Oxygen Cost of Breathing III: Studies in Asthmatic Children*†

JOSEPH THOMAS, M.D.,
Pediatric Allergy Fellow,
CARMEN E. ENECIO, M.D.,‡
Staff Pediatrician,
Greater Southeast Community Hospital,
M. NICK CHEHREH, M.D.,
Clinical Professor of Pediatrics and Child Health,
and
ROSCOE C. YOUNG, JR., M.D.,
Associate Professor of Medicine and Director, Harden Pulmonary Laboratory,
Howard University Hospital,
Washington, D.C.

ENERGETICS is that branch of respiratory mechanics which deals with energy cost of breathing, work done by the respiratory muscles, and their mechanical efficiency. Although studies of energetics on children have been theoretically possible, little or no data currently exist.[1] This may be because some methods used to measure work involve integration of pressure-volume loops obtained from a ballon passed into the esophagus, an objectionable procedure especially among children.

It is reasonable to suspect that oxygen cost of breathing (O_2 cost) or total work of breathing should be higher in asthma when airways obstruction is present than they are in healthy children. The purpose of this study, therefore, was to obtain values for O_2 cost of breathing in asthmatic children by using non-invasive methods and relate these to values in healthy children.

METHODS

The subjects consisted of asthmatic patients from Pediatrics Allergy Clinics of Howard University Freedmen's and District of Columbia General Hospitals. Twenty asthmatic children, ages six to 15, were divided into two groups: those who were asymptomatic (10 children) and those with symptoms and wheezing on examination at the time of study (10 children). Ten healthy nonsmoking children without asthma or other cardiopulmonary disease were tested to serve as control subjects. Height and weight of each of the three groups of children were identical, but the normal group was significantly older than that of the symptom-free asthmatic group, $P<0.01$. Serum immunoglobin E values of the asthmatic children ranged from 450 to 4,050 IU/ml. Whereas, healthy subjects had values from 350-680 IU/ml. Twenty-four children had $alpha_1$ antitrypsin levels measured, which were within the normal range, suggesting that hereditary emphysema was not present. Total eosinophil counts in the asthmatic children were elevated. The study was performed on an out-patient basis. The children came to the laboratory in the fasting condition, at least two hours prior to study, at the same time each day. The data base was reviewed and brief examination accomplished. Each child received a chest radiograph. Arterial oxygen saturation at rest (Sa_{O_2}) was measured with an ear oximeter and routine spirometry per-

*Presented in part at the 42nd Annual Meeting, American Academy of Pediatrics Section on Allergy, October 22, 1973, Chicago, Illinois.
†Supported in part by the Alexander and Margaret Stewart Trust Fund (RPG-8017)
‡Work done during tenure of a Pediatric Allergy Fellowship, Howard University.

formed. Predicted normal spirographic values were those recently published from this laboratory.[2] Respiratory peak flow rate ($\dot{V}$ max) was measured with a Wright Peak Flow Meter. Informed consent was obtained from the parents or guardians after the nature of the procedures has been fully explained.

APPARATUS

The apparatus used for measurement of O_2 cost consisted of a modified Collins 9 L respirometer as originally described by Bartlett and Specht[3] and by Harden and associates.[4] It consisted of placing a one way external valve in the circuit with the inner Sadd valve removed, so the carbon dioxide absorber could be shunted out of the circuit during a period of voluntary hyperventilation. The children rested in a semi-recumbent position for 30 minutes to achieve a steady state. A seven minute period of normal quiet breathing on O_2 was followed by a one minute period of voluntary hyperventilation at a frequency of 20 to 30 breaths/minute for one minute. Another period of normal quiet breathing for seven minutes immediately followed. O_2 cost of the increased ventilation was assumed to be due to O_2 uptake by respiratory muscles.

Oxygen cost of breathing was calculated in ml of oxygen at STPD per liter of ventilation at BTPS.

Data were compiled on punch cards by computer using the SPSS program package.[5] Descriptive statistics were computed for each measurement in three sub populations. Pearson correlations were calculated for oxygen cost and each spirometric parameter, while the significant ones were used to calculate a multiple regression with oxygen cost as dependent variable. Student's T Test was used to compare sample means of sub populations of asthmatic children with healthy control subjects.

RESULTS

Chest radiographs of all children studied were negative for infiltrative lung disease, however, the symptomatic asthmatic group showed hyperaeration of the lungs. As expected this group also showed airways obstruction by their spirographic patterns.

Descriptive statistics for $\dot{V}$ max and maximum voluntary ventilation MVV are shown in Table 1. Both groups of asthmatic children have values significantly lower than healthy control children, $P<0.05$ or better. Values for O_2 cost of breathing for each group are shown in Table 2 with the descriptive statistics below. Oxygen cost of breathing in children who were wheezing was significantly greater than healthy control subjects, $P<0.01$. The test was sensitive enough to detect symptom-free asthmatic children $P<0.01$. The best reproducibility, however, was only ±8%.

Table 1. DESCRIPTIVE STATISTICS FLOW OF PEAK AND MAXIMUM VOLUNTARY VENTILATION

	Healthy Controls		*Asthmatic Patients Symptom-Free*		*Asthmatic Patients Symptomatic*	
	$\dot{V}$ max (L/Sec)	*MVV (L/min)*	*$\dot{V}$ max (L/Sec)*	*MVV (L/min)*	*$\dot{V}$ max (L/Sec)*	*MVV (L/min)*
MEAN	5.9	82.0	4.2	65.0	3.0	52.6
SE	2.8	5.0	0.2	3.8	0.3	6.1
MEDIAN	5.8	86.3	4.0	60.2	2.7	43.6
MODE	4.3	57.7	3.7	48.6	1.6	35.0
SD	9.0	15.7	6.5	12.0	1.1	19.3
MIN	4.3	57.7	3.3	48.6	15.8	35.0
MAX	7.2	101.7	5.4	91.5	53.3	94.3
SIGNIF	—	—	P<0.01	P<0.05	P<0.01	P<0.01

Oxygen cost correlated negatively with $\dot{V}$ max $r = -0.72$, $P<0.001$ and also with MVV $r = -0.54$, $P<0.001$. Correlations of O_2 cost with other pulmonary function tests failed to reach the level of significance. If $\dot{V}$ max and MVV are measured, O_2 cost of breathing can be predicted from the following multiple regression equation.

O_2 Cost (ml/L) = 15.6 – 3.05 $\dot{V}$ max (L/sec) + 0.0008 MVV (L/min)

Standard errors for the multiple regression of O_2 cost on V max is ± 3.11; and of O_2 cost on MVV is ± 3.07. The analysis of variance for the regression is significant, $F = 30.36$, $P<0.05$ and $F = 16.48$, $P<0.05$ respectively.

COMMENTS

The fear that age difference between

healthy children and symptom-free asthmatic children might introduce a sampling error in measurement of energetics parameters was unwarranted, since O_2 cost was found to be age independent. The similarity of energetics data in the present study in children to that of adults reported in the literature is confirmatory.

Table 2. OXYGEN COST OF BREATHING (ml/L)

		Asthmatic Patients	
	Healthy Controls	*Symptom-Free*	*Symptomatic*
	2.0	2.4	13.0
	5.6	9.2	11.0
	2.2	7.2	9.1
	3.5	5.2	13.3
	1.6	5.5	8.1
	6.1	11.2	19.2
	1.9	3.3	10.5
	3.5	13.0	12.8
	4.1	11.0	8.8
	3.3	9.1	9.6
MEAN	3.4	7.7	11.5
SE	0.49	1.1	1.0
MEDIAN	3.3	7.3	10.6
MODE	3.5	2.4	8.1
SD	1.5	3.6	3.3
VAR	2.4	10.6	11.1
RANGE	4.5	10.6	11.1
SIGNIF	—	P<0.01	P<0.01

Oxygen cost is an expression of the total energy required for breathing. Since it is not yet possible to measure O_2 consumption of the respiratory muscle directly, an indirect method was used. Oxygen uptake of the entire body was measured at two levels of ventilation and the increment assumed to represent the metabolic cost of the increased ventilation.[6] Different techniques have been used to achieve the increased ventilation, such as interposition of respiratory dead space,[3,7] addition of carbon dioxide to the inspired gas mixture[8,9] and voluntary hyperventilation.[4,8-14] The latter has consistently produced the highest O_2 cost. It has been noted that O_2 cost increases with increasing ventilation and that O_2 cost is greater at frequencies of 20 breaths/minute than at 30 breaths/minute. This difference was minimal at the lower minute ventilation used in this study. It was essential, however, to obtain a compromise in ventilation to minimize O_2 cost on one hand and to permit obtaining a measurable value on the other.

Variations in O_2 cost in the literature have been great and may be attributed to variations in conditions of measurement. O_2 cost in healthy adult subjects has ranged from 0.5 to as much as 7.9 ml/L. It has been shown to be increased by a variety of other physiologic stimuli, such as breathing hypoxic gas mixtures,[12] being submerged in water,[7] during muscular exercise[16] and in a wide variety of disease states. Abnormalities shown to cause increased work and O_2 cost are emphysema,[10,13] granulomatous pulmonary diseases,[10,14] a few instances of cardiac disease,[10,12] extreme obesity,[17] and in a few adult asthmatic patients, McGregor and Becklake[13] found approximately a two-fold increase in work and O_2 cost in two such patients. The wide variability was of the same order of magnitude and similar to that of the present study. Akogyeram* measured O_2 cost in nine symptom-free asthmatic children and in an equal number of asthmatic children during an attack. Her mean values were similar to those reported in the present study.

It is worth considering that hypoxemia in asthma may contribute to the increased O_2 cost in symptom-free as well as in symptomatic patients. Hypoxemia is often present even in symptom-free asthmatics because of ventilation perfusion inhomogeneities known to exist in their lungs, and is due to disease of small peripheral airways. Since hypoxemia has been shown to increase O_2 cost,[12] this may have been the case among asthmatic patients in the present study even though arterial O_2 saturations of the three groups were not significantly different. Slight differences that did exist represented a greater variance in O_2 tensions since the latter lie on the plateau of the oxyhemoglobin dissociation curve. O_2 cost, therefore, is apparently highest for those who can *least* afford to pay.

The authors conclude, that although oxygen cost of breathing increases with severity of airways obstruction in asthmatic children, and a relationship exists between it and several frequently used lung function tests,

*Dr. Esther A. Akogyeram. Unpublished data from Freedmen's Hospital, 1968.

we do NOT recommend it for clinical use because of the difficulty in obtaining reproducible measurements. This may be related to the lengthy attention span (15 minutes) required of the child on the apparatus. Leaks at the mouthpiece because of dental malocclusion, more likely to occur during the one minute period of voluntary hyperventilation, occasionally invalidated the test and necessitated another trial.

SUMMARY

Oxygen cost of breathing was measured in 10 healthy children and in 20 asthmatics, six to 15 years of age, 10 of whom were symptomatic and wheezing at the time of study. Measurements consisted of oxygen cost, spirometry and peak flow.

Values for healthy children were similar to those published in the literature for healthy adults, and were unrelated to age or body size.

Oxygen cost of breathing was increased in all asthmatics. It was greater in symptomatic than it was in symptom-free asthmatics.

Oxygen cost correlated negatively with peak flow rate and with maximum voluntary ventilation.

The difficulties encountered in the measurement, however, were such, that oxygen cost is not recommended as a routine pulmonary function test for children.

ACKNOWLEDGEMENT

The authors express gratitude to Dr. Charles W. Moore, Educational Computer Services, Howard University Computer Center, for his assistance in compiling the statistics.

LITERATURE CITED

1. POLGAR, G. and V. PROMADHAT. Pulmonary Function Testing in Children, Techniques and Standards. Philadelphia, WB Saunders Co., 1971, p. 194.
2. CHEHREH, M. N. and R. C. YOUNG, JR., H. VIAENE, C. W. ROSS and R. B. SCOTT. Spirometric Standards for Healthy Inner-City Black Children. Am. J. Dis. Child., 126:159-163, 1973.
3. BARTLETT, R. G., JR. and H. SPECHT. Energy Cost of Breathing Determined with a Simplified Technique. J. Appl. Physiol., 11:84-86, 1957.
4. HARDEN, K. A. and R. G. BARTLETT, JR., H. BARNES, L. REID, A. BARTHAUKUR and W. P. WATERS. Oxygen Cost of Breathing: Part I. Am Rev. Resp. Dis., 85:387-391, 1962.
5. NIE, N. H. and C. H. HULL and J. G. JENKINS. Statistical Package for the Social Sciences, 2nd Ed., New York, McGraw-Hill, 1975. pp. 183, 267, 276, 320.
6. OTIS, A. B. The Work of Breathing—In: Handbook of Physiology Section 3, Respiration Volume I. Washington, D. C. American Physiological Society, 1964. p. 470.
7. BARTLETT, R. G., JR and H. F. BRUBACH and H. SPECHT. Oxygen Cost of Submerged Breathing in the Submerged Resting Subject. J. Appl. Physiol., 11:377-382, 1957.
8. LILJESTRAND, G. Untersuchungen uber die Atmungsarbeit. Skandin. Arch. f Physiol., (Leipz) 35:199-293, 1918.
9. MURRAY, J. R. Oxygen Cost of Voluntary Hyperventilation. J. Appl. Physiol., 14:187-190, 1959.
10. COURNAND, A. and D. W. RICHARDS, Jr., A. R. BADER, R. BADER, M. E. BADER and A. P. FISHMAN. The Oxygen Cost of Breathing. Trans. Assn. Amer. Phys., 67:1967-172, 1954.
11. CAMPBELL, E. J. M. and E. K. WESTLAKE and R. M. CHERNIACK. Simple Methods of Estimating Oxygen Consumption and Efficiency of the Muscles of Breathing. J. Appl. Physiol., 11:303-308, 1957.
12. HOESCHEN, R. J. and L. H. A. GOLD, T. E. CUDDY and R. M. CHERNIACK. Oxygen Cost of Efficiency of the Respiratory System in Hypoxia and in Congestive Heart Failure. Circ. Res., 11:825-831, 1962.
13. MCGREGOR, M. and M. R. BECKLAKE. The Relationship of Oxygen Cost of Breathing to Respiratory Mechanical Work and Respiratory Force. J. Clin. Invest., 40:971-980, 1961.
14. HARDEN K. A. and R. C. YOUNG, JR., C. CARR and J. R. LAUREY. Oxygen Cost of Breathing II. Studies in Patients with Sarcoidosis. Am. Rev. Resp. Dis., 97:1127-1130, 1968.
15. CAMPBELL, E. J. M. and E. AGOSTONI and J. N. DAVIS. The Respiratory Muscles: Mechanics and Neural Control. WB Saunders, Philadelphia 1970. pp. 125-128.