Anaerobic threshold and respiratory compensation in pregnant women

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Lotgering, Frederik K., Piet C. Struijk, Marieke B. Van Doorn, Wilma E. M. Spinnewijn, and Henk C. S. Wallenburg. Anaerobic threshold and respiratory compensation in pregnant women. *J. Appl. Physiol.* 78(5): 1772–1777, 1995.—In an effort to explore why CO_2 output ($\dot{V}CO_2$) at peak exercise is lower during pregnancy than postpartum despite little change in the peak O_2 uptake ($\dot{V}O_2$), we determined the $\dot{V}CO_2/\dot{V}O_2$ relationship during rapidly incremental exercise and estimated the anaerobic threshold (AT) and the respiratory compensation (RC) point. We measured heart rate, $\dot{V}O_2$, $\dot{V}CO_2$, and minute ventilation ($\dot{V}E$) at rest and during cycle exercise tests with rapidly increasing exercise intensities until maximal effort in 33 volunteers at 16-, 25-, and 35-wk gestation and postpartum. Through modification of the V-slope method, we estimated the AT and RC point for each test by nonlinear regression analysis in a three-dimensional space (defined by $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$) for a line assumed to have two breakpoints; we found a good fit for all tests. The AT and RC points were found at exercise intensities of ~50 and 80% peak $\dot{V}O_2$, respectively, with no significant differences between test periods. $\dot{V}E$ was significantly higher during pregnancy than during postpartum at rest and throughout incremental exercise. A lower peak $\dot{V}CO_2$ relative to peak $\dot{V}O_2$ during pregnancy compared with postpartum was reflected by a more shallow slope of $\dot{V}CO_2$ vs. $\dot{V}O_2$ above the AT point. This suggests that during pregnancy the buffering of lactic acid is reduced.

ventilation; oxygen uptake; carbon dioxide output; breathing rate; tidal volume; pregnancy

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O_2 UPTAKE ($\dot{V}O_2$) and CO_2 output ($\dot{V}CO_2$) at rest are slightly increased during pregnancy, whereas during exercise peak $\dot{V}O_2$ and peak power are unaffected and peak $\dot{V}CO_2$ is lower during gestation (4). The increased $\dot{V}O_2$ and $\dot{V}CO_2$ at rest during pregnancy reflect the needs of the growing conceptus. The fact that peak $\dot{V}O_2$ is unaffected by pregnancy suggests that muscle mass and physical fitness are not altered by gestation. However, the observation that peak $\dot{V}CO_2$ is reduced during pregnancy cannot be explained easily.

It is known that minute ventilation ($\dot{V}E$) is increased during pregnancy through an increase in tidal volume (V_T), an effect that has been attributed to high circulating levels of progesterone (3) and results in a lower arterial P_{CO_2}. Given the hyperbolic relationship between $\dot{V}E$ and arterial P_{CO_2} (7), higher values of $\dot{V}E$ for a given $\dot{V}CO_2$ are therefore to be expected during pregnancy. However, this does not explain the observation of a lower peak $\dot{V}CO_2$ relative to peak $\dot{V}O_2$ during pregnancy.

Below the anaerobic threshold (AT), the relationship between $\dot{V}CO_2$ and $\dot{V}O_2$ is virtually linear, largely metabolic in origin, and little affected by $\dot{V}E$ (2). Above AT, $\dot{V}CO_2$ increases more steeply relative to $\dot{V}O_2$, predominantly as a result of bicarbonate buffering of lactic acid, and $\dot{V}E$ is closely coupled to $\dot{V}CO_2$ (2). The respiratory compensation (RC) point marks the onset of RC for metabolic acidosis, $\dot{V}E$ rises more rapidly than does $\dot{V}CO_2$, and therefore the behavior of $\dot{V}CO_2$ no longer reflects solely metabolic and buffering events (2). We propose that a reduction in $\dot{V}CO_2$ relative to $\dot{V}O_2$ during exercise in pregnant compared with nonpregnant women most likely reflects a reduction in the buffering of lactic acid above AT during gestation. A reduction in RC of metabolic acidosis above the RC point would result in extreme respiratory acidosis and is unlikely because it is not in keeping with the known respiratory drive in pregnant women and the higher peak $\dot{V}E$ observed in pregnant than in postpartum women (4).

To explore why $\dot{V}O_2$ at peak exercise is lower during pregnancy than postpartum despite little change in peak $\dot{V}O_2$, we examined in greater detail our data from a longitudinal study of $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ during cycle tests with rapidly progressing exercise intensities throughout pregnancy and after delivery (4) and we determined the AT and RC points as well as the slopes of $\dot{V}CO_2$ vs. $\dot{V}O_2$, both below and above the AT and RC points.

METHODS

We studied 33 healthy women at 16, 25, and 35 wk of pregnancy and 7 wk after delivery. All women were healthy and had uncomplicated singleton pregnancies. The physical fitness of the subjects who entered the study was variable, ranging between women with a sedentary lifestyle and competitive sportswomen. The study was approved by the Hospital and University Ethics Committee, and all women included in the study gave informed consent.

Details of subjects, study protocol, and data on peak values of heart rate (HR), $\dot{V}O_2$, $\dot{V}CO_2$, and $\dot{V}E$ have been previously reported (4). In short, a physical and obstetric examination was performed to confirm the health of all individuals participating in the study. After 20 min of rest, the subject was seated on a cycle ergometer and connected to an electrocardiogram monitor, a gas flowmeter and mixing chamber, and an O_2 and CO_2 analyzer (Oxycon-4, Mijnhardt, Bunnik, The Netherlands). After 5 min of rest on the cycle ergometer, during which baseline measurements were taken, the women started to exercise. Three minutes of warming up at 30 W were followed by stepwise increments in exercise intensity of 10 W every 30 s until peak aerobic power was achieved. This was followed by 5 min of cooling down at 10 W. Peak aerobic power was defined by subjective maximal effort in the presence of at least two of the following objective criteria: *1*) an increase in $\dot{V}O_2$ of <5% in response to an increase in exercise

intensity, 2) an increase in HR of <5% in response to an increase in exercise intensity, and 3) a respiratory exchange ratio of >1.0. We continuously measured HR, $\dot{V}E$, $\dot{V}O_2$, $\dot{V}CO_2$, and exercise intensity. Thirty-second average values of all variables were calculated on-line and were stored on diskettes for later analysis.

If we assume linear interdependence of the variables $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ and the presence of an AT point and an RC point according to Beaver et al. (2), the relationship among $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ can be described as a line with two breakpoints in a three-dimensional space. To determine the lines and the breakpoints in a three-dimensional trilinear model, we used nonlinear regression analysis (PC + V4.01, SPSS, Chicago, IL) for each test as described in APPENDIX. We normalized the data of all individual tests to a scale of 0 (rest) to 1 (peak) for $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ to avoid a slight distortion that might occur during regression analysis by $\dot{V}E$, which was almost 50-fold higher than $\dot{V}O_2$ and $\dot{V}CO_2$. We used the values at rest and at peak exercise as well as the data obtained at each step of incremental exercise after exclusion of the first 1 min of incremental exercise to avoid distortion caused by the capacity effect of changing tissue CO_2 stores, according to Beaver et al. After the normalized values of the AT and RC points were calculated, the normalized values were converted back to conventional units of $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$, i.e., liters per minute.

For each test period and each variable under consideration, we computed means $\pm$ SE. We used two-way analysis of variance and the signed-rank test to assess differences between paired variables. $P < 0.05$ was taken as the level of significance.

RESULTS

The 33 women (23 primiparae and 10 multiparae) completed all tests. They remained healthy throughout the study period and delivered healthy infants. Mean age at the time of delivery was 30.9 ± 0.7 (SE) yr, gestational age was 40.3 ± 0.2 wk, and birth weight was 3.43 ± 0.08 kg. Each woman underwent an initial test to become acquainted with the experimental circumstances; the data obtained in this test were discarded. All women subsequently were studied at 16.1 ± 1.0 wk (trimester 1), 25.3 ± 0.7 wk (trimester 2), and 35.0 ± 0.6 wk (trimester 3) of pregnancy and at 6.7 ± 1.4 wk after delivery. Body weight at 16-wk gestation was 68.0 ± 1.7 kg, not different from the postpartum control value of 67.6 ± 1.9 kg, but it increased significantly with advancing gestational age to 71.8 ± 1.8 and 75.3 ± 1.8 kg at 25- and 35-wk gestation, respectively.

Mean HR at rest was significantly increased during pregnancy above postpartum control values (87 ± 2, 89 ± 2, 94 ± 2, and 83 ± 2 beats/min, at 16-, 25-, 35-wk gestation and postpartum, respectively), whereas peak HR values were slightly but significantly reduced during pregnancy (174 ± 2, 174 ± 2, 174 ± 2, and 178 ± 2 beats/min at 16-, 25-, 35-wk gestation and postpartum, respectively). Peak power was not significantly different from postpartum control values during the first and second trimester of pregnancy but was slightly reduced at 35-wk gestation (202 ± 7, 196 ± 7, 191 ± 7, and 199 ± 7 W at 16-, 25-, 35-wk gestation and postpartum, respectively).

When we assumed a trilinear relationship among $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$, regression analysis showed a good fit for
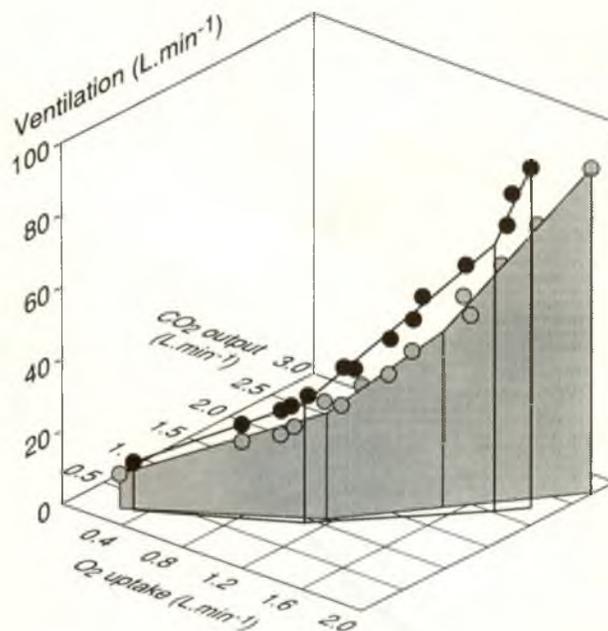

FIG. 1. Trilinear relationship among ventilation, O_2 uptake, and CO_2 output in single volunteer (subject 9) at 16-wk gestation (shaded circles) and postpartum (filled circles).

all tests: the median value of the average distance from the data points to the regression line of a test was 1.2 (0.6–2.2), 1.0 (0.6–2.2), 1.3 (0.6–2.2), and 1.1 (0.6–2.7)% of normalized values at 16-, 25-, and 35-wk gestation and postpartum, respectively. Figure 1 shows an example of the trilinear relationship among $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ in a single volunteer at 16-wk gestation and postpartum. Figure 2 shows the same trilinear relationship in the same volunteer projected onto two-dimensional planes. In addition, it shows that a visually correct fit is maintained for the derived variables $\dot{V}E/\dot{V}O_2$ vs. $\dot{V}O_2$, $\dot{V}E/\dot{V}CO_2$ vs. $\dot{V}CO_2$, and $\dot{V}CO_2/\dot{V}O_2$ vs. $\dot{V}O_2$.

We found a clearly discernible AT and RC point in 125 of 132 tests (95%), and in all 33 volunteers two breakpoints were found in at least three of the four tests. In seven tests, breakpoints were found that might suggest a bilinear rather than a trilinear relationship among variables. In three of these tests the AT point was found between the resting value and the lowest value measured during incremental exercise, in three tests the AT and RC points were found to coincide, and in one test the RC point was found between the peak value and the highest value measured during incremental exercise below the peak. These breakpoints are not necessarily incorrect nor do they markedly distort the overall picture. Therefore, these breakpoints have not been excluded from further analysis.

Table 1 shows the mean values of $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, breathing rate, and VT at rest and at peak exercise as well as at the two calculated breakpoints (AT and RC) in the relationship among $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$. The AT and RC points were found at exercise intensities of ~50 and 80% peak $\dot{V}O_2$, respectively, with no significant differences between the four test periods (53.4 ± 4.3, 52.2 ± 5.6, 52.3 ± 4.8, and $50.5 \pm 6.4\%$ peak $\dot{V}O_2$ for AT and
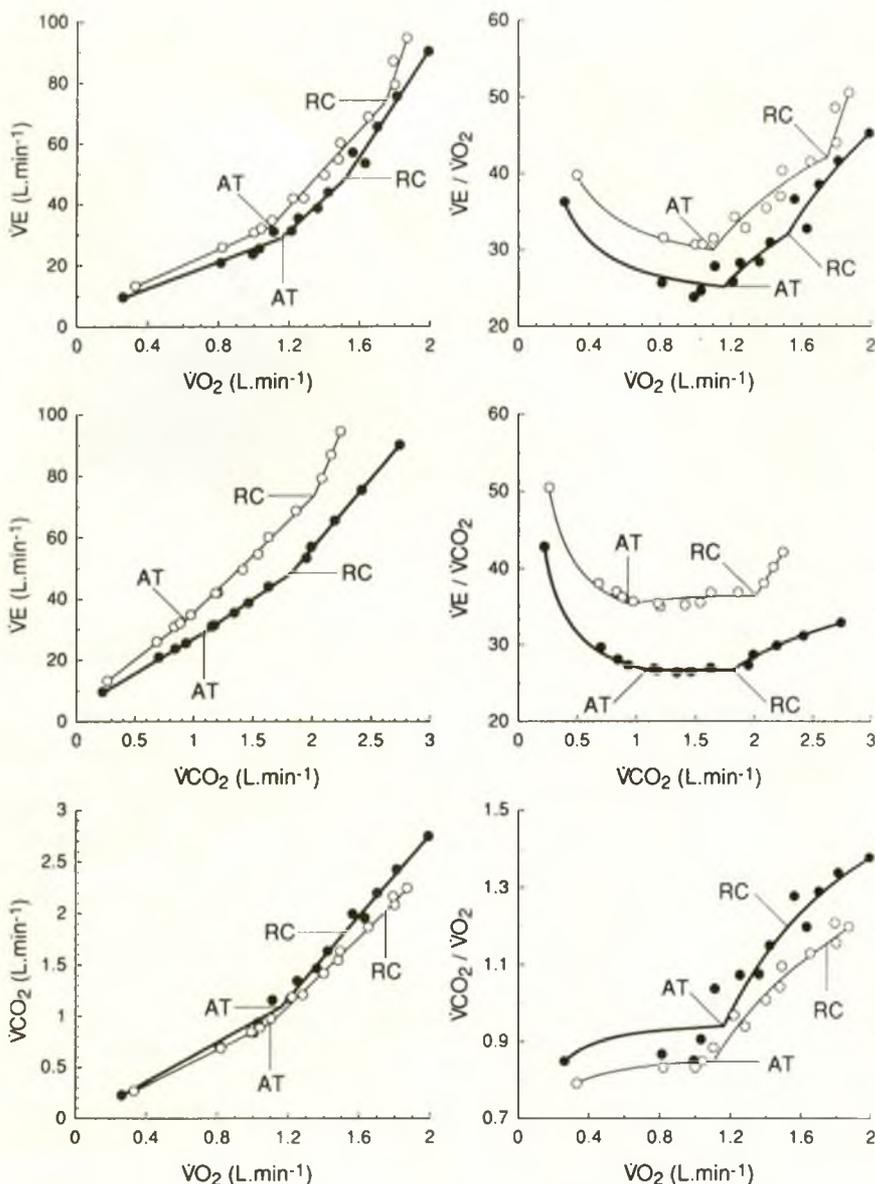
FIG. 2. Trilinear relationship among ventilation ($\dot{V}E$), O_2 uptake ($\dot{V}O_2$), and CO_2 output ($\dot{V}CO_2$), and derived variables in single volunteer (*subject 9*) at 16-wk gestation (○) and postpartum (●). RC, respiratory compensation; AT, anaerobic threshold.

79.3 ± 8.4, 79.0 ± 9.4, 76.9 ± 8.0, and 78.2 ± 6.9% peak $\dot{V}O_2$ for RC at 16-, 25-, and 35-wk gestation and postpartum, respectively). $\dot{V}O_2$ at the AT and RC points correlated with peak $\dot{V}O_2$ in all four test periods (0.73 < r < 0.91) and, therefore, with physical condition.

$\dot{V}E$ was significantly higher during gestation at rest and throughout incremental exercise. This was accomplished by a significantly higher VT without a significantly different breathing rate during pregnancy compared with postpartum. $\dot{V}O_2$ and $\dot{V}CO_2$ were higher during pregnancy than during postpartum at rest and not significantly different between periods at the AT and RC points. At peak effort, $\dot{V}O_2$ was similar and $\dot{V}CO_2$ was lower in pregnant than in postpartum women.

Table 2 shows the slopes of the lines in relation to the AT and RC points. The data are presented as medians with 10th to 90th percentiles to exclude some extreme values of slopes that resulted from the questionable presence of an AT or RC point in 7 of the 132 tests. Above AT, the slopes of $\dot{V}E$ vs. $\dot{V}O_2$ and $\dot{V}CO_2$ vs. $\dot{V}O_2$ were significantly steeper than those below AT for all periods, whereas the slopes of $\dot{V}E$ vs. $\dot{V}CO_2$ were not different from those below AT. Above the RC point, the slopes showed a significant further increase for all three relationships and all four periods. Consequently, the $\dot{V}E$ vs. $\dot{V}O_2$ and $\dot{V}CO_2$ vs. $\dot{V}O_2$ relationships are trilinear, with an AT and RC point, whereas $\dot{V}E$ vs. $\dot{V}CO_2$ is in fact bilinear with no AT point.

Pregnancy significantly increased the slopes of $\dot{V}E$ vs. $\dot{V}CO_2$ throughout incremental exercise, whereas for $\dot{V}E$ vs. $\dot{V}O_2$ it increased the slopes below and above AT but not above the RC point. Most notably, however, the slopes of $\dot{V}CO_2$ vs. $\dot{V}O_2$ that were similarly steep between periods below AT were significantly shallower above AT during gestation. Above the RC point, the slopes of $\dot{V}CO_2$ vs. $\dot{V}O_2$ were significantly more shallow than postpartum only during the third trimester of pregnancy.

TABLE 1. *Effect of pregnancy on values at rest and at peak cycle exercise as well as at AT and onset of RC*

	$\dot{V}_{O_2}$, l/min	$\dot{V}_{CO_2}$, l/min	$\dot{V}_E$, l/min	Breathing Rate, breaths/min	V_T, liters
Rest					
16 wk	0.29±0.01†	0.23±0.01*	11.4±0.3*	15.7±0.4	0.74±0.02*
25 wk	0.29±0.01*	0.24±0.01*	11.5±0.3*	15.6±0.4	0.75±0.02*
35 wk	0.31±0.01*	0.25±0.01*	12.3±0.3*	15.7±0.4	0.80±0.02*
Postpartum	0.27±0.01	0.21±0.01	9.5±0.2	16.1±0.4	0.60±0.02
AT					
16 wk	1.24±0.05	1.05±0.04	35.8±1.1*	21.1±0.6	1.72±0.06*
25 wk	1.19±0.03	1.01±0.04	35.1±0.8*	21.8±0.5	1.64±0.05*
35 wk	1.21±0.04	1.02±0.04	37.1±1.0*	22.3±0.6	1.71±0.07*
Postpartum	1.17±0.03	0.98±0.03	29.8±0.8	21.9±0.6	1.39±0.05
RC					
16 wk	1.84±0.07	1.88±0.08	62.6±2.7	30.0±1.0	2.10±0.06*
25 wk	1.83±0.07	1.88±0.08	63.8±2.7*	30.3±1.0	2.11±0.07*
35 wk	1.79±0.07	1.83±0.07	63.8±2.4*	30.0±1.0	2.16±0.08*
Postpartum	1.81±0.06	1.92±0.07	54.8±2.2	28.8±1.0	1.93±0.07
Peak					
16 wk	2.20±0.08	2.56±0.09*	95.6±3.2*	45.2±1.3	2.13±0.07*
25 wk	2.16±0.08	2.51±0.08*	94.6±2.9*	44.1±1.3	2.14±0.07*
35 wk	2.15±0.08	2.46±0.09*	96.1±3.5*	42.7±1.1	2.20±0.08*
Postpartum	2.19±0.08	2.70±0.09	89.5±3.0	43.9±1.6	2.02±0.06

Values are means ± SE; $n = 33$ women. AT, anaerobic threshold; RC, respiratory compensation; $\dot{V}_{O_2}$, O_2 uptake; $\dot{V}_{CO_2}$, CO_2 output; $\dot{V}_E$, minute ventilation; V_T, tidal volume. Significantly different compared with postpartum control values: * $P < 0.01$; † $P < 0.05$.

DISCUSSION

AT is defined as the level of exercise $\dot{V}_{O_2}$ above which aerobic energy production is supplemented by anaerobic mechanisms (7). Traditional methods for AT detection rely on visual inspection of graphical plots of ventilatory equivalents and end-tidal gas concentrations (2). The large inter- and intraobserver variation in the visual assessment of the ventilatory threshold led us, like others (2, 5), to search for a mathematical method applicable to the data from our longitudinal study of $\dot{V}_E$, $\dot{V}_{O_2}$, and $\dot{V}_{CO_2}$ during incremental exercise in pregnancy and after delivery, as previously reported (4). The fact that we had not measured end-tidal P_{CO_2} or arterial blood gas values in that study and had stored only 30-s average values limited our options to determine AT.

The physiological basis for our analysis of the data was provided by the V-slope method of Beaver et al. (2). Beaver et al. start their analysis by considering $\dot{V}_E$ vs. $\dot{V}_{CO_2}$ as a bilinear relationship to detect an RC point. Subsequently, the data below the RC point are selected to derive AT as the breakpoint of the $\dot{V}_{CO_2}$ vs. $\dot{V}_{O_2}$ relationship, which is bilinear below the RC point. When we tried this method, exclusion of the data above the RC point resulted in such a reduction of our 30-s average data points that the AT point could not be identified reliably in several cases. By modifying the V-slope method into a single routine in which we consider the relationship among the three variables $\dot{V}_E$, $\dot{V}_{O_2}$, and $\dot{V}_{CO_2}$ as a line in a three-dimensional space with two breakpoints, AT and RC, there was no need to exclude any of our data points, and we were able to detect reliably two breakpoints in 95% of the tests.

TABLE 2. *Effect of pregnancy on slopes of trilinear relationship between $\dot{V}_E$, $\dot{V}_{O_2}$, and $\dot{V}_{CO_2}$*

	Slope Below AT	Slope Between AT and RC	Slope Above RC
$\dot{V}_E$ vs. $\dot{V}_{O_2}$			
16 wk	25.1* (22.4–30.2)	44.3* (30.1–59.1)	95.3 (54.5–170)
25 wk	25.9* (23.9–30.2)	47.1* (28.9–56.8)	85.4 (56.6–245)
35 wk	26.9* (23.9–34.3)	48.6* (31.2–60.9)	86.4 (48.9–180)
Postpartum	22.9 (19.3–26.1)	39.4 (23.9–52.1)	86.1 (46.8–178)
$\dot{V}_E$ vs. $\dot{V}_{CO_2}$			
16 wk	29.6* (27.2–32.6)	31.3* (24.5–37.4)	49.2* (33.7–67.4)
25 wk	30.8* (27.9–34.2)	33.0* (25.2–37.3)	48.5* (34.5–77.4)
35 wk	31.7* (29.3–37.0)	34.0* (25.1–39.4)	49.0 (32.0–64.7)
Postpartum	26.3 (23.4–30.8)	26.2 (20.3–32.5)	42.7 (26.4–65.7)
$\dot{V}_{CO_2}$ vs. $\dot{V}_{O_2}$			
16 wk	0.87 (0.74–0.94)	1.37* (1.21–1.62)	1.94 (1.47–2.88)
25 wk	0.85 (0.78–0.96)	1.42* (1.06–1.56)	1.83 (1.44–3.16)
35 wk	0.84 (0.77–0.95)	1.36† (1.18–1.75)	1.76† (1.26–2.58)
Postpartum	0.87 (0.75–0.94)	1.44 (1.15–1.75)	2.14 (1.61–2.71)

Values are medians, with 10th to 90th percentiles in parentheses; $n = 33$ women. Significantly different compared with postpartum control values: * $P < 0.01$, † $P < 0.05$.

There are three reasons why we feel that our mathematical modification of the V-slope method is justified. First, we very consistently found two breakpoints for the $\dot{V}E$ vs. $\dot{V}O_2$ and $\dot{V}CO_2$ vs. $\dot{V}O_2$ relationships and only one breakpoint, the RC point, for $\dot{V}E$ vs. $\dot{V}CO_2$, as one would expect. Second, the breakpoints were found at exercise intensities that one would expect for the AT and RC points and very close in terms of percent peak $\dot{V}O_2$ to the AT and RC points found by Beaver et al. Third, a visually correct fit was maintained for derived variables, as shown in Fig. 2.

Our data show that the marked reduction in peak $\dot{V}CO_2$ relative to peak $\dot{V}O_2$ during pregnancy results from a shallower slope of $\dot{V}CO_2$ vs. $\dot{V}O_2$ above AT compared with postpartum. This most likely reflects a reduction in the buffering of lactic acid by bicarbonate. Because our data do not allow identification of the underlying cause, we may only speculate about the possible mechanisms. A reduction in the rate of lactic acid production is unlikely as maximal power was virtually unaffected by gestation. Increased utilization of lactate during pregnancy by the liver (6) or by the fetoplacental unit, for which it is the second most important substrate (1), might possibly explain the observed reduction in maximal $\dot{V}CO_2$ in pregnancy.

APPENDIX

To determine a line with two breakpoints in a three-dimensional space while assigning approximately equal weight to the variables, we converted the data of all individual tests to a scale of 0–1 for $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$.

Normalization procedure. The mean value at rest was set at 0; the peak value was set at one. The data of each step of incremental exercise were assigned a value between 0 and 1: for $\dot{V}O_2$, on the x-axis as $x_i = (\dot{V}O_2$ incremental $- \dot{V}O_2$ rest)/(peak $\dot{V}O_2 - \dot{V}O_2$ rest) and, similarly, as y_i for $\dot{V}CO_2$ on the y-axis and as z_i for $\dot{V}E$ on the z-axis.

Finding the regression line. If we assume that the AT point is $\begin{pmatrix} x_1 \\ y_1 \\ z_1 \end{pmatrix}$ and the RC point is $\begin{pmatrix} x_2 \\ y_2 \\ z_2 \end{pmatrix}$, we can describe the three segments (rest to AT, AT to RC, and RC to peak) as the vector equations

$$\begin{pmatrix} x \\ y \\ z \end{pmatrix} = a \begin{pmatrix} x_1 \\ y_1 \\ z_1 \end{pmatrix} \tag{A1}$$

$$\begin{pmatrix} x \\ y \\ z \end{pmatrix} = \begin{pmatrix} x_1 \\ y_1 \\ z_1 \end{pmatrix} + b \begin{pmatrix} x_2 - x_1 \\ y_2 - y_2 \\ z_2 - z_2 \end{pmatrix} \tag{A2}$$

$$\begin{pmatrix} x \\ y \\ z \end{pmatrix} = \begin{pmatrix} x_2 \\ y_2 \\ z_2 \end{pmatrix} + c \begin{pmatrix} 1 - x_2 \\ 1 - y_2 \\ 1 - z_2 \end{pmatrix} \tag{A3}$$

in which x_1, y_1, z_1 and x_2, y_2, z_2 can be determined by minimizing the sum of squared distances of the data points to the regression line, as

$$d(Q,l) = \frac{\|\mathbf{r} * (\bar{\mathbf{q}} - \bar{\mathbf{p}})\|}{\|\mathbf{r}\|} \tag{A4}$$

in which d (Q,l) is the distance of a point Q with a position vector $\bar{\mathbf{q}}$ to line l, $\bar{\mathbf{p}}$ is the position vector, and $\mathbf{r}$ is the direction vector of the line segment under consideration.

The following SPSS commands specify the three-segmented model in which join points AT and RC are to be estimated.

```
COMPUTE ZERO = 0
MODEL PROGRAM  Y1=0.4  Z1=0.3  Y2=0.6  Z2=0.5.
IF ( X <= 0.5 )
PRED1 = SQRT((Y1*Z−Z1*Y)**2 + (Z1*X−0.5*Z)**2 +
(0.5*Y−Y1*X)**2) /
        SQRT(0.5**2 + Y1**2 + Z1**2).
IF ( X > 0.5 AND X < 0.75 )
PRED1 = SQRT(((Y2−Y1)*(Z−Z1)−(Z2−Z1)*(Y−Y1))**2 +
        ((Z2−Z1)*(X−0.5)−(0.75−0.5)*(Z−Z1))**2 +
        ((0.75−0.5)*(Y−Y1)−(Y2−Y1)*(X−0.5))**2) /
        SQRT((0.75−0.5)**2 + (Y2−Y1)**2 + (Z2−Z1)**2).
IF ( X >= 0.75 )
PRED1 = SQRT(((1−Y2)*(Z−Z2)−(1−Z2)*(Y−Y2))**2 +
        ((1−Z2)*(X−0.75)−(1−0.75)*(Z−Z2))**2 +
        ((1−0.75)*(Y−Y2)−(1−Y2)*(X−0.75))**2) /
        SQRT((1−0.75)**2 + (1−Y2)**2 + (1−Z2)**2).
NLR ZERO WITH X Y Z / PRED=PRED1 / OUTFILE=
   'ESTIM.SYS'.
MODEL PROGRAM  X1=0.5 Y1 Z1 X2=0.75 Y2 Z2.
IF ( X <= X1)
PRED = SQRT((Y1*Z−Z1*Y)**2 + (Z1*X−X1*Z)**2
   + (X1*Y−Y1*X)**2)/
        SQRT(X1**2 + Y1**2 + Z1**2).
IF ( X > X1 AND X < X2 )
PRED = SQRT(((Y2−Y1)*(Z−Z1)−(Z2−Z1)*(Y−Y1))**2 +
        ((Z2−Z1)*(X−X1)−(X2−X1)*(Z−Z1))**2 +
        ((X2−X1)*(Y−Y1)−(Y2−Y1)*(X−X1))**2) /
        SQRT((X2−X1)**2 + (Y2−Y1)**2 + (Z2−Z1)**2).
IF ( X >= X2)
PRED = SQRT(((1−Y2)*(Z−Z2)−(1−Z2)*(Y−Y2))**2 +
        ((1−Z2)*(X−X2)−(1−X2)*(Z−Z2))**2 +
        ((1−X2)*(Y−Y2)−(1−Y2)*(X−X2))**2) /
        SQRT((1−X2)**2 + (1−Y2)**2 + (1−Z2)**2).
NLR ZERO WITH X Y Z / FILE ='ESTIM.SYS' / SAVE PRED .
```

The nonlinear regression routine can determine the parameters by minimizing the squared sum of residuals. As a first estimate of the necessary initial values, the routine was run as an intermediate step with $x_1 = 0.5$ and $x_2 = 0.75$ as constant values and $y_1 = 0.4$, $z_1 = 0.3$, $y_2 = 0.6$, and $z_2 = 0.5$ as initial values. The estimates of x_1 to z_2 thus obtained were used to run a subsequent routine to calculate the normalized values of the AT and RC points that were then converted back to conventional units and reported in the text.

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