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## Coupling of Ventilation and CO<sub>2</sub> Production during Exercise in Children

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**ABSTRACT.** The purpose of this study was to determine how ventilation ( $\dot{V}_E$ ) and CO<sub>2</sub> production ( $\dot{V}CO_2$ ) in response to exercise change during the growth process in children and teenagers. Dynamic gas exchange responses were measured in two types of studies: 1) 128 healthy children ranging in age from 6 to 18 yr performed progressive exercise tests ("ramp" type protocol) for measurement of the slope of the relationship between  $\dot{V}_E$  and  $\dot{V}CO_2$ — $\Delta\dot{V}_E/\Delta\dot{V}CO_2$ ; and 2) the response characteristics of  $\dot{V}_E$  and  $\dot{V}CO_2$  in the transition between rest and exercise were measured in 11 teenagers and 11 younger children. Gas exchange was measured breath by breath. We found a small but significant decrease in  $\Delta\dot{V}_E/\Delta\dot{V}CO_2$  with increasing body weight ( $r = -0.46, p < 0.05$ ), height, or age (mean slope of 27 in the youngest in 21 in the oldest subjects). The response characteristics of  $\dot{V}_E$  and  $\dot{V}CO_2$  (measured as the time constant of the best-fit exponential response) were longer than for  $\dot{V}O_2$  in both younger children and teenagers; but the time constants for  $\dot{V}_E$  and  $\dot{V}CO_2$  were each approximately 30% faster in younger children compared to teenagers. In addition, end-tidal PCO<sub>2</sub> during exercise was significantly lower in the younger subjects (mean value of 39.6 torr) compared to the teenagers (mean value of 43.5 torr). The results suggest that the process of respiratory control in exercise matures to a small degree during childhood in that PCO<sub>2</sub> may be regulated at lower levels in younger children and there may be growth-related differences in the relative amounts of CO<sub>2</sub> that can be stored in tissues. (*Pediatr Res* 21: 568–572, 1987)

### Abbreviations

$\dot{V}_E$ , ventilation  
 $\dot{V}CO_2$ , CO<sub>2</sub> output  
 $\dot{V}O_2$ , O<sub>2</sub> uptake  
AT, anaerobic threshold  
RCP, respiratory compensation point

Babies have different respiratory control than do adults. For example, the arterial PCO<sub>2</sub> is regulated at lower levels, the pattern of breathing is erratic and marked by periodicity, and the ventilatory response to hypoxia and hyperoxia differs from the adult (1, 2). Thus, while it is apparent that the respiratory control apparatus undergoes maturation in the normal human being,

there is a dearth of information on the ontogeny of these mechanisms during childhood. We hypothesized, therefore, that maturation of respiratory control could be detected and characterized during growth in children.

In adults, it is known that the degree of  $\dot{V}_E$  is linked to the metabolic production of CO<sub>2</sub> (3–8). This linkage is marked by homeostasis for CO<sub>2</sub> concentration in the blood, such that PCO<sub>2</sub> is kept within a very narrow range despite large fluctuations in the  $\dot{V}CO_2$  as occur during exercise. But the child is faced with problems not encountered by the mature individual—while the ventilatory apparatus in both the adult and child must quickly respond to the increased CO<sub>2</sub> load induced by physical activity, the child must, in addition, deal with greater CO<sub>2</sub> loads imposed by the increasing body size of the growth process itself. This research is focused on the precise linkage between  $\dot{V}CO_2$  and  $\dot{V}_E$  during exercise in growing children.

This was done by first examining the dynamic  $\dot{V}_E$  and  $\dot{V}CO_2$  response kinetics during progressive cycle ergometer exercise in a large group of children and teenagers. Following this, in a separate experiment, detailed analysis of the response kinetics in the transition between rest and constant work rate exercise was done in a small group of children and teenagers. These types of studies utilizing breath-by-breath analysis of gas exchange and dynamic exercise protocols are particularly useful in children—a population in which more invasive methods are unfeasible.

### METHODS

**Population.** All subjects were volunteers obtained through local schools and community organizations. Obese children, children with a history of chronic disease, and children not allowed to participate in normal physical education programs at school were excluded from the study. No attempt was made to select subjects who were particularly active; *i.e.* there was no recruitment through physical education or sports programs.

All children were within the normal range for height and weight by reference tables of the National Center for Health Statistics. The subjects were predominantly of the middle socioeconomic class. Eighty-six percent of the subjects were Caucasian; the remainder consisted of Oriental, Hispanic, and black children. This project was approved by the Human Subjects Committee of Harbor-UCLA Medical Center. Informed consent was obtained from each subject and, when appropriate, from a guardian before participation.

Two types of exercise protocols were used: a) a progressive exercise test for which 128 children (68 boys and 60 girls, range 6–18 yr old) comprised the sample, b) a constant work rate test for which 11 younger children (five boys and six girls, range 7–10 yr old) and 11 teenagers (five boys and six girls, range 15–18 yr old) comprised the sample. These latter subjects were randomly chosen from the larger group. In addition, we analyzed the relationship between  $\dot{V}CO_2$  and work rate from 15 ramp

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protocols randomly chosen from children ranging in age from 6 to 8 yr and from 15 ramp protocols randomly chosen from normal adults ranging in age from 18 to 20 yr previously tested in our laboratory.

**Measurement of gas exchange.** The subjects breathed through a low-impedance turbine volume transducer for measurement of inspiratory and expiratory volumes. Dead-space of the mouth-piece and turbine device was 90 ml. Respired  $PO_2$  and  $PCO_2$  were determined by mass spectrometry from a sample drawn continuously from the mouthpiece at 1 ml/s. The electrical signals from these devices underwent analog to digital conversion for the on-line breath to breath computation of  $\dot{V}O_2$  (STPD),  $\dot{V}CO_2$  (STPD), and  $\dot{V}_E$  (BTPS) as previously described (3). The external deadspace ventilation was subtracted in the calculation of  $\dot{V}_E$ . The data from each test were displayed on line and stored on digital tape for subsequent analysis.

**Progressive exercise protocol.** The protocol consisted of a ramp pattern of increasing work rate (9, 10) utilizing an electromagnetically braked cycle ergometer. Subjects began with a minimum of a 3 min warm-up cycling at 0 W (unloaded) work rate. The work rate was then continuously increased at a constant rate. The increase in work rate per min was selected so that the total exercise duration would be greater than 6 min and less than 14 min. The mean time for the test (not counting the warm-up) was 9 min. The children were instructed to raise a hand when they could not continue, and on this signal, the work rate was reduced to 0 W. The children were actively encouraged throughout the test.

The children were instructed to maintain as constant a pedaling rate as possible between 50 and 70 rpm. A pedaling rate meter was in full view of each subject, and a servomechanism in the electronic braking system of the ergometer maintained the work rate performed to an accuracy of 1% within a range of pedaling rates of 50–90 rpm.

The progressive exercise tests were used to measure the AT. The AT indicates the point during exercise at which lactate concentrations begin to increase in the blood. As  $CO_2$  is liberated by the bicarbonate buffering of the lactic acid,  $\dot{V}_E$  and  $\dot{V}CO_2$  increase out of proportion to the increase in  $\dot{V}O_2$ , thereby allowing the noninvasive determination of the AT (11). In each subject, the AT was measured by finding the  $\dot{V}O_2$  above which  $\dot{V}_E/\dot{V}O_2$  and  $P_{ET}O_2$  increased without an increase in  $\dot{V}_E/\dot{V}CO_2$  or a decrease in  $P_{ET}CO_2$ , as previously described (9).

**Constant work rate exercise protocol.** The work rate for the constant work rate protocols was taken as 75% of the work rate corresponding to the subject's AT. The mean work rate was 64 W for the teenagers and 22 W for the younger children. When normalized to body weight, the rest to steady-state exercise

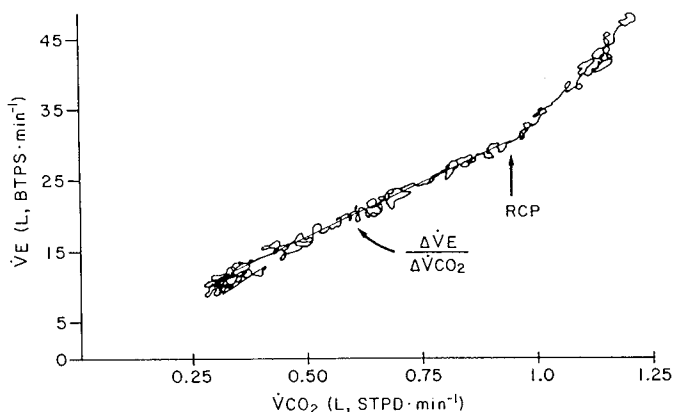


Fig. 1. Breath by breath measurement of  $\dot{V}_E$  as a function of  $\dot{V}CO_2$  during a progressive exercise protocol (ramp test) in an 8-yr-old child. Solid line indicates the best-fit line from 1-min after the onset of the ramp to the RCP (see text) as indicated. The slope of the line is given as  $\Delta\dot{V}_E/\Delta\dot{V}CO_2$ .

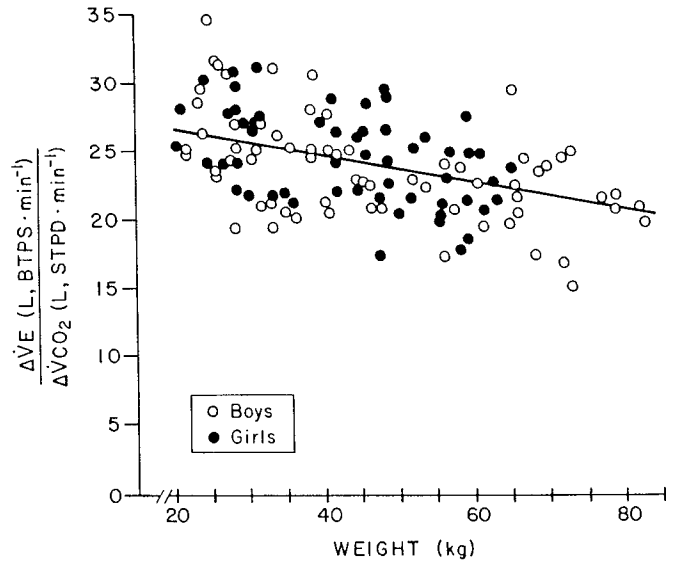


Fig. 2. Slope of the  $\dot{V}_E$ - $\dot{V}CO_2$  relationship as a function of body weight in 128 normal subjects ranging in age from 6 to 18 yr. Boys are represented by open circles; girls by closed circles. There was a small but significant negative correlation between the slope and body weight (see text).

increase in  $\dot{V}O_2$  did not differ significantly between the younger children (mean, 16 ml  $O_2$   $min^{-1}$   $kg^{-1}$ ) and the teenagers (mean, 13 ml  $O_2$   $min^{-1}$   $kg^{-1}$ ). In eight of the teenagers, constant work rate tests were also performed to study gas exchange dynamics at 20 W to match the work rate performed by the younger children.

Each subject performed a minimum of six rest-to-constant work rate transitions. Exercise periods were 6 min each, and heart rate,  $\dot{V}O_2$ ,  $\dot{V}_E$ , and  $\dot{V}CO_2$  returned to the preexercise resting values before a repetition was performed. The subjects began exercise with the activation (at the end of an exhalation) of a green light signal; there was no voice command. To avoid the expenditure of energy required to overcome the inertia of the fly-wheel at the start of exercise, the ergometer fly-wheel was motorized and maintained at a rate of 60 rpm until the onset of pedaling. When the subject starts to pedal, the motor maintaining the fly-wheel is turned off.

**Data analysis.** 1) Progressive exercise protocol—a graphical presentation of  $\dot{V}_E$  (liter, BTPS  $min^{-1}$ ) as a function of  $\dot{V}CO_2$  (liter, STPD  $min^{-1}$ ) (Fig. 1) was used to determine the point at which  $\dot{V}_E$  increased out of proportion to  $\dot{V}CO_2$ —the RCP. This occurs at higher work rates than the AT at which point  $\dot{V}_E$  is still coupled to  $\dot{V}CO_2$ . Linear regression techniques were then used to find the best-fit line from the data starting at 60 s after the onset of exercise to the RCP, and the slope ( $\Delta\dot{V}_E/\Delta\dot{V}CO_2$ ) of the best-fit line was calculated for each subject. The slopes were then plotted as a function of body weight (Fig. 2), height, and age, and the linear regression and correlation coefficients were determined by standard techniques. The data were also analyzed using polynomial, logarithmic, and exponential fitting models. In 15 younger children and in 15 young adults, the relationship between  $\dot{V}CO_2$  and work rate during ramp protocols was quantified. This was done by using linear regression techniques to find the slope ( $\Delta\dot{V}CO_2/\Delta WR$ ) of the best-fit line below the subjects' AT.

2) Constant work rate protocol— $\dot{V}CO_2$  and  $\dot{V}_E$  kinetics [following the cardiodynamic phase (4, 12)] were studied at a work rate which was 75% of the subject's AT. The time constant ( $\tau$ ) of the response (Fig. 3) was determined from the following equation (4, 12):

$$\Delta\dot{V}(t) = \Delta\dot{V}_{ss} \times (1 - e^{-t/\tau})$$

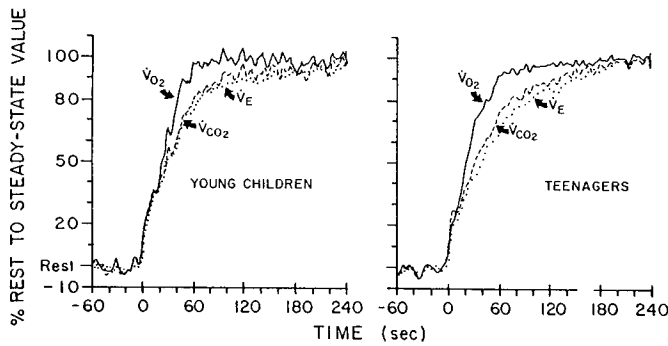


Fig. 3. Kinetics of  $\dot{V}O_2$ ,  $\dot{V}CO_2$ , and  $\dot{V}_E$  in children and teenagers. The response of  $\dot{V}O_2$  (solid line),  $\dot{V}CO_2$  (dashed line), and  $\dot{V}_E$  (dotted line) are shown. Each line represents the averaged, superimposed data of either the 11 younger children or the 11 teenagers. Time 0 on the x-axis indicates the onset of constant work rate exercise. In order to compare the gas exchange responses of the different sized groups, the y-axis represents the gas exchange response as a percent of the rest to steady-state exercise difference. The responses of  $\dot{V}CO_2$  and  $\dot{V}_E$  were slower than for  $\dot{V}O_2$  in both younger children and the teenagers; however, the responses of  $\dot{V}_E$  and  $\dot{V}CO_2$  were somewhat faster in the younger children compared to the teenagers.

where  $\Delta\dot{V}(t)$  is the increase in either  $\dot{V}_E$  or  $\dot{V}CO_2$  above the prior control values at any exercise time ( $t$ );  $\Delta\dot{V}_{ss}$  is the difference between rest and steady-state exercise  $\dot{V}$ ; and  $\tau$  is the time constant or the time to reach 63%  $[(1 - 1/e) \times 100\%]$  of  $\Delta\dot{V}_{ss}$ .

The fitting window was between 20 to 120 s after the onset of exercise, and a best-fit exponential (characterized by  $\tau$ ) was found using iterative techniques (4). The model calculated a delay representing the difference in time between the onset of exercise and the extrapolated onset of the best-fit exponential. The mean end-tidal  $PCO_2$  during the steady-state exercise was measured in each subject.

3) Statistical analysis—Independent  $t$  tests were used to compare the time constants for  $\dot{V}_E$  and  $\dot{V}CO_2$  in the teenagers with those of the younger children. In the teenagers, dependent  $t$  tests were used to compare the time constants for  $\dot{V}_E$  and  $\dot{V}CO_2$  at the higher work rate with those obtained at the lower work rate. Statistical significance was taken at the  $p < 0.05$  level.

## RESULTS

**Progressive exercise protocol.** Linear regression analysis demonstrated that the slope of the  $\dot{V}_E$ - $\dot{V}CO_2$  relationship decreased to a small but significant degree with increasing body weight (Fig. 2). The regression line showed that the average values were 27 for the smallest subjects and 21 for the largest subjects. The data were also analyzed using polynomial and exponential regressions with no improvement in correlation. Similar linear regression correlations were observed for  $\Delta\dot{V}_E/\Delta\dot{V}CO_2$  as a function of age and body weight. There were no significant differences in these values between the boys and girls of the study. The linear regression equations ( $Y$  is the slope,  $\Delta\dot{V}_E/\Delta\dot{V}CO_2$ ), SE estimates ( $S_{Y,X}$ ), and  $r$  were as follows:

1) for weight (kg)

$$Y = -0.099 \times \text{weight} + 28.7, S_{Y,X} = 3.26, r = -0.46, p < 0.05$$

2) for height (cm)

$$Y = -0.096 \times \text{height} + 38.6, S_{Y,X} = 3.17, r = -0.50, p < 0.05$$

and 3) for age (yr)

$$Y = -0.474 \times \text{age} + 30.1, S_{Y,X} = 3.26, r = -0.45, p < 0.05.$$

There was no statistical difference between  $\Delta\dot{V}CO_2/\Delta WR$  in the 15 young adults [mean value  $11.7 \pm 2.5$  (SD)  $ml CO_2 min^{-1}$

$W^{-1}$ ] compared to the younger children ( $12.5 \pm 2.3 ml CO_2 min^{-1} W^{-1}$ ).

**Constant work rate exercise protocol** (Table 1). The time constants for  $\dot{V}CO_2$  were significantly shorter in the 11 younger children compared to the 11 teenagers. Similarly, time constants for  $\dot{V}_E$  were significantly shorter in the 11 younger children compared to the 11 teenagers. The mean end-tidal  $PCO_2$  during exercise was significantly lower in the 11 younger children compared to the 11 teenagers. There were no significant differences in the steady-state respiratory exchange ratios during rest or exercise between the younger children and teenagers (mean resting  $r$  in younger children was 0.92 and in the teenagers, 0.94; mean exercise  $r$  in younger children was 0.92 and in the teenagers, 0.94).

The difference in time constants was not work rate dependent since the time constants for  $\dot{V}CO_2$  in the teenagers did not differ between the higher work rate [mean  $52 \pm 6$  s (SEM)] and lower work rate [mean  $54 \pm 7$  s (SEM)]. Similarly, the time constants for  $\dot{V}_E$  in the teenagers at the higher work rate [mean  $56 \pm 2$  s (SEM)] did not differ significantly from the lower work rate [mean  $64 \pm 8$  s (SEM)].

## DISCUSSION

The slope of the  $\dot{V}_E$ - $\dot{V}CO_2$  relationship during exercise was to a small but significant degree greater in younger children compared to teenagers (Fig. 2), and the time constants for  $\dot{V}_E$  and  $\dot{V}CO_2$  were faster in younger children compared to teenagers (Table 1). These were somewhat surprising results for two reasons. First, we have previously found other dynamic relationships of progressive exercise (*e.g.* work efficiency, derived from the relationship between  $\Delta\dot{V}O_2$  and  $\Delta\text{work rate}$ ) to be independent of age or body size (19). Second, we had also observed that the time constant for oxygen uptake ( $\tau\dot{V}O_2$ ) was independent of age or body size in children (13).

The relationship between  $\dot{V}_E$  and  $\dot{V}CO_2$  is given by a modification of the alveolar gas equation:

$$\dot{V}_E = [863 \times PaCO_2^{-1} \times (1 - V_D/V_T)^{-1}] \times \dot{V}CO_2$$

where  $\dot{V}_E$  is ventilation,  $\dot{V}CO_2$  is  $CO_2$  production,  $PaCO_2$  is arterial  $CO_2$  tension, and  $V_D/V_T$  is deadspace to tidal volume ratio. As can be seen, the factors affecting the relationship between  $\dot{V}_E$  and  $\dot{V}CO_2$  will be the  $PaCO_2$  and the  $V_D/V_T$ . The equation implies that as the regulated level of  $PCO_2$  decreases, more ventilation will be required for a given increase in  $\dot{V}CO_2$ . We estimated the  $PaCO_2$  with measurements of  $P_{ET}CO_2$  during steady-state exercise (direct measurements of arterial  $PCO_2$  during exercise are not available in children), and lower values of end-tidal  $PCO_2$  were found in the younger children (Table 1). Steeper slopes in the younger children may be a manifestation of a lower  $CO_2$  set-point. Since the  $CO_2$  produced per increase in work rate is independent of age, our data suggest that younger children breathe more for a given increase in metabolic demand than do teenagers.

Relatively larger deadspace ventilation (both the external and physiologic deadspace) could also account for increased slopes in the younger subjects, but previous studies suggest that this is not a major factor. First, as noted in the "Methods" section, the external deadspace ventilation is subtracted from the total ventilation in our calculation of  $\dot{V}_E$ . Moreover, it has been demonstrated that when the external deadspace ventilation is subtracted, the relationship between  $\dot{V}_E$  and  $\dot{V}CO_2$  is virtually unaffected even when the size of the external deadspace is varied experimentally (14). Finally, previous work in children using a variety of indirect measurements indicate that  $V_D/V_T$  during exercise is constant throughout childhood (15-17).

Recently, Brischetto *et al.* (18) found that  $\Delta\dot{V}_E/\Delta\dot{V}CO_2$  was larger in older adults (aged 67-79 yr) than in younger adults (22-37 yr). The mean value of the slope in the older individuals was similar to that obtained in the youngest children in our study. The difference in the ventilatory response was attributed to

Table 1. Age, wt, time constants for  $\dot{V}O_2$ ,  $\dot{V}CO_2$ , and  $\dot{V}_E$ , preexercise and mean exercise  $\dot{V}O_2$ , and mean exercise end-tidal  $CO_2$  in 11 younger children and 11 teenagers

Gender	Age (yr)	Wt (kg)	$\tau\dot{V}O_2$ (s)	$\tau\dot{V}CO_2$ (s)	$\tau\dot{V}_E$ (s)	Preexercise $\dot{V}O_2$ (liter/min)	Mean exercise $\dot{V}O_2$ (liter/min)	Mean exercise $P_{ET}CO_2$ (mm Hg)
F	10.1	30.5	29.2	44.2	45.8	0.25	0.85	41
F	9.2	26.0	25.1	41.7	46.8	0.21	0.62	37
F	8.4	27.2	25.1	48.8	52.8	0.25	0.85	39
F	7.7	23.3	21.8	32.3	31.1	0.24	0.60	40
F	8.2	26.4	31.9	47.9	55.0	0.23	0.51	43
F	9.5	33.4	24.7	39.4	25.9	0.21	0.51	40
M	8.3	31.8	23.2	23.1	18.3	0.19	0.63	41
M	8.2	28.6	30.4	47.6	56.0	0.26	0.64	37
M	7.8	26.1	23.7	37.7	43.9	0.11	0.77	39
M	9.8	31.7	26.9	31.7	32.0	0.25	0.85	39
M	7.7	27.7	28.5	44.0	46.6	0.20	0.63	40
F	18.0	60.0	32.5	58.0	60.0	0.25	1.32	46
F	17.8	92.0	37.0	60.3	55.9	0.28	1.55	43
F	18.7	70.4	32.9	51.9	55.1	0.38	0.95	43
F	18.1	63.2	21.0	40.0	45.3	0.40	1.50	47
F	15.3	59.0	34.7	55.4	57.5	0.31	1.21	44
F	18.0	60.0	31.3	58.4	68.5	0.31	1.20	44
M	16.1	56.4	27.6	49.5	55.6	0.25	1.00	38
M	17.1	56.4	24.6	48.4	44.0	0.35	1.20	43
M	18.1	64.8	21.7	47.2	37.7	0.30	0.96	41
M	18.3	78.6	25.1	46.6	55.8	0.25	1.30	43
M	18.0	64.5	22.6	39.0	41.5	0.40	0.98	46
Younger children								
Mean	8.6*	28.4*	26.4	39.9*	41.3*	0.22*	0.68*	39.6*
SD	0.9	3.1	3.2	8.1	12.5	0.04	0.13	1.7
Teenagers								
Mean	17.5	65.9	28.3	50.4	52.4	0.32	1.20	43.5
SD	1.0	10.8	5.6	7.2	9.2	0.06	0.21	2.5

\* Significantly differed from teenagers.

increased  $V_D/V_T$  which is known to occur in elderly subjects (19). The results of our study, combined with those of Brischetto *et al.* (18), suggest that the  $\Delta\dot{V}_E/\Delta\dot{V}CO_2$  is at its minimum beginning late in adolescence and extending through middle age. This may represent a period of ventilatory control and function when  $CO_2$  excretion in man is most efficient.

When the work rate input is below the subject's AT, the gas exchange dynamics following the onset of exercise are normally well described by a first-order exponential (after the early cardiodynamic phase) (4, 20). The response characteristics become more complex for work rates above the AT (11), and the present study was designed so that the work rate input was below the AT for both the teenagers and young children. In adults, kinetics for  $\dot{V}O_2$  are known to be faster than for  $\dot{V}CO_2$  (4, 11), reflecting the much larger storage capacity for  $CO_2$  relative to  $O_2$  (21). Similarly, we found that  $\dot{V}CO_2$  and  $\dot{V}_E$  kinetics were slower than  $\dot{V}O_2$  kinetics in both the teenagers and younger children.

In a previous study (13), we found that for the same rest-to-exercise increase in metabolic demand ( $\Delta\dot{V}O_2/kg$ ), younger children had the same time constant of  $\dot{V}O_2$  as did teenagers. In contrast, the analysis of  $\dot{V}CO_2$  and  $\dot{V}_E$  kinetics show them to be more rapid in younger children than in teenagers (Table 1). The differences in time constants are unlikely to be attributable to nonlinearities of the  $\dot{V}_E$  and  $\dot{V}CO_2$  response since these values were the same at two different work rates in the teenage subjects.

The slower responses in the teenagers means that less  $CO_2$  (per kg body weight) was exhaled into the atmosphere in the transition from rest to exercise. What is the fate of this "unaccounted for"  $CO_2$ ? One possibility is that in exercise transitions, younger children actually produce less  $CO_2$  per  $O_2$  consumed at the cellular level than do teenagers. However, this is highly unlikely

as the steady-state values for R during rest and exercise were the same in children and teenagers suggesting the same patterns of substrate utilization.

A more likely explanation is that greater amounts of  $CO_2$  are stored in the teenagers compared to the younger children. A major site for rapid  $CO_2$  storage is the blood (21), and teenagers have generally higher levels of hemoglobin than do younger children (22). In addition, it is not known whether  $CO_2$  storage capacity of tissues such as muscle and fat are different in younger children compared to teenagers. In the presence of relatively smaller  $CO_2$  stores,  $CO_2$  originating in the exercising muscle cells may saturate the tissue stores more quickly to the new venous  $PCO_2$  value and reach the central and pulmonary circulation faster as well, thereby accounting for the more rapid  $\dot{V}_E$  kinetics in the younger children. Previous studies from this laboratory have demonstrated that ventilatory responses can be modified by changing the amount of  $CO_2$  stored (*e.g.* by hyperventilation) (23).

The results of this study suggest that the complex process of respiratory control does undergo gradual change during childhood. Differences in body stores for  $CO_2$  may explain the observed differences in  $\dot{V}_E$  and  $\dot{V}CO_2$  kinetics, and, for reasons as yet unclear, younger children appear to regulate  $CO_2$  at lower levels. However, the magnitude of the observed differences between the youngest and oldest subjects was small ( $\Delta\dot{V}_E/\Delta\dot{V}CO_2$  decreased by 19%;  $\tau\dot{V}CO_2$  increased by 31%) relatively to the 4-fold increase in body mass suggesting that the respiratory control mechanisms are close to maturity early in life. It seems, then, that the coupling of cellular  $CO_2$  production to ventilation is well regulated throughout childhood, and may be viewed as one of the homeostatic mechanisms of the growth process itself.

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## Erratum

An error has been found in the recently published article by Lee Frank titled “Oxygen Toxicity in Neonatal Rats: the Effect of Endotoxin Treatment on Survival during and post-O<sub>2</sub> Exposure (*Pediatr Res* 21:109–115, 1987).

On page 110, top of column 2, the endotoxin dosage used for the electron micrographic study should read: **neonatal rats treated with saline or endotoxin in progressive doses of 10 µg/kg at 0 time, 50 µg/kg at 24 h, 250 µg/kg at 72 h, and 1.25 mg/kg at 72 h of O<sub>2</sub> exposure** instead of “neonatal rats treated in the same manner as described above with saline or endotoxin. . . .”

The results obtained in the survival and light morphometric studies were similar with either endotoxin regimen (20 µg/kg at 0 time and 40 µg/kg at 24 h of O<sub>2</sub> exposure, or the 4 progressive dose regimen).