Modeling the blood lactate kinetics at maximal short-term exercise conditions in children, adolescents, and adults

Ralph Beneke,1,3 Matthias Hüttler,2,3 Marcus Jung,3 and Renate M. Leithäuser1

1Centre for Sports and Exercise Science, Department of Biological Sciences, University of Essex, Colchester, United Kingdom; 2Department of Physical Medicine and Rehabilitation, Haukeland University Hospital, Bergen, Norway; and 3Institute of Sports Medicine, Free University, Berlin, Germany

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Beneke, Ralph, Matthias Hüttler, Marcus Jung, and Renate M. Leithäuser. Modeling the blood lactate kinetics at maximal short-term exercise conditions in children, adolescents, and adults. J Appl Physiol 99: 499–504, 2005; doi:10.1152/japplphysiol.00062.2005.—Whether age-related differences in blood lactate concentrations (BLC) reflect specific BLC kinetics was analyzed in 15 prepubescent boys (age 12.0 ± 0.6 yr, height 1.54 ± 0.06 m, body mass 40.0 ± 5.2 kg), 12 adolescents (16.3 ± 0.7 yr, 1.83 ± 0.07 m, 68.2 ± 7.5 kg), and 12 adults (27.2 ± 4.5 yr, 1.83 ± 0.06 m, 81.6 ± 6.9 kg) by use of a biexponential four-parameter kinetics model under Wingate Anaerobic Test conditions. The model predicts the lactate generated in the extravascular compartment (A), invasion (k1), and evasion (k2) of lactate into and out of the blood compartment, the BLC maximum (BLCmax), and corresponding time (TBLCmax). BLCmax and TBLCmax were lower (P < 0.05) in boys (BLCmax 10.2 ± 1.3 mmol/l, TBLCmax 4.1 ± 0.4 min) than in adolescents (12.7 ± 1.0 mmol/l, 5.5 ± 0.7 min) and adults (13.7 ± 1.4 mmol/l, 5.7 ± 1.1 min). No differences were found in A related to the muscle mass (AMM) and k1 between boys (AMM 22.8 ± 2.7 mmol/l, k1 0.865 ± 0.115 min⁻¹), adolescents (22.7 ± 1.3 mmol/l, 0.692 ± 0.221 min⁻¹), and adults (24.7 ± 2.8 mmol/l, 0.687 ± 0.287 min⁻¹). The k2 was higher (P < 0.01) in boys (2.87 10⁻¹ ± 0.75 10⁻² min⁻¹) than in adolescents (2.03 10⁻¹ ± 0.98 10⁻² min⁻¹) and adults (1.99 10⁻¹ ± 0.93 10⁻² min⁻¹). Age-related differences in the BLC kinetics are unlikely to reflect differences in muscular lactate or lactate invasion but partly faster elimination out of the blood compartment. 

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BLC to the Wingate Anaerobic Test (WAnT) in prepubescent boys, adolescents, and adults using a biexponential four-parameter kinetics model based on BLC measurements pre- and up to 20 min postexercise. This analysis intends to provide indicators of the invasion and evasion of the BLC and of the lactate generated in the extravascular compartment. Furthermore, it allows the calculation of the maximum of the postexercise BLC (BLC_max), the corresponding time (TBLC_max), and the dynamics of the subsequent decrease of the BLC postexercise.

**MATERIAL AND METHODS**

**Subjects.** Fifteen prepubescent boys, 12 male adolescents, and 12 men participated in the present study (Table 1). All subjects were physically active, healthy nonsmokers, and no one was under pharmacological or specific dietetic treatment. Informed consent was obtained from all subjects or their guardians after explanation of the nature and risks involved in participation in the experiments, which conformed to internationally accepted policy statements regarding the use of human subjects as approved by the local ethic committee.

**Procedures.** The subjects started with an incremental load test on an electrodynamically braked cycle ergometer (Excalibur Sport, Lode). The test started with a workload of 1.0 W/kg, which was increased by 0.5 W/kg after every second minute. The incremental load test was finished at individual maximal power output indicated by volitional fatigue after strong vocal encouragement. The incremental load test was finished at individual maximal power output indicated by use of human subjects as approved by the local ethic committee.

The interrelationships between selected variables were examined by use of a four-parameter biexponential model. This model requires a BLC value at the start of exercise (BLC0), and a series of BLC values for as little as 20 min postexercise. It approximates an extravascular increase (A) in lactate generated by exercise metabolism, and two constants describing the kinetics of appearance (k1) and disappearance (k2) of lactate in the blood compartment (Eq. 1).

\[
BLC(t) = \frac{A \cdot k_1}{k_1 - k_2} \cdot (e^{-k_1 \cdot t} - e^{-k_2 \cdot t}) + BLC_0
\]

where t is time. Rearrangement of Eq. 1 enables for the calculation of BLC_max (Eq. 2), the TBLC_max (Eq. 3), and the turn point (TP), the time after that the decrease (Δ) of the posttest BLC can be described monoexponentially (Eq. 4).

\[
BLC_{\text{max}} = BLC_0 + A \cdot \left( \frac{k_1}{k_1 - k_2} \right) e^{\frac{t}{k_2}}
\]

\[
TBLC_{\text{max}} = \frac{1}{k_1 - k_2} \cdot \ln \left( \frac{k_1}{k_2} \right)
\]

\[
TP = \frac{2}{k_1 - k_2} \cdot \ln \left( \frac{k_1}{k_2} \right) = 2T\Delta BLC_{\text{max}}
\]

The change of the extravascular lactate concentration related to MM (Aслим) was estimated based on the assumption that the total lactate water space of the body represents ~62.5% and 60% of the body mass in the boys and in the adolescents and adults, respectively (3, 12, 13, 38).

Descriptive results are reported as mean values and standard deviations (SD). A multiple nonlinear regression analysis was used to test whether the biexponential four-parameter model sufficiently describes the behavior of the BLC over time and to determine the constants A, k1, and k2. Differences between subjects were analyzed by using a one-way ANOVA model with Tukey post hoc analyses. The interrelationships between selected variables were examined by simple linear and nonlinear regression analyses. For all statistics, the significance level was set at P < 0.05.

**RESULTS**

In the incremental load test, BLC_peak was lower (P < 0.05) in the boys than in adolescents and adults. P_peak was higher (P < 0.05) in adolescents than in boys and adults, whereas

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**Table 1. Anthropometric data**

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Boys</th>
<th>Adolescents</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0±0.6</td>
<td>16.3±0.7*</td>
<td>27.2±4.5*†</td>
<td></td>
</tr>
<tr>
<td>Height, m</td>
<td>1.54±0.07</td>
<td>1.83±0.07*</td>
<td>1.83±0.06*</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>40.0±5.2</td>
<td>68.2±7.5*</td>
<td>81.6±6.9*†</td>
</tr>
<tr>
<td>Muscle mass, kg</td>
<td>14.3±2.1</td>
<td>28.6±3.4*</td>
<td>34.3±2.9*†</td>
</tr>
</tbody>
</table>

Values are means ± SD. *Significantly different from boys; †significantly different from adolescents (P < 0.05).
Ppeak related to muscle mass was lower in the adults than in boys and adolescents. No difference in V\textsubscript{O2peak} was found between the three groups but V\textsubscript{O2peak} related to muscle mass was lower (P < 0.05) in adults than in boys and adolescents (Table 2).

Under W\textsubscript{AnT} conditions, the BLC was higher (P < 0.05) in adolescents and adults than in boys from the second postexercise minute on, but no difference in the BLC could be proven between adolescents and adults (Fig. 1). The test-by-test analysis of the kinetics of each single W\textsubscript{AnT} using the four-parameter biexponential model revealed relative explanations of the variance of the BLC over time of 98.7 ± 0.7, 98.3 ± 1.3, and 97.2 ± 2.6%, which were not different between boys, adolescents, and adults, respectively. Further analysis of residuals provided Durbin-Watson coefficients of 1.71, 1.56, and 1.12 in boys, adolescents, and adults, respectively, and showed that in the adults the four-parameter biexponential model slightly overestimated the BLC response during the initial 4 min combined with a slight underestimation of the BLC between the 9th and 16th minute post-W\textsubscript{AnT}, which was not the case in the adolescents and boys (Fig. 1). A and BLC\textsubscript{max} were lower (P < 0.05) and TBLC\textsubscript{max} and TP were shorter (P < 0.05) in boys than in adolescents and adults with no difference between the latter groups. The k\textsubscript{2} was higher (P < 0.05) in boys in than in adolescents and adults. A (Fig. 2), BLC\textsubscript{max} (Fig. 3), and k\textsubscript{2} (r = −0.38, y = −0.001x + 0.033, P < 0.05) were interrelated with age; k\textsubscript{2} was also correlated with BLC\textsubscript{max} (Fig. 4). No differences between the groups were found in k\textsubscript{1} and A\textsubscript{MM} (Table 3). BLC\textsubscript{max} was higher (P < 0.05) than BLC\textsubscript{peak} in all groups. The latter difference, 1.5 ± 1.1, 0.7 ± 0.8, and 1.1 ± 1.0 mmol/l, was higher (P < 0.05) than BLC\textsubscript{peak} in adolescents and adults, respectively (Tables 2 and 3).

In boys AP was lower (P < 0.05) than in adolescents and adults, whereas PP was only lower (P < 0.05) in boys than in adults, but there were no differences between adults and adolescents and boys and adolescents, respectively. MP was lower (P < 0.05) in adults than in adolescents, but no differences between adolescents and adults and boys and adults were found. Adults had a higher (P < 0.05) PD than adolescents, but there was no difference between boys and adolescents or boys and adults. However, if the latter measures of W\textsubscript{AnT} performance were related to MM, no difference between any of the age groups was found (Table 4).

**DISCUSSION**

The present study is the first approach to analyze age-related differences in the dynamic response of the BLC to high-intensity, short-term exercise based on a model comprising parameters for the extravascular increase in lactate generated by exercise metabolism, and the kinetics of appearance and disappearance of lactate into and out of the blood compartment. Previous, more complex system models that allow an objective analysis of theories on the regulation of ATP production in muscle cells, partly combined with the consideration of theories about limiting factors of oxygen transport to the muscle cell (3, 4, 30, 35, 36, 37) have not been applied on
age-related changes in the BLC response to exercise. Furthermore, and particularly when applied to maximal short-term exercise, they strongly rely on assumptions concerning the dynamics of the onset of the glycolytic system during the initial seconds of exercise and are therefore highly speculative.

The applied biexponential four-parameter model well described the behavior of the BLC under WAnT conditions as a cumulative effect of all related factors, irrespective of whether their specific behavior may be described adequately by using exponential models as well. The present results confirm previous results that both incremental load tests and also the WAnT generate lower \((P < 0.05)\) levels of BLC in children compared with adolescents and adults (26, 47). Differences in the BLC response to exercise are more likely to be seen between children and adults or adolescents than between adolescents and adults (18, 26, 32). Differences in model parameters between boys, adolescents, and adults give support to the hypothesis that the difference in BLCmax is a result of a lower \((P < 0.05)\) extravascular increase in lactate generated by the exercise metabolism during physical activity combined with faster elimination of the BLC from the intravascular compartment in boys compared with adolescents and adults, respectively. The latter also seems to explain differences \((P < 0.05)\) in TBLCmax and TP.

However, the present results of lower \((P < 0.05)\) levels of BLCmax as result of a lower \((P < 0.05)\) extravascular increase in lactate generated by exercise do not support the idea of a reduced muscular glycolytic rate at younger age (18, 19, 23, 24). It seems that A has a maximum during the third decade of life. However, the finding that AMM and \(k_1\) are almost identical in all three age groups of the present study seems to be more in line with studies that could not confirm age-related divergences in anaerobic muscular metabolism (9, 25). The latter appears to get further support by similar measures of WAnT performance if expressed related to MM combined with good to excellent levels of performance under WAnT and incremental load conditions (5, 6, 8, 28, 30). Furthermore, AMM values of \(-23 \text{ mmol/kg}\), which is equivalent to an intramuscular rate of lactate increase of \(-0.77 \text{ mmol-kg}^{-1} \cdot \text{s}^{-1}\), are well in the range of the magnitude of intramuscular lactates and energetic equivalents of anaerobic lactic energy production of previous studies using maximal cycling or electrical stimulation of comparable duration in adults (30, 31, 46). Such levels of intramuscular lactate increase are higher than corresponding levels found after \(V_{\text{O2 peak}}\) tests, which also showed age-related differences based on muscle biopsies (18, 32). However, in the present study the higher difference between BLCmax and BLCpeak in boys compared with adolescents and adults may support the idea of age-related differences in intramuscular lactate levels at \(V_{\text{O2 peak}}\) if determined by an incremental load test. Under the assumption that BLCpeak is found when lactate attained equilibrium in its total dilution space, in line with previous findings (18, 32), the present values of BLCpeak indicate a lower increase in muscle lactate in the magnitude of \(-2–3 \text{ mmol/kg}\) in the boys compared with the adolescents and adults at the incremental test. The latter differences in the lactate response to incremental load and WAnT combined with lower \((P < 0.05)\) levels of \(V_{\text{O2 peak}}\) and \(P_{\text{peak}}\) related to muscle mass in adults than in boys may indirectly provide further evidence for consistent findings of higher activities of aerobic muscular enzymes in children (9, 19, 25) and faster \(V_{\text{O2}}\) kinetics in children compared with adults (34, 45).

### Table 3. Lactate response to the WAnT

<table>
<thead>
<tr>
<th></th>
<th>Boys</th>
<th>Adolescents</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, mmol/l</td>
<td>10.4±1.2</td>
<td>12.7±0.7*</td>
<td>13.8±1.6*</td>
</tr>
<tr>
<td>(k_1), min⁻¹</td>
<td>0.86±0.115</td>
<td>0.60±0.032</td>
<td>0.67±0.028</td>
</tr>
<tr>
<td>(k_2), min⁻¹</td>
<td>2.87×10⁻²±0.75×10⁻²</td>
<td>2.03×10⁻²±0.89×10⁻²</td>
<td>1.99×10⁻²±0.93×10⁻²</td>
</tr>
<tr>
<td>AMM, mmol/kgMM</td>
<td>22.8±2.8</td>
<td>22.7±1.3</td>
<td>24.7±2.8</td>
</tr>
<tr>
<td>BLCmax, mmol/l</td>
<td>10.2±1.3</td>
<td>12.7±1.0*</td>
<td>13.7±1.4*</td>
</tr>
<tr>
<td>TBLCmax, min</td>
<td>4.1±0.4</td>
<td>5.5±0.7*</td>
<td>5.7±1.1*</td>
</tr>
<tr>
<td>TP, min</td>
<td>8.3±0.8</td>
<td>11.0±1.4*</td>
<td>11.5±2.2*</td>
</tr>
</tbody>
</table>

Values are means ± SD. A, lactate generated in the extravascular compartment during Wingate Anaerobic Test (WAnT); \(k_1\), constant of invasion into the blood compartment; \(k_2\), constant of evasion out of the blood compartment; BLCmax, highest BLC; TBLCmax, time of BLCmax; TP, turn point, the time after that the decrease of the post-test BLC can be described monoexponentially. *Significantly different from boys \((P < 0.05)\).
The result that the elimination of BLC was almost 30% faster ($P < 0.05$) in the boys compared with adolescents and adults gives further evidence to the hypothesis that, compared with adults, children are superior in the decrease of BLC even under resting conditions (6). On the one hand, the latter may be attributed to higher resting metabolic rates in children compared with adolescents and adults (2); on the other hand, it may also be an effect of lower $BLC_{\text{max}}$ (Fig. 3), an interrelationship described earlier (39). Both of the latter are accelerators of the BLC kinetics shortening TBLC$_{\text{max}}$ in the boys compared with adolescents and adults.

The negative correlation between $k_2$ and $BLC_{\text{max}}$ (Fig. 4) supports previous reports that $k_2$ decreases and the time constant ($\tau$) or the half-time of the BLC during recovery ($T_{1/2}$) increases, if the postexercise maximum of the BLC is higher (39). The present data also clearly indicate that most approaches based on the difference in the BLC between selected time points during the recovery period may be significantly flawed by the dynamics of the lactate invasion. The $k_1$ values determined in the present study are more or less equivalent to a $\tau$ of 1.3 min, indicating that 5–6 min are required for a sufficient completion of the invasion of lactate into the blood compartment. Furthermore, if monoexponential models are applied, the inclusion of data before the TP of the postexercise BLC curve, e.g., data close to the highest level of the postexercise BLC leads to a systematic underestimation of $k_2$ and corresponding overestimations of $\tau$ and $T_{1/2}$ of between 10 and 25%, respectively.

Consequently the findings of no difference in $k_1$ combined with age-related differences in $k_2$ and a negative correlation between $k_2$ and $BLC_{\text{max}}$ does not support the conclusion of a most recent study that in boys the disappearance dynamics of the BLC after maximal short-term exercise are not different from those of men (17), although almost identical levels of BLC had been measured and equally to the present results $BLC_{\text{max}}$ values of $\sim 10.5$ mmol/l were combined with a value of $T_{1/2}$ of $\sim 20$ min. However, in the latter study similar levels of $BLC_{\text{max}}$ had been achieved by using shorter tests in adults compared with children (17). In a within-subject design, $BLC_{\text{max}}$ and $A$ are a function not only of exercise intensity but also of the duration of exercise, whereas $k_2$ decreases if the test duration is increased from 10 to 30 s (Beneke R, Masen DJ, Leithäuser RM, unpublished data). Consequently, similar rates in the decrease of the BLC after short-term exercise of different duration resulting in similar levels of $BLC_{\text{max}}$ in children and adults (17) are more likely the effect of test duration rather than similar kinetics of the disappearance of the BLC.

In conclusion, after maximal short-term exercise the $BLC_{\text{max}}$ is lower and earlier reached in boys than adolescents and adults. There are almost no differences in the BLC response between the latter two groups. The difference in the kinetics of the BLC between boys, adolescents, and adults appears to reflect a lower extravascular increase in lactate generated by the maximal short-term exercise combined with a faster elimination of the BLC. The extravascular increase of lactate seems to have a maximum during the third decade of life. Nevertheless, the latter does not support the hypothesis of a reduced muscular glycolytic rate, but it is consistent with lower relative muscle mass, higher relative total lactate water space, and favorable conditions for the aerobic metabolic system in boys than in adolescents and adults, respectively.

REFERENCES