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Oxygen uptake dynamics during high-intensity exercise in children and adults

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ARMON, YAACOV, DAN M. COOPER, RICARDO FLORES, STEFANIA ZANCONATO, AND THOMAS J. BARSTOW. *Oxygen uptake dynamics during high-intensity exercise in children and adults.* J. Appl. Physiol. 70(2): 841–848, 1991.—We hypothesized that the O_2 uptake ($\dot{V}O_2$) response to high-intensity exercise would be different in children than in adults. To test this hypothesis, 22 children (6–12 yr old) and 7 adults (27–40 yr old) performed 6 min of constant-work-rate cycle-ergometer exercise. Sixteen children performed a single test above their anaerobic threshold (AT). In a separate protocol, six children and all adults exercised at low and high intensity. Low-intensity exercise corresponded to the work rate at 80% of each subject's AT. High-intensity exercise (above the AT) was determined first by calculating the difference in work rate between the AT and the maximal $\dot{V}O_2$ (Δ). Twenty-five, 50, and 75% of this difference were added to the work rate at the subject's AT, and these work rates were referred to as 25%Δ, 50%Δ, and 75%Δ. For exercise at 50%Δ and 75%Δ, $\dot{V}O_2$ increased throughout exercise (O_2 drift, linear regression slope of $\dot{V}O_2$ as a function of time from 3 to 6 min) in all the adults, and the magnitude of the drift was correlated with increasing work rates in the above-AT range ($r = 0.91$, $P < 0.0001$). In contrast, no O_2 drift was observed in over half of the children during above-AT exercise. The O_2 drifts were much higher in adults (1.76 ± 0.63 ml $O_2 \cdot kg^{-1} \cdot min^{-2}$ at 75%Δ) than in children (0.20 ± 0.42, $P < 0.01$). The average O_2 cost (ml $O_2 \cdot min^{-1} \cdot W^{-1}$) was greater in children at all work rates (11.5 ± 1.2 at 75%Δ in children, 9.6 ± 1.0 at 75%Δ in adults; $P < 0.01$), and the pattern of the response was different in the two groups. These data suggest that a process of maturation takes place in the integrated adjustment to exercise as reflected in the dynamics of $\dot{V}O_2$.

gas exchange; anaerobic threshold; oxygen drift; oxygen cost; growth; development

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CARDIORESPIRATORY AND METABOLIC RESPONSES to exercise are regulated in healthy children to maintain cellular homeostasis in a period characterized by rapid change in body size and organ development (7). Although the maximal O_2 uptake ($\dot{V}O_{2\,max}$) and anaerobic threshold (AT) change in almost direct proportion with body weight, other responses, such as the time course of the rise in O_2 uptake ($\dot{V}O_2$) during moderate-intensity (below-AT) constant-work-rate exercise, are the same in children and young adults (9). The dynamics of ventilation ($\dot{V}E$) and CO_2 output ($\dot{V}CO_2$) after the onset of moderate-intensity exercise are faster in children than in adults (10), but the differences in $\dot{V}E$ and $\dot{V}CO_2$ are not nearly as great as the discrepancy in age and body size.

The mechanisms of these growth-related differences are not fully understood but may result from factors such as differences in CO_2 storage capacity and cellular metabolic adjustment to sudden increases in energy demand (10, 29). These responses are particularly important during high-intensity (above-AT) exercise when the relationship between O_2 delivery and tissue metabolic demand reaches physiological limitations. The goal of this study was to determine whether growth-related differences in the $\dot{V}O_2$ response existed for work performed in the high-intensity range. Finding such differences could be helpful in determining the mechanism of maturation of cellular energy metabolism.

Previous studies of the $\dot{V}O_2$ response to constant-work-rate low-intensity exercise have demonstrated that the steady-state $\dot{V}O_2$ is achieved by 3 min (~6 time constants) (16). However, when adults perform constant-work-rate exercise in the high-intensity range, the difference between the $\dot{V}O_2$ at 6 and 3 min is positive, indicating that the attainment of a steady state is delayed if it is ever achieved (3, 23). The high correlation between lactate concentration and the magnitude of the O_2 drift in adults (as indicated by the slope in the $\dot{V}O_2$ response between 3 and 6 min of exercise) prompted speculation that the O_2 drift was, in fact, related to lactate metabolism (3, 23).

Whether an O_2 drift existed in children was not known, but there were reasons to speculate that $\dot{V}O_2$ responses to high-intensity exercise in children would be different from those in adults. Children reach lower lactate concentrations and are less able to sustain exercise in the high-intensity range than are adults (1). These observations suggest that the magnitude of the O_2 drift would likely be lower in children than in adults. This hypothesis was tested by examining the dynamic $\dot{V}O_2$ response to exercise in a group of adults and children. Studies were done over a range of work rates from below to above the subjects' AT. Although methodological constraints prohibit direct measurements of cellular energy metabolism in children (such as might be obtained by muscle biopsy), there is growing evidence that gas exchange measured at the mouth indirectly reflects cellular function (5, 8, 27).

METHODS

Study Population

Twenty-two healthy children [12 females and 10 males, age range 6–12 yr, mean 10.0 ± 2.2 (SD); mean body weight 33.0 ± 11.1 kg] and seven healthy adult males (27–40 yr of age, mean 32 ± 5; mean body weight 70 ± 8 kg) participated in the study. Informed consent was obtained from each subject or, when appropriate, a parent.

Protocols

The first protocol consisted of an incremental cycle-ergometer exercise. Each subject performed a progressive exercise test to the limit of tolerance by use of a ramp pattern of increasing work rate as described previously (11, 32). This was used to determine the peak $\dot{V}O_2$ or $\dot{V}O_{2\,max}$ and the AT. The AT corresponds to the metabolic rate ($\dot{V}O_2$) above which anaerobic metabolism supplements aerobic energy production. Lactic acidosis then occurs, and its noninvasive determination has been previously described (30, 31). The difference between work rates corresponding to the AT and to the $\dot{V}O_{2\,max}$ (Δ) was also determined from the ramp protocols.

The second protocol consisted of constant work rate exercise. Sixteen children performed a single ergometer exercise test. Our goal was to select a work rate that was above the AT corresponding to 50% of the difference between $\dot{V}O_{2\,max}$ and the AT (e.g., 50%Δ means the sum of the work rate at the AT and 50% of the work rate difference between the AT and $\dot{V}O_{2\,max}$). However, we found that some children were unable to complete 6 min of exercise at this work rate, and in others the lack of an apparent slope of $\dot{V}O_2$ led us to believe that the chosen work rate was not sufficiently high for the particular subject. (Six minutes of exercise is about the limit of tolerance for many subjects exercising in the high-intensity range but still provides sufficient data for linear regression analysis.) In these cases, the children repeated the studies at appropriately higher or lower work rates and only the repeated data were included in the study. All in all, work rates ranged from 27 to 100%Δ in these 16 children.

Based on the analysis of the initial 16 children, we then studied individual adults and children who performed constant-work-rate ergometer exercise at a series of exercise intensities. All the adults and six additional children (age range 6–12; 5 males) performed constant-work-rate ergometry for 6 min corresponding to 80% AT and to 25%Δ, 50%Δ, and 75%Δ. For example, if the subject's AT corresponded to 100 W and if the Δ was 100 W, then the 25%Δ work rate would be chosen as 125 W. Not all subjects performed all four protocols. A 3-min period of unloaded pedaling preceded the constant-work exercise.

Gas Exchange Measurement

The subjects breathed through a mouthpiece connected to a low-impedance turbine volume transducer and a breathing valve with a combined dead space of 90 ml. O_2 and CO_2 tensions were determined by mass spectrometry from a sample drawn continuously from the mouthpiece at 1 ml/s. The inspired and expired volumes and gas tension signals underwent analog-to-digital conversion, from which $\dot{V}O_2$ (STPD), $\dot{V}CO_2$ (STPD), and $\dot{V}E$ (BTPS) were calculated on-line breath by breath as previously described (2). The breath-by-breath data were then interpolated to 1-s time intervals.

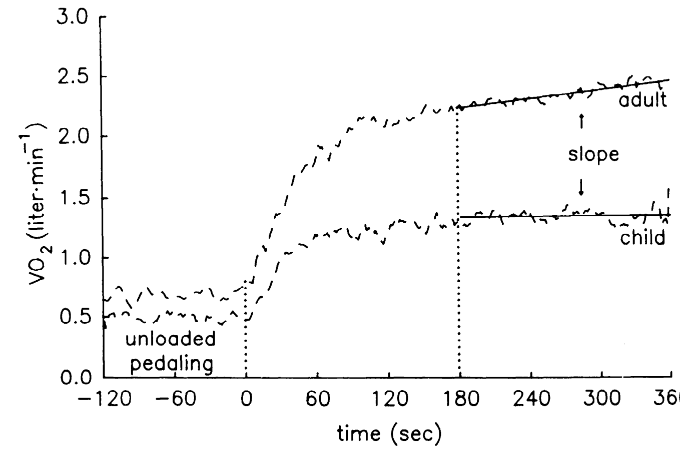

FIG. 1. $\dot{V}O_2$ response to high-intensity exercise (50%Δ) in a representative adult and child. A 6-min constant-work-rate exercise started at *time 0*. Slope was calculated using linear regression techniques to correlate $\dot{V}O_2$ with time between 3rd and 6th min of exercise.

Data Analysis

Normalization. To compare $\dot{V}O_2$ responses of different-sized subjects, we used two strategies.

WORK RATES. The effort of each subject was scaled to his/her metabolic capability by using the physiological landmarks AT and $\dot{V}O_{2\,max}$ rather than absolute work rate. We used the work intensity to connote the relative work rate as %AT or %Δ. In addition, the work rate divided by body weight provided a numerical means to compare the work performed by adults and children.

O_2 UPTAKE PER KILOGRAM. The breath-by-breath $\dot{V}O_2$ data were divided by body weight for each subject.

O_2 drift. We used linear regression techniques to correlate $\dot{V}O_2$ with time between the 3rd and 6th min of exercise. The slope of the best-fit line was considered to be positive if the 95% confidence interval was >0. The slopes were normalized to body weight (ml · min^{-2} · kg^{-1}), and the normalized slopes were defined as the O_2 drift. Typical responses to high-intensity constant-work-rate exercise in an adult and child are shown in Fig. 1. As can be seen in these examples, the linear model was a good description of the $\dot{V}O_2$ response in the 3- to 6-min portion of the exercise study.

O_2 cost. To calculate the O_2 cost, the breath-by-breath data were scaled to work performed (in watts) for each subject at each work rate. This was done by finding the difference between $\dot{V}O_2$ at *time t* during exercise and the preexercise $\dot{V}O_2$ (baseline, unloaded pedaling). This value was then divided by the work rate (in watts). Careful calibration of our ergometers revealed that unloaded cycling represented 12 W for the adults' ergometer and 7 W for the children's ergometer. Thus these respective values were subtracted from the constant work rate value to correctly describe the $\Delta\dot{V}O_2$-Δ watt relationship. To exclude mechanical differences between the two ergometers that might contribute to differences in the responses between the two groups, one adult subject repeated the exercises on the children's ergometer at work rates below and above the AT. Analysis of his data showed virtually

no difference between the two ergometers in the subject's $\dot{V}O_2$ response.

Mathematical modeling of responses. In addition to the linear regression analysis of the $\dot{V}O_2$ response from 3 to 6 min of constant exercise, we attempted to characterize the whole response (i.e., from the onset of exercise through the 6th min). When exercise is performed below a subject's AT, the $\dot{V}O_2$ response can be modeled by a single-exponential equation (16)

$$\text{net } \dot{V}O_2(t) = \Delta\dot{V}O_2 \times [1 - e^{-(t/\tau)}] \qquad (1)$$

where net $\dot{V}O_2(t)$ is the increase in $\dot{V}O_2$ above the baseline (during unloaded pedaling) at any given time (t) after onset of exercise, $\Delta\dot{V}O_2$ is the difference between baseline and the steady-state $\dot{V}O_2$ (asymptote), and τ is the time constant of the response (the time to reach 63% of $\Delta\dot{V}O_2$). For moderate-intensity exercise, τ can be well fit using the first 2 min of data (16). Because observations from adult studies show a linear component of the O_2 response for high-intensity exercise (3), we modified the above equation by adding a linear term

$$\text{net } \dot{V}O_2(t) = \Delta\dot{V}O_2 \times [1 - e^{-(t/\tau)}] + s \times t \qquad (2)$$

where s represents the coefficient of the linear term. Nonlinear iterative curve-fitting techniques were used to calculate the parameters of this model (i.e., τ and s) for each subject at each work rate (3). In addition to the analysis of each curve for each subject, we used the noise-reducing technique of superimposing and averaging values. In this manner we could graphically display the differences between adults and children for a given work intensity (i.e., 80%AT, 25%Δ, 50%Δ, and 75%Δ).

The finding of a linear component for high-intensity exercise complicates the use of τ to compare the temporal response dynamics of $\dot{V}O_2$ in children and adults. If an asymptote (steady state) of $\dot{V}O_2$ is not achieved, selection of an end point for determining temporal responses is necessarily arbitrary. In the particular case of the $\dot{V}O_2$ cost for the highest-intensity work rates where both adults and children reached the same value by the 6th min of exercise, we calculated the half time ($t_{1/2}$) of the response (i.e., the time required to achieve one-half of the baseline to end-exercise value). The $t_{1/2}$ was then used to compare the overall speed of response between the adults and children in this case.

Statistical Analysis

For the 16 children who performed a single high-intensity exercise test, linear regression was used to determine whether there was a correlation between the work rate (as work rate per kilogram) and the magnitude of the O_2 drift (as the slope of the best-fit line). In the remaining children and adults who completed the several work rates, analysis of variance and modified t tests were used to compare the effect of different work intensities within each group and the differences between the groups. To compare the group mean average curves, we used nonparametric analyses. Results are presented as means ± SD.

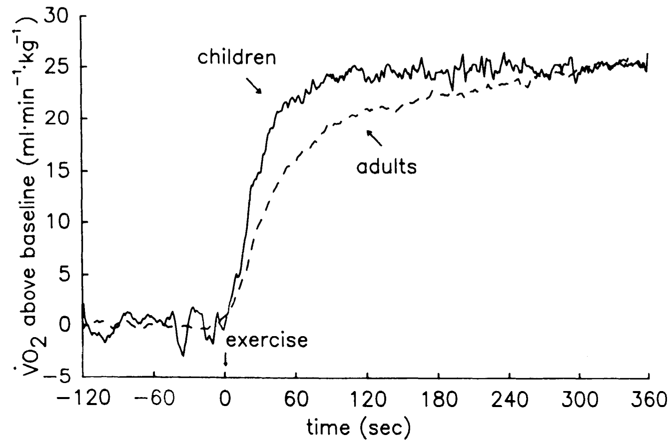

FIG. 2. Group mean $\dot{V}O_2$ response (normalized to body weight, above baseline) to the same work rate exercise (2 W/kg) in children and adults. Note different $\dot{V}O_2$ kinetics in children and adults.

RESULTS

The $\dot{V}O_{2\,max}$ per kilogram body weight in children (43 ± 6 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$) was not statistically different from that in adults (40 ± 10 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$). The average work rate per kilogram body weight in those children who performed the serial protocol was 0.83 ± 0.12, 1.60 ± 0.09, 1.78 ± 0.27, and 2.02 ± 0.31 W/kg for 80%AT, 25%Δ, 50%Δ, and 75%Δ, respectively. In adults these values were 0.84 ± 0.26, 1.52 ± 0.37, 2.02 ± 0.38, and 2.49 ± 0.52 W/kg, corresponding to 80%AT, 25%Δ, 50%Δ, and 75%Δ. In comparing adults and children, a statistically significant difference in work rate per kilogram was found only at the highest work intensity ($P < 0.05$). We used the chance observation that 50%Δ in adults represented precisely the same work rate increment as 75%Δ in children (2.02 W/kg) and constructed a graph showing the $\dot{V}O_2$ normalized per kilogram for the two groups at these respective work intensities (Fig. 2).

O_2 Drift

In adults, positive slopes were found in some subjects at all work rates (in 57% of the adults at 80% AT, in 83% at 25%Δ, and in 100% at 50%Δ and 75%Δ). The slopes increased with increasing work intensities in adults (Fig. 3). The difference between the mean slope at 80% AT (0.17 ± 0.11 ml $O_2 \cdot kg^{-1} \cdot min^{-2}$) was not significantly less than the slope at 25%Δ (0.48 ± 0.42). However, the 25%Δ value was significantly less than both 50%Δ (1.27 ± 0.50, $P < 0.05$) and 75%Δ (1.76 ± 0.63, $P < 0.01$). In addition, linear regression of above-AT slopes as a function of work rate per kilogram revealed a correlation coefficient of 0.91 ($P < 0.0001$).

In the children who performed exercise at the four work rates, positive slopes were found in half of them at the 80% AT work intensity, in 75% at 25%Δ, in 50% at 50%Δ, and only in 25% at the highest work intensity. There were no differences between the slopes at 80% AT (0.19 ± 0.32 ml $O_2 \cdot kg^{-1} \cdot min^{-2}$), 25%Δ (0.28 ± 1.18), 50%Δ (0.27 ± 0.73), and 75%Δ (0.20 ± 0.42). Thus, in contrast to adults, the slope did not increase with greater work intensity in children. In addition, there was no correlation between the slope and work rate per kilogram

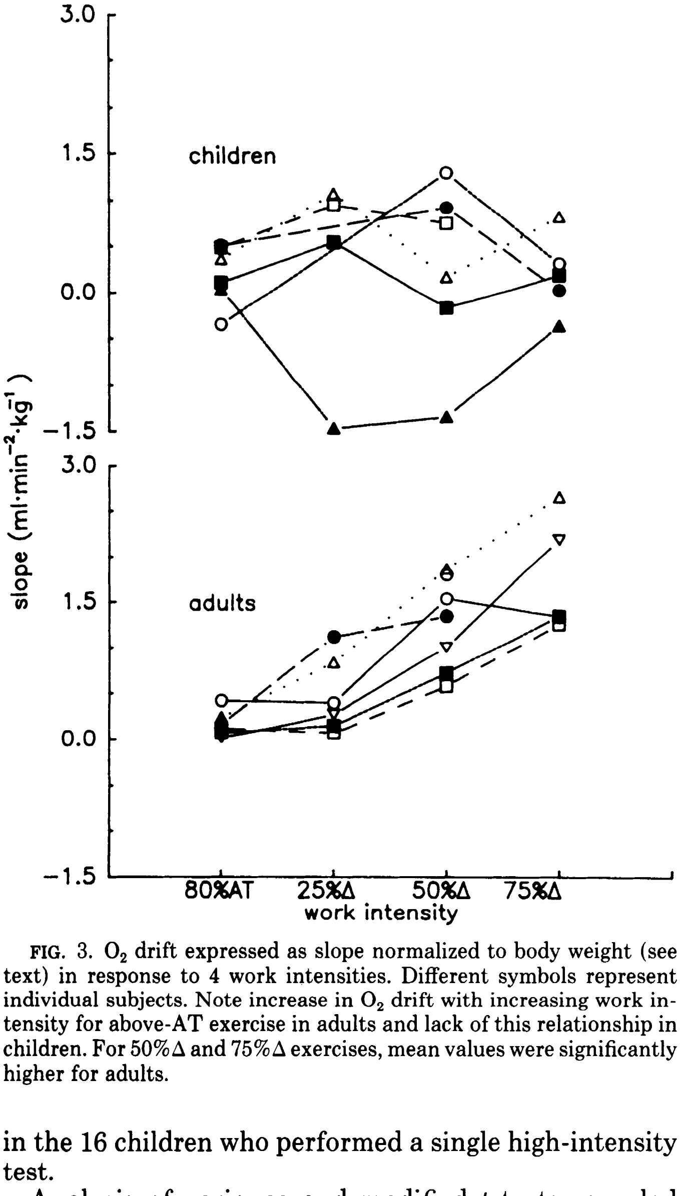

FIG. 3. O_2 drift expressed as slope normalized to body weight (see text) in response to 4 work intensities. Different symbols represent individual subjects. Note increase in O_2 drift with increasing work intensity for above-AT exercise in adults and lack of this relationship in children. For 50%Δ and 75%Δ exercises, mean values were significantly higher for adults.

in the 16 children who performed a single high-intensity test.

Analysis of variance and modified t tests revealed marked differences between the adults and children. At both 75%Δ and 50%Δ the slopes in adults were significantly greater than in children ($P < 0.01$). The difference in the $\dot{V}O_2$ response between children and adults is demonstrated graphically in Fig. 4, showing group mean responses of $\dot{V}O_2$ per kilogram for the lowest (80% AT) and highest (75%Δ) work intensities.

O_2 Cost

The O_2 cost of high-intensity exercise in adults differed from that in children in both pattern and magnitude. The average O_2 cost was greater in children (at 80% AT, 11.92 ± 1.12 ml $O_2 \cdot min^{-1} \cdot W^{-1}$; 25%Δ, 11.63 ± 1.72; 50%Δ, 11.47 ± 1.71; 75%Δ, 11.46 ± 1.21) than in adults (80% AT, 9.34 ± 1.77; 25%Δ, 9.88 ± 1.10; 50%Δ, 9.90 ± 0.71; 75%Δ, 9.57 ± 1.03) at all work intensities ($P < 0.01$). The mean values were not affected by the work intensity in either the children or the adults.

In addition, the pattern of the responses was different (Fig. 5). During high-intensity exercise, the O_2 cost of

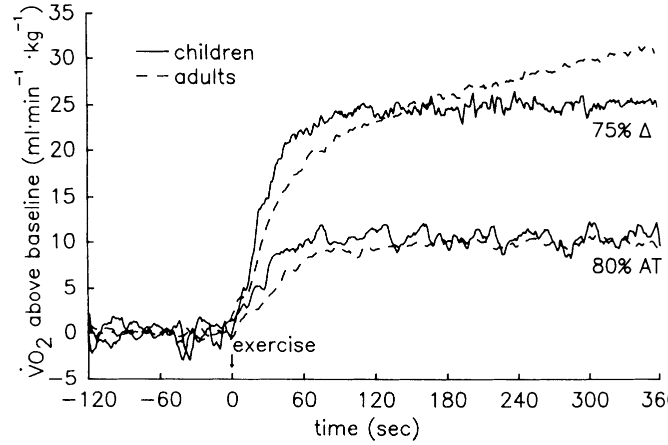

FIG. 4. Group mean $\dot{V}O_2$ response (normalized to body weight, above baseline) for lowest- (80% AT) and highest- (75%Δ) intensity exercise in children and adults. For below-AT exercise, response was similar in both groups. For high-intensity exercise, note faster initial $\dot{V}O_2$ adjustment in children but higher $\dot{V}O_2$ toward the end of exercise in adults.

exercise was lower in adults during the first 3 min of exercise, but by the last 3 min, there was no statistical difference between the two groups (12.56 ± 1.33 ml $O_2 \cdot min^{-1} \cdot W^{-1}$ for 75%Δ in children compared with 11.4 ± 1.30 in adults). Statistical analysis of the group mean curves revealed significant differences between children and adults at all four work intensities ($P < 0.0001$). For the highest work intensity (75%Δ, where both groups reached the same value by the 6th min of exercise), the $t_{1/2}$ was 20 s in children and 45 s in adults (Fig. 5). Finally, we compared the mean value of the O_2 cost of the last minute of exercise at the different work intensities. Analysis of variance and modified t tests revealed that in adults the O_2 cost was significantly higher at the end of the highest-intensity exercise (12.4 ± 1.38 ml $O_2 \cdot min^{-1} \cdot W^{-1}$) than at the end of the 80% AT work rate (10.88 ± 2.25, $P < 0.05$). In children, the last-minute O_2 cost of the highest-intensity exercise (12.68 ± 1.52 ml $O_2 \cdot min^{-1} \cdot W^{-1}$) was not statistically different from that of the below-AT exercise (13.12 ± 1.30).

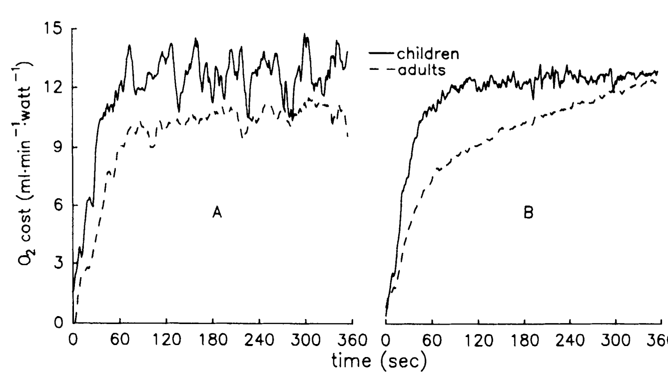

FIG. 5. Group mean O_2 cost of lowest- (*A*, 80% AT) and highest- (*B*, 75%Δ) intensity exercise in children and adults. For both low- and high-intensity exercise, average O_2 cost was significantly higher in children. Note difference in response time between the 2 groups at high-intensity exercise. Adults achieve the children's value only toward the end of exercise. During the last minute of exercise, O_2 cost in adults was significantly higher at 75%Δ than at 80% AT exercise.

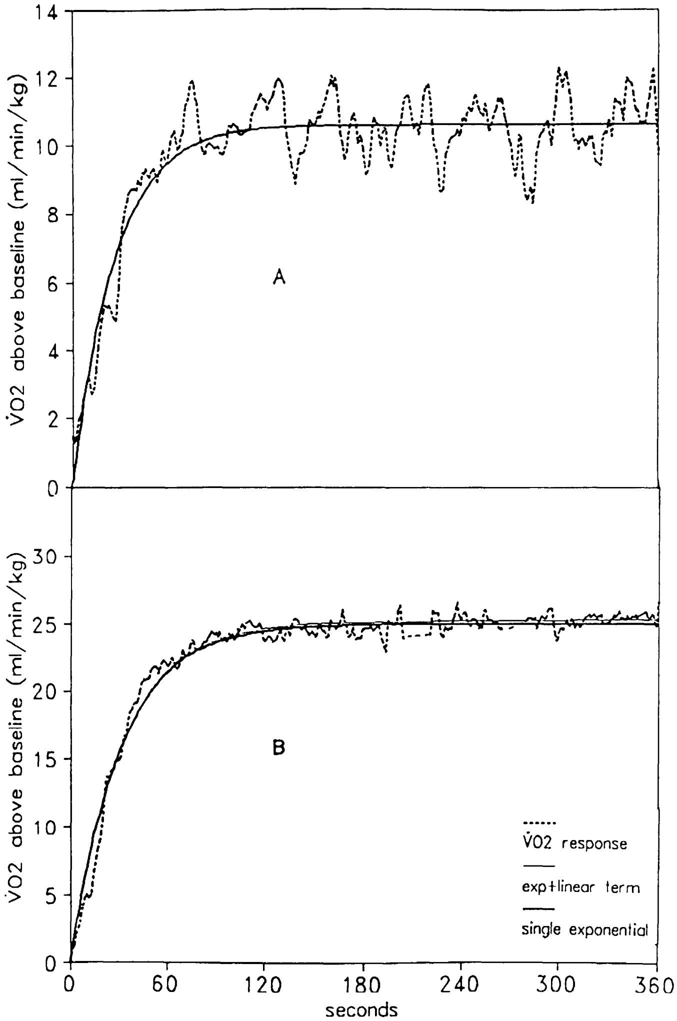

FIG. 6. Characterization of $\dot{V}O_2$ response by a mathematical model in children. Single-exponential model provided a good fit for $\dot{V}O_2$ response in both 80% AT (*A*) and high-intensity (*B*) exercise. The more complex model [an exponential + linear term] was not necessary to accurately describe $\dot{V}O_2$ response in high-intensity range.

Modeling

The pattern of the $\dot{V}O_2$ response to 6 min of exercise in children was different from that in adults. Although a single-exponential function could be used to accurately describe the low-intensity as well as the above-AT exercise in children (Fig. 6), the monoexponential model was not an appropriate description of the response in adults for most work rates above the AT. The addition of a linear term (*Eq. 2*), however, provided a good fit for the $\dot{V}O_2$ response in the high-intensity range in adults (Fig. 7). In fact, when a model consisting of the sum of two exponentials was tried for the group mean responses, the time constant for the second-exponential component became so large that it acted virtually as a linear term.

The time constant of $\dot{V}O_2$ did not change with work rate intensity in either adults or children. The values were significantly lower in children than in adults for all work rates (children: 80% AT, 26 ± 8 s; 25%Δ, 25 ± 4; 50%Δ, 29 ± 7; 75%Δ, 29 ± 6; adults: 80% AT, 44 ± 7 s; 25%Δ, 50 ± 6; 50%Δ, 44 ± 7; 75%Δ, 41 ± 3; $P < 0.01$).

The value of the linear coefficient (*Eq. 2*) correlated well with the slope of the O_2 drift ($r = 0.94$, $P < 0.0001$). The value of the linear term was 0 in all adults in the 80% AT work intensity, while positive values were found for the above-AT protocols in all but one subject (this at 25%Δ). In children, the linear term was 0 for all below-AT protocols but was positive in 73% of the above-AT exercises. Finally the linear coefficients in children for all above-AT exercise intensities were significantly lower than the mean values in adults (children: mean 0.24 ml $O_2 \cdot kg^{-1} \cdot min^{-2}$, range 0.21–0.55; adults: mean 0.97, range 0.27–1.73; $P < 0.01$).

DISCUSSION

These data demonstrate that the pattern of the $\dot{V}O_2$ response to high-intensity exercise in children is qualitatively and quantitatively different from that in adults. Fewer children than adults develop an O_2 drift during high-intensity exercise, and in children the magnitude of the drift both in absolute terms and when normalized to body weight is smaller and not correlated with work intensity. However, despite a smaller or absent O_2 drift, the O_2 cost of exercise (as $\dot{V}O_2$ per watt) is greater in children than in adults. Finally, children demonstrate faster ad-

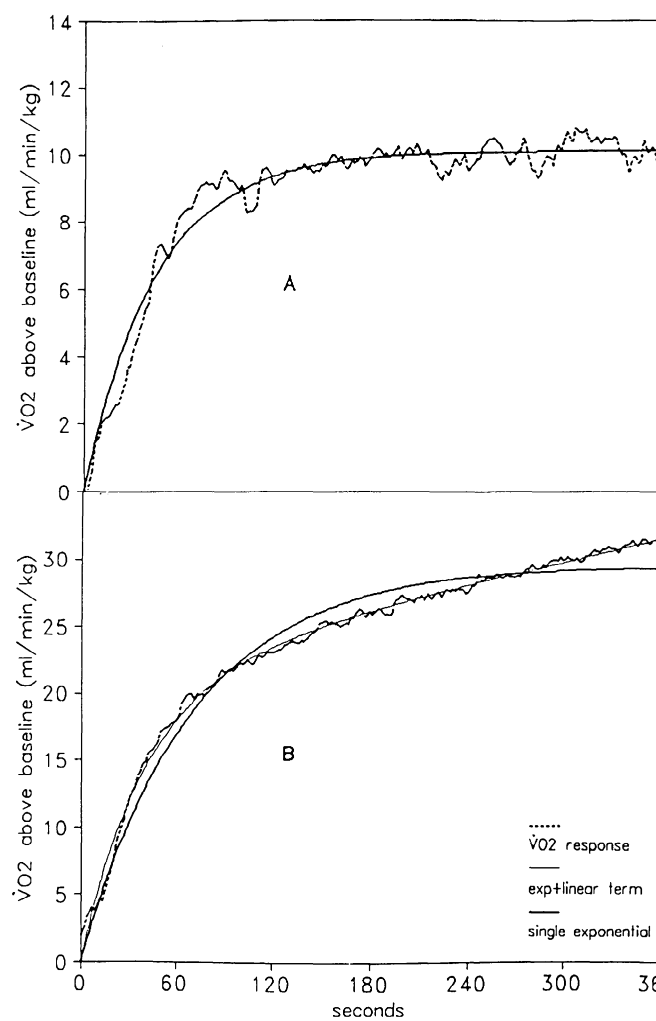

FIG. 7. Characterization of $\dot{V}O_2$ response by a mathematical model in adults. For 80% AT exercise (*A*), the $\dot{V}O_2$ response was well described by a single-exponential model. However, for high-intensity exercise (*B*), addition of a linear term to exponential equation was needed to provide a good fit for $\dot{V}O_2$ response.

justments of $\dot{V}O_2$ during high-intensity exercise than do adults.

Scaling metabolic rate to body size is of critical importance when attempting to assess growth of the cardiorespiratory system (7, 15, 19). To determine whether a particular response truly differs between adults and children, it is first necessary to minimize the effects of size alone on the response in question. For example, metabolic rates ($\dot{V}O_2$) in adults and children are determined in large part by the mass of metabolizing tissue. Although direct noninvasive measurements of muscle mass are not available, body weight is an accurate and easily obtained index. Some aspects of physiological function in mature mammals of different sizes are known to scale to body weight to a power <1.0 by use of the allometric equation (19)

$$\text{metabolic function} \propto \text{body mass}^b \qquad (3)$$

where b is the scaling factor. However, our studies of exercise responses in children demonstrated the scaling factor to be 1.01 (95% confidence interval, 0.90–1.11) for the $\dot{V}O_{2\,max}$ and 0.92 (95% confidence interval, 0.80–1.02) (11).

The data cited above support our use of unscaled body weight (i.e., $mass^1$) and suggest that growth in children is a unique case of the relationship between size and function in biology. The relationship between body size and metabolic function during growth in a species may not be regulated by the same mechanisms that apply to the relationship between size and function in mature animals of different species. Moreover, even if our data had been scaled to a factor <1, the effect would be to amplify the differences in drift between adults and children.

A number of different mechanisms have been proposed to explain the O_2 drift. The increasing $\dot{V}O_2$ could represent the increased energy expenditure associated with dissipation of heat generated during exercise (15). The larger surface area-to-body mass ratio in children than in adults would facilitate passive heat exchange to a greater extent in children and might have contributed to a relatively smaller increment in the temperature-related $\dot{V}O_2$. However, recent studies in adults demonstrated that fitness training lowered the magnitude of the O_2 drift without affecting the increase in core temperature during exercise (4). These investigators concluded that heat exchange was not a major determinant of the O_2 drift in high-intensity exercise.

Alternative explanations center on the high correlation between the increase in lactate concentration during exercise and the magnitude of the O_2 drift. Current theory holds that the rate of ATP degradation with increasing concentration of ADP in contracting muscle cells stimulates mitochondrial oxidative phosphorylation (5). For low-intensity exercise, O_2 is sufficiently available so that ATP regeneration is supplied solely by oxidative phosphorylation. Consequently, $\dot{V}O_2$ and concentrations of ADP, PCr, P_i, and O_2 at the cellular level reach a new steady state. During heavy exercise, insufficient availability of cellular O_2 leads to anaerobic regeneration of ATP and net lactate release. Increasing lactate concentrations could stimulate metabolism of lactate to glucose via the Cori cycle (an O_2-dependent process) or the oxidation of lactate in muscle cells (18, 30). Lactate levels are known to be lower at comparable levels of work intensity in children than in adults (13, 22). Thus, our finding of smaller O_2 drifts in children is consistent with the hypothesis that the O_2 drift reflects metabolism of lactic acid.

The O_2 cost measured in the present study represents the integrated response of the organism to a known increase in the cellular energy requirement. Thus, any observed differences in the O_2 cost between adults and children or among the different work rates reflect differences in the way the cellular energy requirement is supplied. In adults, we observed the tendency [also seen previously (14)] for higher O_2 costs of high- vs. low-intensity exercise. The drift in $\dot{V}O_2$ during heavy exercise did not simply reflect a longer time required by the organism to achieve the same value of $\dot{V}O_2$ per watt reached at lower work rates. Rather, by the 6th min of exercise, adults were utilizing more $\dot{V}O_2$ per watt during heavy exercise than they did during below-AT work.

The O_2 cost pattern was different in children. As noted, the values in children were higher than in adults at all work rates, and children demonstrated less tendency to increase $\dot{V}O_2$ during high-intensity exercise. It was only by the last minute of the heaviest exercise that adults and children achieved comparable O_2 costs. In a previous study, we calculated the work efficiency from the slope of the relationship between $\dot{V}O_2$ and work rate measured during progressive exercise tests (ramp-type protocols) (11), and we found a small but statistically significant decrease in the O_2 cost (measured as an increase in the work efficiency) with increasing body weight in girls. There was a small decrease of O_2 cost with increasing weight in boys as well, but the slope of the regression was not statistically significant. The discrepancy in results could be due to several factors: first, in our previous study the O_2 cost was measured from ramp protocols and not from constant-work-rate tests. Nonlinearities in the nature of the $\dot{V}O_2$-work rate relationship could affect the resulting calculation of O_2 cost. In addition, the design of the present study (i.e., comparing a group of younger subjects with a group of older ones rather than a continuum of ages and body sizes) was fundamentally different from that of the previous study. The current design would make it easier to detect subtle differences in O_2 cost between adults and children.

Do higher values of $\dot{V}O_2$ per watt indicate a more effective cardiorespiratory response to exercise in children than in adults, or, alternatively, do the higher values result from a less developed ability of children to support anaerobic ("O_2-sparing") mechanisms of ATP metabolism? Bar-Or and others (1, 12, 22) have suggested that children are less able than adults to sustain exercise in the supramaximal range, indicating a reduced anaerobic "potential" in children. Lower lactate levels found during exercise in children are consistent with relatively less ability to utilize anaerobic glycolytic processes for ATP turnover. In one investigation of glycolytic enzymes in children during exercise (13), lower levels of phosphofructokinase were found in 11- to 13-yr-old children than in young adults.

In contrast to this hypothesis of reduced anaerobic potential in children, lactate levels alone cannot be used to determine overall lactate metabolism, because blood lactate concentration is determined by the balance between production and removal. Children may metabolize lactate more quickly than adults. The latter mechanism is not inconsistent with our results. The higher $\dot{V}O_2$ per watt seen in children at all work intensities could indicate a greater ability to oxidize the lactate produced during exercise. In this context, it is noteworthy that the neonatal heart muscle is less sensitive to hypoxia than the adult myocardium, specifically because of the neonates' greater capacity for anaerobic glycolysis and more rapid removal of lactate (6, 28).

The time constant of the exponential term (*Eq. 2*) was not affected by the work intensity in either children or adults, but the linear coefficient increased with increasing work rates in adults. This suggests that the underlying physiological adjustments of $\dot{V}O_2$ responsible for the exponential phase of the response were independent of the magnitude of the input. Significant differences in time constants were observed between the adults and children at both low- and high-intensity exercise. [This was somewhat surprising to us because in two previous independent studies we observed that the time constants for $\dot{V}O_2$ for below-AT exercise were slightly smaller in children than in adults but not significantly so (9, 26). Methodological differences in the data analysis and population (subjects' age) between the previous and present studies may have contributed to the different results.] The faster kinetics in children during high-intensity exercise may represent less dependence on anaerobic responses early in exercise in children than in adults. Alternatively, there is evidence that $\dot{V}O_2$ kinetics are faster after fitness training, presumably because of the increase in mitochondrial density and capillarization that occurs in muscles (17, 20, 24). The $\dot{V}O_{2\,max}$ per kilogram was the same in adults and children, but to the extent that "fitness" can be gauged by faster kinetics, children may be generally more fit than adults.

Our data demonstrate that the response to short periods of constant-work-rate exercise can be modeled in a simple way by using the sum of an exponential and linear term. The coefficient of the linear term correlated well with the magnitude of an independently measured slope of the O_2 drift in both adults and children. This approach may be useful in a number of clinical instances where both the exponential and linear components of the response may be affected. For example, in adult patients with severe cyanotic congenital heart disease, the dynamic $\dot{V}O_2$ response is markedly slowed (25). Similarly, the $\dot{V}O_2$ time constant is prolonged in patients with chronic obstructive lung disease (21). This approach could prove useful for investigations of growth and development in healthy children, as well as in a variety of childhood diseases, as a tool to gauge pathophysiological responses.

This study adds to the growing body of evidence demonstrating maturation of energy metabolism during growth in children. We speculate that the mechanism of the greater O_2 cost in children than in adults reflects the kinetics of high-energy phosphate metabolism in muscle cells. Noninvasive techniques, such as magnetic resonance spectroscopy, may prove useful in resolving the development of the "anaerobic potential" that occurs during growth in humans.

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REFERENCES

1. BAR-OR, O. *Pediatric Sports Medicine for the Practitioner.* New York: Springer-Verlag, 1983.
2. BEAVER, W. L., N. LAMARRA, AND K. WASSERMAN. Breath-by-breath measurement of true alveolar gas exchange. *J. Appl. Physiol.* 51: 1662–1675, 1981.
3. CASABURI, R., T. J. BARSTOW, T. ROBINSON, AND K. WASSERMAN. Influence of work rate on ventilatory and gas exchange kinetics. *J. Appl. Physiol.* 67: 547–555, 1989.
4. CASABURI, R., T. W. STORER, I. BEN-DOV, AND K. WASSERMAN. Effect of endurance training on possible determinants of $\dot{V}O_2$ during heavy exercise. *J. Appl. Physiol.* 62: 199–207, 1987.
5. CHANCE, B., J. S. LEIGH, B. J. CLARK, J. MARIS, J. KENT, S. NIOKA, AND D. SMITH. Control of oxidative metabolism and oxygen delivery in human skeletal muscle: a steady-state analysis of the work/energy cost transfer function. *Proc. Natl. Acad. Sci. USA* 82: 8384–8388, 1985.
6. CHIU, R. C. J., AND W. BINDON. Why are newborn hearts vulnerable to global ischemia? The lactate hypothesis. *Circulation* 76, *Suppl.* V: V-146–V-149, 1987.
7. COOPER, D. M. Development of the oxygen transport system in normal children. In: *Advances in Pediatric Sport Sciences. Biological Issues,* edited by O. Bar-Or. Champaign, IL: Human Kinetics, 1989, vol. 3, p. 67–100.
8. COOPER, D. M. Exercise and metabolism in the growing child. In: *Basic Mechanisms of Pediatric Respiratory Disease: Cellular and Integrative.* Philadelphia, PA: Decker. In press.
9. COOPER, D. M., C. BERRY, N. LAMARRA, AND K. WASSERMAN. Kinetics of oxygen uptake and heart rate at onset of exercise in children. *J. Appl. Physiol.* 59: 211–217, 1985.
10. COOPER, D. M., M. KAPLAN, L. BAUMGARTEN, D. WEILER-RAVELL, B. J. WHIPP, AND K. WASSERMAN. Coupling of ventilation and CO_2 production during exercise in children. *Pediatr. Res.* 21: 568–572, 1987.
11. COOPER, D. M., D. WEILER RAVELL, B. J. WHIPP, AND K. WASSERMAN. Aerobic parameters of exercise as a function of body size during growth in children. *J. Appl. Physiol.* 56: 628–634, 1984.
12. ERIKSSON, B. O. Muscle metabolism in children—a review. *Acta Paediatr. Scand.* 283: 20–28, 1980.
13. ERIKSSON, B. O., J. KARLSSON, AND B. SALTIN. Muscle metabolites during exercise in pubertal boys. *Acta Paediatr. Scand.* 217, *Suppl.*: 154–157, 1971.
14. HANSEN, J. E., R. CASABURI, D. M. COOPER, AND K. WASSERMAN. Oxygen uptake as related to work rate increment during cycle ergometer exercise. *Eur. J. Appl. Physiol. Occup. Physiol.* 57: 140–145, 1988.
15. KLEIBER, M. *The Fire of Life.* New York: Krieger, 1975, p. 178–222.
16. LAMARRA, N. *Ventilatory Control, Cardiac Output, and Gas Exchange Dynamics During Exercise Transients in Man* (PhD thesis). Los Angeles: University of California, 1982.
17. LARSSON, L. Physical training effects on muscle morphology in sedentary males at different ages. *Med. Sci. Sports Exercise* 14: 203–206, 1982.
18. MCGILVERY, R. W. *Biochemistry: A Functional Approach.* Philadelphia, PA: Saunders, 1983.
19. MCMAHON, T. A. *Muscles, Reflexes, and Locomotion.* Princeton, NJ: Princeton Univ. Press, 1984, p. 234–296.
20. MUSCH, T. I., G. C. HAIDET, G. A. ORDWAY, J. C. LONGHURST, AND J. H. MITCHELL. Training effects on regional blood flow response

to maximal exercise in foxhounds. *J. Appl. Physiol.* 62: 1724–1732, 1987.

21. NERY, L. E., K. WASSERMAN, J. D. ANDREWS, D. J. HUNTSMAN, J. E. HANSEN, AND B. J. WHIPP. Ventilatory and gas exchange kinetics in chronic obstructive lung disease. *J. Appl. Physiol.* 53: 1594–1602, 1982.
22. PATERSON, D. H., D. A. CUNNINGHAM, AND L. A. BUMSTEAD. Recovery O_2 and blood lactic acid: longitudinal analysis in boys aged 11 to 15 years. *Eur. J. Appl. Physiol. Occup. Physiol.* 55: 93–99, 1986.
23. ROSTON, W. L., B. J. WHIPP, J. A. DAVIS, D. A. CUNNINGHAM, R. M. EFFROS, AND K. WASSERMAN. Oxygen uptake kinetics and lactate concentrations during exercise in humans. *Am. Rev. Respir. Dis.* 135: 1080–1084, 1987.
24. SALTIN, B. The interplay between peripheral and central factors in the adaptive response to exercise and training. *Ann. NY Acad. Sci.* 301: 224–231, 1977.
25. SIETSEMA, K. E., D. M. COOPER, J. K. PERLOFF, M. H. ROSOVE, J. S. CHILD, M. M. CANOBBIO, B. J. WHIPP, AND K. WASSERMAN. Dynamics of oxygen uptake during exercise in adults with cyanotic congenital heart disease. *Circulation* 73: 1137–1144, 1986.
26. SPRINGER, C., T. J. BARSTOW, K. WASSERMAN, AND D. M. COOPER. Oxygen uptake and heart rate responses during hypoxic exercise in children and adults. *Med. Sci. Sports Exercise.* In press.
27. SYSTROM, D., D. KANAREK, S. KOHLER, AND H. KAZEMI. ^{31}P nuclear magnetic resonance spectroscopy of the anaerobic threshold in humans. *J. Appl. Physiol.* 68: 2060–2066, 1990.
28. SU, J. Y., AND W. F. FRIEDMAN. Comparison of the responses of fetal and adult cardiac muscle to hypoxia. *Am. J. Physiol.* 224: 1249–1253, 1973.
29. WARD, S., B. J. WHIPP, S. N. KOYAL, AND K. WASSERMAN. Influence of body CO_2 stores on ventilatory dynamics during exercise. *J. Appl. Physiol.* 55: 742–749, 1983.
30. WASSERMAN, K. Anaerobiosis, lactate, and gas exchange during exercise: the issues. *Federation Proc.* 45: 2904–2909, 1986.
31. WASSERMAN, K., B. J. WHIPP, S. N. KOYAL, AND W. L. BEAVER. Anaerobic threshold and respiratory gas exchange during exercise. *J. Appl. Physiol.* 35: 236–243, 1973.
32. WHIPP, B. J., J. A. DAVIS, F. TORRES, AND K. WASSERMAN. A test to determine parameters of aerobic function during exercise. *J. Appl. Physiol.* 50: 217–221, 1981.