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Kinetics of oxygen uptake and heart rate at onset of exercise in children

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COOPER, DAN M., COLIN BERRY, NORMAN LAMARRA, AND KARLMAN WASSERMAN. Kinetics of oxygen uptake and heart rate at onset of exercise in children. J. Appl. Physiol. 59(1): 211-217, 1985.—Requirements for cellular homeostasis appear to be unchanged between childhood and maturity. We hypothesized, therefore, that the kinetics of O_2 uptake ($\dot{V}O_2$) in the transition from rest to exercise would be the same in young children as in teenagers. To test this, Vo_2 and heart rate kinetics from rest to constant work rate (75% of the subject's anaerobic threshold) in 10 children (5 boys and 5 girls) aged 7– 10 yr were compared with values found in 10 teenagers (5 boys and 5 girls) aged 15–18 yr. Gas exchange was measured breath to breath, and phases I and II of the transition and phase III (steady-state exercise) were evaluated from multiple transitions in each child. Phase I (the Vo_2 at 20 s of exercise expressed as percent rest-to-steady-state exercise $\dot{V}O_2$) was not significantly correlated with age or weight [mean value $42.5 \pm 8.9\%$ (SD)] nor was the phase II time constant for $\dot{V}O_2$ [mean 27.3 ± 4.7 (SD) s]. The older girls had significantly slower kinetics than the other children but were also found to be less fit. When the teenagers exercised at work rates well below 75% of their anaerobic threshold, phase I VO₂ represented a higher proportion of the overall response, but the phase II kinetics were unchanged. The temporal coupling between the cellular production of mechanical work at the onset of exercise and the uptake of environmental O2 appears to be controlled throughout growth in children.

time constant for O_2 uptake; growth and development; cardiodynamic hyperpnea; phase I and II O_2 uptake kinetics

THE PROCESS OF GROWTH IN children is dynamic. The body increases in size and the organs develop and mature until the organism's structure and function are "optimized" for the human being's particular ecological niche. During this period, the gas exchange system must adapt to increasing metabolic demands. In previous work with children, we have characterized cardiorespiratory growth by identifying aspects of gas exchange responses to exercise which appear to remain constant despite changes in body size and age (7, 8). In this way we are beginning to determine which aspects of cardiorespiratory function appear to be controlled throughout the growth period.

We reasoned that age- or size-independent variables of cardiorespiratory function might be found by examining the dynamics of O_2 uptake (VO_2) in response to exercise. During transitions from rest to exercise, or from one level of energy requirement to another, the response of the organism is structured to maintain homeostasis at the cellular level (16); thus the supply of environmental O_2 is determined by the needs of the cells. Since the stores of O_2 in the body are very small relative to metabolic demand, dynamics of $\dot{V}O_2$ measured at the mouth during exercise transitions are closely coupled in time to cellular events. Furthermore, although young children differ in size from adults, resting requirements of cellular homeostasis, as reflected by body temperature, pH, PCO₂, and PO₂ are the same (2, 4, 12). It seemed likely, then, that kinetics of $\dot{V}O_2$ in response to exercise would be influenced primarily by the need for cellular homeostasis and would be age and size independent.

The hypothesis was tested by analyzing the kinetics of Vo₂ using breath-to-breath measurements of gas exchange during repeated rest-to-constant-work-rate cycle ergometry (square-wave protocol). The kinetics of $\dot{V}O_2$ during exercise transitions in normal adults have been characterized by three phases (5, 6, 17, 18, 23). Phase I is the abrupt increase in VO_2 within the first 20 s of exercise, the cardiodynamic phase, and represents the increase in pulmonary blood flow due to the sudden increase in venous return from the exercising limbs. The effect of age, body size, or different work rate inputs on the magnitude of $\dot{V}O_2$ in phase I is not known. Phase II is the exponential rise in Vo₂ culminating in the steadystate $\dot{V}O_2$ (phase III). There is evidence that the phase II Vo_2 response is significantly longer when the work rate input is above the subject's anaerobic threshold (AT) compared with transitions below the AT (23); i.e., it is not described by first-order linear equations for all ranges of work rate transitions.

To compare $\dot{V}O_2$ kinetics in different-sized children, the magnitude of the work rate transition for each subject was chosen to be below the subject's AT and to represent a similar increase in metabolic demand $(\Delta \dot{V}O_2/kg)$ in all subjects regardless of size. The constant work rate for each child was determined by finding the work rate corresponding to the $\dot{V}O_2$ at ~75% of the AT. We further examined the "linearity" of the $\dot{V}O_2$ response by measuring kinetics in the older (larger) children at a work rate transition which was much lower than 75% of their AT and comparable with the work rate used for the younger children, 20 W. Finally, since the O_2 uptake at the mouth is coupled to O_2 consumption by the cell through the cardiovascular system, the kinetics of heart rate during the exercise transition were measured and compared with the $\dot{V}O_2$ kinetics.

METHODS

Study Groups

Ten children (5 boys and 5 girls), ranging in age from 7 to 10 yr, comprised the group of "younger" subjects, and 10 teenagers (5 boys and 5 girls), ranging in age from 15 to 18 yr, comprised the group of "older" subjects. All volunteers were in good health, participated in physical education courses at school, did not smoke, and did not use drugs or medications. Informed consent was obtained according to the guidelines of the Institutional Review Board at Harbor-UCLA Medical Center. Age, weight, and height of the subjects are provided in Table 1.

Protocol

A ramp exercise protocol was used to determine the AT and the maximum O_2 uptake (VO_{2max}) for each subject during cycle ergometer exercise (23). The average values for all groups are shown in Table 1 and were within the normal limits established for children in this laboratory (7, 8). The work rate for the square-wave protocol was determined by estimating the work rate that would result in ~75% of the subject's VO_2 at AT. The average work rate for square-wave testing in each group is shown in Table 1. In eight of the older subjects, square-wave tests were also performed at a constant work rate of 20 W.

Each subject performed a minimum of six rest-toexercise transitions. Exercise periods were 6 min each, and at least 6 min of rest followed an exercise period. Heart rate and $\dot{V}o_2$ returned to the preexercise resting values before a repetition was performed. In the older subjects, all transitions were usually completed in one session. Most of the younger children, however, had patience for only one or two transitions and multiple sessions on separate days were required.

The subject was signaled to begin exercise by a green light that was activated at the end of an exhalation. No vocal command was given. In addition, the ergometer flywheel was motorized and maintained at a rate of 60

TABLE 1. Study sample profile

	n	Age, yr	Weight, kg	Work Rate,	ml $O_2 \cdot min^{-1} \cdot kg^{-1}$		
- -	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			W	AT/kg	Vo _{zmax} /kg	
Younger boys	5	8.4	29.2	24	26.3	40.1	
		± 0.8	± 2.5	± 9	± 4.3	± 6.0	
Younger girls	5	8.8	28.2	20	27.1	36.6	
		± 0.9	± 3.9	±7	± 3.8	± 3.5	
Older boys	5	17.5	64.1	67	23.5	43.3	
		± 0.9	± 9.1	± 16	± 6.1	± 4.7	
Older girls	5	17.3	68.9	61	18.3	33.8	
		± 1.3	± 14.0	± 26	± 4.8	± 4.3	
All younger	10	8.6	28.7	22	26.7	38.4	
subjects		± 0.9	± 3.1	±8	± 4.0	± 4.8	
All older	10	17.4	66.5	64	20.9	38.6	
subjects		± 1.1	± 11.6	± 21	± 5.4	± 4.5	

Values are means \pm SD. AT, anaerobic threshold.

rpm until the onset of pedaling so that the subjects would not have to expend energy in overcoming the inertia of the flywheel at the start of exercise.

The subjects 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. A servomechanism in the electronic braking system of the ergometer maintained the input work rate to an accuracy of 1% within a range of pedaling rates of 50–90 rpm.

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 mouthpiece 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 analogto-digital conversion for the on-line breath-to-breath computation of O_2 uptake (VO₂, STPD), CO₂ output $(\dot{V}CO_2, STPD)$, and expired ventilation $(\dot{V}E, BTPS)$ as previously described (3). Heart rate (HR) was measured beat by beat using a modified standard lead I electrocardiogram (ECG) for which three leads were placed on the chest. The ECG was in continuous view via a highpersistence ECG oscilloscope. The data from each test were displayed on-line and stored on digital tape for subsequent analysis.

Data Analysis

The $\dot{V}O_{2max}$ was the highest $\dot{V}O_2$ achieved by the subject. The AT- $\dot{V}O_2$ was measured noninvasively from gas exchange data by finding the $\dot{V}O_2$ above which $\dot{V}E/\dot{V}O_2$ and end-tidal partial pressures of O_2 (PET_{O2}) increased without an increase in $\dot{V}E/\dot{V}CO_2$ or a decrease in end-tidal PCO₂ (23, 26). To determine the work rate for the square-wave protocols, a rough estimate of the time constant and system delay was made from the $\dot{V}O_2$ response during the ramp exercise test (7, 25). This was then subtracted from the time at which the AT- $\dot{V}O_2$ occurred and ~75% of the corresponding work rate was selected.

The results of each rest-to-exercise transition for each subject were time-interpolated in 1-s intervals and superimposed to obtain an averaged second-by-second response.

For each subject, we calculated the following.

*Phase I Vo*₂. Since the change in Vo₂ from rest to steady-state exercise (ΔVO_{2ss}) varied greatly in the study population, we measured the phase I Vo₂ as a proportion of ΔVO_{2ss} . The Vo₂ at 20 s after the onset of exercise (end of phase I) was expressed as the percent of ΔVO_{2ss} .

Phase II $\dot{V}o_2$ time constant. When the work rate is below the subject's AT, phase II has been shown to be characterized by the following equation (17):

$$\Delta \dot{\mathrm{V}} \mathbf{O}_{2}(t) = \Delta \dot{\mathrm{V}} \mathbf{O}_{2\mathrm{ss}} \times (1 - e^{-t/\tau})$$

where $\Delta \dot{V}O_2(t)$ is the increase in $\dot{V}O_2$ above resting values at any exercise time (t); $\Delta \dot{V}O_{2ss}$ is the difference between rest and steady-state exercise $\dot{V}O_2$; and τ is the time constant or the time to reach 63% $[(1 - 1/e) \times 100\%]$ of $\Delta \dot{V}O_{2ss}$. With the use of linear regression and iterative techniques, a best-fit exponential was found for phase II (17). The fitting window was between 20 and 120 s after the onset of exercise, and the exponential was characterized by the time constant $(\tau \dot{V}O_2)$.

 $t_{\frac{1}{2}}$ heart rate. The half time, rather than the time constant, was calculated, since previous investigators have shown that the heart rate response is not well defined by first-order kinetics (17). Both the "group mean" responses (18) and each individual's $\dot{V}O_2$ and HR responses were used for data analysis. The group mean response (a noise reducing technique) consisted of superimposing and averaging the results of all the subjects of a particular group. This is especially useful for comparing the results of the older and younger subjects.

Statistical Analysis

Linear regression techniques were used to assess the dependence of $\dot{V}O_2$ and HR kinetics in individual subjects as a function of age and weight. Analysis of variance (ANOVA) was used to test for differences in these responses in the four groups studied (older boys, older girls, younger boys, and younger girls). When ANOVA was significant, intergroup means were compared using the modified t test by the method of Bonferroni (22). The paired t test was used to test differences in $\dot{V}O_2$ kinetics at the low and high work rates in the older children. Results are presented as means \pm SD. Statistical significance was taken at the P < 0.05 level.

RESULTS

Kinetics of $\dot{V}O_2$

The time-interpolated breath-by-breath data from six transitions of rest to constant work rate are shown in a 17-yr-old boy and a 9-yr-old girl in Fig. 1, A and B. The best-fit exponential is also shown for each child.

The mean resting and steady-state exercise $\dot{V}O_2/kg$ of the individual subjects were significantly lower in the older group. Resting $\dot{V}O_2/kg$ in the younger subjects was 9.4 ± 0.8 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$ and in the older subjects was 5.8 ± 0.8 . Steady-state exercise $\dot{V}O_2/kg$ in the younger subjects was 23.7 ± 3 and in the older subjects was 18.6 ± 3.9 . This represented a rest-to-exercise increase of 12.8



FIG. 1. O_2 uptake ($\dot{V}O_2$) response to transitions between rest and work rate (75% of subject's anaerobic threshold) in a 10-yr-old girl (A) and a 17 yr-old-boy (B). Time is plotted on X-axis; time 0 indicates onset of exercise. Y-axis represents $\dot{V}O_2$. Note that it is scaled differently in the 2 subjects for easier visual comparison of the $\dot{V}O_2$ kinetics. Solid lines, mean of 6 transitions performed by each subject; dashed lines, best-fit exponentials. $\tau \dot{V}O_2$ for both subjects was 25 s.

 \pm 3.5 ml O₂·min⁻¹·kg⁻¹ in the older subjects and 14.3 \pm 3.5 ml O₂·min⁻¹·kg⁻¹ in the younger subjects. These two values were not significantly different.

Phase I. There was no significant correlation between phase I and age (r = 0.26) in the study population (Figs. 2 and 3), nor was there a significant correlation with weight (r = 0.36). At 20 s (end of phase I), the mean $\dot{V}O_2$ for all subjects was $42.5 \pm 8.9\%$ of the $\Delta\dot{V}O_{2ss}$. By contrast, in all eight older children studied at the 20-W work rate, $\dot{V}O_2$ at the end of phase I represented a higher proportion ($63.5 \pm 5.6\%$) of the ΔVO_{2ss} (Fig. 4). The absolute increase of $\dot{V}O_2$ (ml O_2/min) above base-line levels was significantly lower (mean 25%) at the lower work rate (Fig. 4).

Phase II. The group mean responses for the younger and older subjects are shown for $\dot{V}O_2$ in Fig. 3. There was no correlation of the $\tau \dot{V}O_2$ with age (Fig. 2), weight, or height. However, the older girls had significantly higher values for $\tau \dot{V}O_2$ than did the other three groups (Table 2). The older girls also had the lowest values for AT/kg and $\dot{V}O_{2\max}/kg$ (Table 1). Additionall in the study population as a whole, there was a negative correlation between $\tau \dot{V}O_2$ and both the AT/kg and $\dot{V}O_{2\max}/kg$ (Fig. 5). (However, this correlation was not observed for the boys alone.)

In contrast to the different phase I response observed



FIG. 2. Individual values of phase I of the O_2 uptake ($\dot{V}O_2$) response (A) and $\dot{V}O_2$ of phase II (B) as a function of age. Closed circles, girls; open circles, boys. Phase I $\dot{V}O_2$ presented as percent change from rest to steady-state ($\Delta \dot{V}O_{2ss}$;) $\tau \dot{V}O_2$ s. There were no significant correlations for either phase I $\dot{V}O_2$ or $\tau \dot{V}O_2$ and age in the study sample as a whole. Older girls, however, had significantly higher values of $\tau \dot{V}O_2$ than did the other children.



FIG. 4. Effect of different work rate inputs on phase I O_2 uptake $(\dot{V}O_2)$ response. Left panel shows that $\dot{V}O_2$ at end of phase I represented a higher proportion of change from rest to steady state $(\Delta \dot{V}O_{2ss})$ at the lower work rate in all 8 subjects. Right panel shows that $\dot{V}O_2$ at end of phase I was 25% higher at higher work rates.

TABLE 2. Time constant for $\dot{V}O_2$ and $t_{1/2}$ for heart rate in younger and older children

	Younger Boys	Younger Girls	Older Boys	Older Girls	All Younger subjects	All Older Subjects
τ [.] VO ₂	26.5	26.5	24.3	31.6*	26.5	28.0
-	± 3.0	± 4.0	± 2.3	± 6.2	± 3.4	± 5.9
$t_{1/2}$ HR	18.9	22.1	13.4	17	20.5	15.2
	± 5.7	± 5.8	±8.9	± 8.6	± 5.7	± 8.5

Values are means \pm SD in seconds. $\tau \dot{V}O_2$, time constant for O_2 uptake; t_{ν_2} HR, half time of heart rate (HR).

at the different work rates in the older subjects, the time constants of phase II did not differ significantly. The $\tau \dot{V}O_2$ of the group mean response in the eight older subjects at the higher work rate was 28.0 s ± 1 compared with 26.4 ± 1 at the 20-W work rate transition (Fig. 6).

Kinetics of heart rate

The group mean responses for heart rate in the younger and older subjects are shown in Fig. 7A, and these data are normalized as the percent of the rest to steady-state heart rate differences in Fig. 7B for comparison between the younger and older subjects. The $t_{1/2}$

FIG. 3. Dashed lines, group mean response of O_2 uptake ($\dot{V}O_2$) in all younger subjects in rest-to-exercise transitions; Solid lines, all older subjects. Time is plotted on X-axis; time 0 indicates onset of exercise. A: $\dot{V}O_2$ in l/min is plotted on the Y-axis; B: percent change from rest to steady state ($\Delta \dot{V}O_{2\,ss}$) is plotted on the Y-axis (see text). Time constants did not differ between the 2 groups.

HR for the group mean response of the older subjects was 11 s and for the younger subjects 20 s, as seen in Fig. 7B. Consistent with the group mean response for heart rate were the individual $t_{\frac{1}{2}}$ HR responses, which demonstrated a significant negative correlation with increasing age (r = -0.43) and weight (r = -0.51). Analysis of variance of the four subject groups did not reveal significant differences related to gender (Table 2). The $t_{\frac{1}{2}}$ HR was significantly correlated with the resting heart rate (r = 0.67); the lower the resting heart rate, the faster the kinetics (Fig. 8).

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We observed no difference in the kinetics of $\dot{V}O_2$ during exercise transitions below the AT between a group of 7to 9-yr-old children and 15- to 18-yr-old teenagers (Figs. 2 and 3). The results of this study support the hypothesis that the dynamic response of $\dot{V}O_2$ in the transition from rest to exercise is independent of size and age during growth. It is noteworthy that deVries and co-workers (10) found no differences in $\dot{V}O_2$ response using submaximal work rates between a group of older (60–69 yr) and younger men (21–29 yr). Thus the kinetics of $\dot{V}O_2$ in response to exercise may reflect the organism's ability to maintain cellular homeostasis in response to increased metabolic demand and are controlled in a relatively narrow range throughout the normal growth process.

Mácek and Vávra previously reported that 10- to 11yr-old boys had a more rapid increase in Vo_2 in response to exercise than did 20- to 22-yr-old men (20). Their protocol consisted of work rates at 90–100% of maximal lasting to the limit of the subject's tolerance (4–5 min), and, notably, the Vo_{2max}/kg was significantly lower in the boys than in the young men. The kinetics of Vo_2 in response to exercise become progressively slower as work rates increase above the AT (17, 26). It is possible, then, that the faster kinetics of the younger subjects of Mácek and Vávra represented the response to relatively lower work rate inputs and did not indicate a growth-related difference in the temporal coupling of gas exchange to metabolic demand.

The older girls had significantly higher time constants for $\dot{V}O_2$ than did the other groups and had the lowest AT/kg and $\dot{V}O_{2 max}/kg$ (Table 2). This suggests that they are less fit (9, 27). The significant negative correlation



FIG. 5. Time constant for O₂ uptake $(\dot{V}O_2)$ as a function of anaerobic threshold (AT)/kg (A) and maximum O₂ uptake $(\dot{V}O_{2max})/kg$ (B). Closed circles, girls; open circles, boys. There was a significant negative correlation of $\tau\dot{V}O_2$ with both AT/kg (r = -0.45) and VO_{2max}/kg (r = -0.60).

FIG. 6. Effect of different work rate inputs on O_2 uptake ($\dot{V}O_2$) kinetics. *Time 0* represents onset of exercise. *Left panel* shows group mean responses in the 8 subjects for work rate representing 75% of anaerobic threshold (*solid line*) and the 20-W protocol (*dashed line*) in terms of $\dot{V}O_2$ (l/min). *Right panel* shows response scaled as percent change from rest to steady state ($\Delta \dot{V}O_{2m}$). There was no difference in the kinetics of phase II responses between the 2 work rates.

> FIG. 7. Group mean response to heart rate (HR) in all younger subjects (dashed lines) and in all older subjects (solid lines) in rest-to-exercise transitions. Time is plotted on the X-axis, and time 0 indicates onset of exercise. A: HR in beats/min is plotted on Y-axis; B: Heart rate is presented as a percent of the difference between preexercise and steady-state HR value (% delta). t_{V_2} decreased with age (see text).

of both AT/kg and $\dot{V}O_{2 max}/kg$ with the time constants for $\dot{V}O_2$ during phase II (Fig. 5) is consistent with the findings of other investigators who have shown that fitness training programs shortened the $\dot{V}O_2$ kinetics (14, 15). Training increases the level of oxidative enzymes in muscle cells, the density and number of their mitochondria, and the number and density of capillaries to the muscles (1, 9, 11, 13, 27). Each of these factors could contribute to a more rapid increase in muscle cell $\dot{V}O_2$. It is likely then, that the slower time constants observed in the older girls result, in large part, from low levels of physical exercise (quite possibly due to social and cultural factors) rather than from specific physiological mechanisms related to gender.

At the onset of exercise, phase I $\dot{V}O_2$ is thought to be the consequence of a sudden increase in cardiac output (\dot{Q}), largely, stroke volume (SV) occurring before any change in the arteriovenous content difference $(a-\bar{v})O_2$ (24, 26). The phase I response (as $\% \Delta \dot{V}O_{2ss}$) did not differ between the younger and older subjects (Fig. 2).



FIG. 8. Relationship between $t_{\frac{1}{2}}$ heart rate (HR) and preexercise HR. Open circles, older subjects; closed circles, younger subjects. $t_{\frac{1}{2}}$ HR increased significantly with preexercise HR (r = 0.81).

But we speculate from our data that the increase in stroke volume during phase I may have been larger in the older subjects. By the Fick equation

$$Vo_2 = SV \times HR \times (a-\bar{v})O_2$$

In the younger subjects, HR increased at 20 s (the end of phase I) by 20% over base-line values and in the older children by 27%, but $\dot{V}O_2$ increased over base line by much greater amounts for both the younger (232%) and older (316%) children. This means that SV increased by 193% in the younger children but by 248% in the older children. A smaller increase in SV of younger children is consistent with the fact that they have relatively higher resting metabolic rates ($\dot{V}O_2/kg$) than do the older children. Thus their preexercise SV may have been closer to the exercise SV than in the older subjects. The approximate doubling of SV at the onset of exercise has been measured by other investigators using more direct measurements (19).

In the older children, phase I response represented a greater proportion of ΔVo_{2ss} at the lower work rates (Fig. 4). Whereas the work rate at 75% of AT was more than three times the 20-W protocol, the $\dot{V}o_2$ at the end of phase I had increased by only 25%. These data suggest that the cardiodynamic response at the onset of exercise is only moderately dependent on the magnitude of the work rate input. The phase II dynamics were the same at the two different work rate protocols (Fig. 6). This suggests that the achievement of the steady-state $\dot{V}o_2$ (after phase I) is a process in which feedback mechanisms are operant and is approximately linear for work rates below the AT.

The kinetics of the heart rate response were to a small, but significant degree, faster in the older subjects (Fig. 7). The heart rate response to exercise is not first-order linear, and there is evidence that heart rate kinetics are slower in transitions that begin at higher heart rates (17). Thus the heart rate kinetics in the younger subjects may be slower because the base-line heart rate in the younger subjects is higher. In fact, there was a significant correlation between the resting heart rate and the $t_{\frac{1}{2}}$ HR as shown in Fig. 8.

Our data suggest that the response characteristics of $\dot{V}o_2$ are controlled throughout the growth period, and that the structure of the cardiorespiratory system must change in such a way that these response characteristics

are held within an optimal range. Abnormalities in these dynamics may result from childhood disease (21), and measurements of gas exchange kinetics may prove useful in assessing the effect of such disease on subsequent cardiorespiratory growth. Finally, the results highlight the careful attention that must be paid to gender, levels of physical fitness, and the dynamics of the cardiorespiratory response when designing exercise protocols for children.

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