

Minute-by-minute mean heart rates, ventilation volumes, and volumes per cent of oxygen absorbed from expired air in normal subjects, together with range of variations expressed as standard deviations from each mean value. The vertical lines for each minute represent the variation of plus or minus one standard deviation from the corresponding mean. The expired air values on the right side of the graph are in terms of volumes per cent.

transport per heart beat, which is a measure of the change in the A–V oxygen difference and the stroke volume.[9]

3. *Variability of multiple exercise tests in the same individuals*

Table IV presents the statistical findings obtained from the study of 17 exercise tests in normals, and 54 tests in seven abnormal patients with clinical cardio-respiratory impairment. All tests were done at the rate of 2.6 mph level walking for 10 minutes, or to the limits of tolerance for those who could not walk for as long as 10 minutes, and the data are based upon the average of the one minute observations serially throughout exercise. It will be seen that in all instances the coefficient of variability for the averages of the normals is less than the corresponding value for the averages of the abnormals, except for oxygen debt where the reverse relationship is found. The factors which exhibit the least variability for either normals or abnormals are the duration of walking ("endurance"), respiratory efficiency, heart rate, oxygen consumption, oxygen transport per heart beat, and ventilation volume. The appreciably greater variability of values for volumes per cent of CO_2 excreted and respiratory quotient are attributed to technique, since the CO_2 analyzer employed is neither as stable nor accurate as the oxygen analyzer. Hence these observations cannot be interpreted to invalidate Pelnar's claim that observations of the R.Q. and CO_2 concentration are as important and reliable as those for oxygen concentration.

From these data the limits of variation observed by this standardized exercise test for both normals and abnormals can be estimated from the coeffi-

[9] Any variations in blood volume, hematocrit (4), or arterial oxygen saturations are considered insignificant in relation to the magnitude of change in stroke volume and A–V oxygen difference indicated by the change in oxygen transport per heart beat.

TABLE III

Exercise and recovery mean values in normal subjects (expressed as percentage change from resting measurements)

	Exercise	Recovery
Decrease during exercise		
Ventilatory reserve	−16.7	−2.1
Respiratory quotient	−5.3	+10.0
Ventilation equivalents for oxygen	−25.4	+1.2
Increase during exercise		
Cardiovascular measurements:		
Heart rate	29.5	3.7
Systolic pressure	13.5	2.8
Diastolic pressure	1.5	2.0
Pulse pressure	32.4	4.2
Oxygen transport per heart beat	124.0	15.9
Calories of heat production*	108.0	—
Oxygen consumption	193.0	18.9
Respiratory gases		
Vol. % O_2 absorbed	24.8	−0.5
Vol. % CO_2 excreted	19.4	9.2
Mid-capacity vol. % O_2	22.0	1.5
Ventilation		
Total minute ventilation	135.5	18.3
Respiratory rate	37.5	2.8
Tidal air	69.1	12.0
Mid-capacity ventilation	141.0	29.0
Dead space	68.0	19.6

* Calculated from oxygen consumption, observed R. Q. and corrected for oxygen debt in recovery.

TABLE IV

Variability of multiple exercise tests (2.6 mph level walking, expressed as mean exercise values, standard deviations and coefficients of variation)

Diagnosis	Number of tests	Heart rate	Ventilation volume	Respiratory efficiency	Oxygen consumption	Vol. % CO_2	R. Q.
Normal	4	91± 1.0	6.72± .18	4.85±.16	327± 7.6	3.96± .33	.85±.06
Normal	8	91± 4.4	9.06± .23	4.18±.19	378±14.0	3.80± .40	.87±.11
Normal	5	101± 6.0	7.04± .70	5.05±.20	357±37.0	4.28± .41	.82±.05
Average		94± 3.8	7.61± .37	4.70±.18	354±19.5	4.01± .38	.85±.07
		4.0%	4.9%	3.9%	5.5%	9.5%	8.6%
Beryl. granul.	15	143±10.7	12.56±1.27	3.03±.17	376±25.7	2.16± .09	.74±.03
Beryl. granul.	18	122± 5.8	12.61± .61	2.93±.10	360±23.9	2.38± .62	.83±.20
Bronchostenosis	5	94± 8.4	10.95± .42	3.20±.24	352±25.0	2.95± .40	.93±.10
Pericardiectomy	4	113± 7.2	8.40± .83	4.95±.40	413±10.0	3.90± .60	.79±.11
Coron. insuf.	3	117± 7.5	14.85±1.14	2.94±.23	443±35.0	2.54± .25	.83±.13
Coron. insuf.	4	108± 6.0	12.60±1.45	3.65±.15	461±33.0	3.23± .23	.86±.04
Pulm. stenosis	3	133± 6.5	10.09±2.00	2.29±.01	231±44.0	1.8 ±0.10	.79±.41
Average		113± 7.4	11.72±1.10	3.28±.18	377±28.1	2.71± .33	.82±.15
		6.5%	9.4%	5.6%	7.5%	12.1%	17.8%

Diagnosis	Number of tests	Endurance	Oxygen Debt	Oxygen Transport
Normal	4	10 ±0	8.5±7.6	3.56±.09
Normal	8	10 ±0	7.3±3.4	4.16±.10
Normal	5	10 ±0	11.1±4.0	3.68±.12
Average		10 ±0	9.0±5.0	3.80±.10
		0%	55.3%	2.7%
Beryl. granul.	15	10 ±0	16.1±3.3	2.64±.19
Beryl. granul.	18	9.7±1.2	10.9±3.9	2.93±.24
Bronchostenosis	5	10 ±0	9.5±4.6	3.74±.13
Pericardiectomy	4	10 ±0	7.8±2.6	3.68±.26
Coron. insuf.	3	3.8± .3	38.0±6.4	3.78±.40
Coron. insuf.	4	6.5± .9	21.0±1.7	4.23±.29
Pulm. stenosis	3	5.3± .6	36.3±8.1	1.73±.25
Average		7.9± .43	20.0±4.0	3.25±.25
		5.4%	20.0%	7.7%

Over-all average coefficient of variability: Normals 5%, Patients 10.2%

cients of variability for each factor. Depending upon the level of significance one wishes to consider in evaluating differences in results between any two tests in the same patient, one may employ various multiples of the coefficient of variability. For example, since the range of plus or minus two standard deviations encompasses 95% of the possible values to be expected in a given representative sample, four times the coefficient of variability would approach an estimate of the range of nonsignificant variability for any measurement. In terms of exercise heart rate in patients with clinical disease, four times 6.5% would indicate 26% range of variation of exercise heart rate values which would be within the limits of variability. Hence a 30% change in heart rate, for the same individual, could be interpreted as being significant, *i.e.*, beyond the range of variation of patient and testing procedure.

DISCUSSION

The variability, expressed in terms of per cent coefficients, for various respiratory and circulatory measurements has been determined by statistical analysis of the data obtained from the following: single exercise tests in 20 normal males and 15 normal females, and consecutive one minute observations of the primary measurements of heart rate, ventilation volume and respiratory efficiency, or volumes per cent of oxygen absorbed from expired air, including 17 repeated tests in normals, and 54 repeated tests in seven patients with definite disease entities. From these analyses there was no evidence of increased variability in the three primary measurements during exercise or recovery as compared with rest, and of these three, the respiratory efficiency showed the least variability. The overall average coefficient of variability for all factors considered during exercise was about 12% in 35 normal subjects, and in repeated testing of either normals or patients with disease 5% or 10%, respectively. The factors which showed the least variation were, in addition to the duration of walking, the three primary measurements mentioned above, and the secondary measurements obtained by calculation, such as the oxygen consumption and oxygen transport per heart beat. When the three measurements of ventilation volume, oxygen consumption and oxygen removal or respiratory efficiency are considered for the 35 normal subjects, the average coefficient of variability is 13% during rest and 11.3% during exercise. These values are to be compared with those of Baldwin *et al.* who found 10% variation during rest in the basal state and 17% during one minute of exercise in 92 normal subjects (3).

In view of these findings, the technique of standardizing exercise tolerance testing described is considered satisfactory for the investigations of dyspnea in clinical patients. The essence of this technique is the combination of multiple continuous observations of responses to a standardized stress of exercise. The latter is controlled automatically by treadmill walking. The rate of energy expenditure is moderate, averaging just over twice the resting value, and the duration of 10 minutes is sufficiently long to screen out patients with circulatory insufficiency. Finally since the range of variation is less than previously reported values for observations in the basal state, it does not appear necessary to have this as a prerequisite to satisfactory testing technique when problems of metabolism are not under consideration. Furthermore it permits observations of respiratory and circulatory performance to controlled work-loads under ordinary conditions of diet and preceding activity for the patients studied.

SUMMARY

1. A statistical analysis of the cardio-respiratory performance of 35 normal adults to a standardized stress of activity has been made to determine the normal limits and range of variability in the non-fasting state.

2. The average coefficient of variability for the several factors observed during rest, exercise, and recovery was about 12%.

3. Similar analyses of data from multiple tests on the same individual—either normal subjects or patients with clinical disease—showed average coefficients of variability of about 5% and 10%, respectively.

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