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GAS EXCHANGE ANALYSIS OF IMMEDIATE CO_2 STORAGE AT ONSET OF EXERCISE

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Abstract. The immediate storage of CO_2 at the onset of exercise was estimated in 5 subjects as the difference between measured and predicted CO_2 production at work rates of 33, 53 and 75% $\dot{V}_{O_2}$max. Three time varying models of respiratory exchange ratio (RER) were used to obtain an expected range of predicted CO_2 production. Calculated CO_2 storage in the transition from rest to 33% $\dot{V}_{O_2}$max ranged from 0.33 to 0.38 ml · kg^{-1} · torr^{-1}; from 33 to 53% $\dot{V}_{O_2}$max, corresponding values were −0.04 to 0.14 ml · kg^{-1} · torr^{-1}; and, from 53 to 75% $\dot{V}_{O_2}$max, values ranged from −0.25 to 0.16 ml · kg^{-1} · torr^{-1}. In two models, CO_2 storage decreased significantly at the highest work rate. Estimates of CO_2 storage by hyperventilation in the steady state of exercise yielded significantly greater storage. It was concluded that immediate CO_2 storage at the onset of exercise was less than hyperventilation estimates, and that it tended to decrease with metabolic acidosis.

Acidosis	Carbon dioxide stores	Hyperventilation
Blood acid–base	Human	Onset of exercise

At the onset of exercise, metabolic CO_2 production ($\dot{V}_{CO_2}$) increases in proportion to the oxygen consumption ($\dot{V}_{O_2}$). However, kinetic analyses of respiratory gas exchange have shown the clear differences in the time constants for these two variables. Oxygen uptake ($\dot{V}_{O_2}$) adapts to the steady state of moderate exercise with a time constant (τ) of about 30 sec, while carbon dioxide output ($\dot{V}_{CO_2}$) adapts with a τ = 50 sec (Hughson and Morrissey, 1982; Linnarsson, 1974; Whipp *et al.*, 1982). This slower adaptation of $\dot{V}_{CO_2}$ is a consequence of CO_2 storage. Observation of the respiratory exchange ratio (RER) at the onset of exercise reflects this difference in time constants as the RER decreases transiently before rising to a new steady state (Whipp *et al.*, 1982).

The kinetics of $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ are dependent on the exercise transitions studied. From rest or zero load to work, the time constants reported above are appropriate. However, when exercise proceeds from light to moderate or heavy work rates, the $\dot{V}_{O_2}$ kinetics

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become slower while the $\dot{V}_{CO_2}$ kinetics are either unchanged or become faster (Hughson and Morrissey, 1982; 1983). Thus, the pattern of CO_2 storage changes such that less CO_2 must be stored at higher work rates. Jones and Jurkowski (1979) found that CO_2 storage studied by hyperventilation in the steady state of exercise decreased at higher work rates. They concluded that the total body CO_2 dissociation curve tended to flatten out at the high levels of mixed venous P_{CO_2} observed with heavy exercise.

To date, there have been no attempts to estimate the immediate CO_2 storage capacity at the onset of exercise by measurement of respiratory gas exchange. This study has calculated the CO_2 storage from breath-by-breath measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ during the transition from one steady state to the next. Three levels of exercise were examined with the highest being approximately 75% $\dot{V}_{O_2}$max. The hyperventilation technique for assessing CO_2 storage was also performed at each of these three work rates to permit comparison of values. It was hypothesized that the immediate CO_2 storage at the onset of exercise would be considerably smaller than the storage determined by hyperventilation. It was further hypothesized that at the highest work rate both methods will yield smaller values of CO_2 storage as a consequence of metabolic acidosis.

Methods

Five healthy subjects (3 male, 2 female) volunteered for this study (table 1). All subjects exercised at least 3–5 days per week in some form of activity. The protocol was explained in detail prior to obtaining each subject's consent to participate.

All testing was conducted on a Siemens electric cycle ergometer. An initial progressive exercise test to exhaustion was performed by all subjects. On the basis of this test, work rates of 70, 140 and 210 W were selected for the males and of 50, 100 and 150 W for the females. The lower work rates were below the ventilatory threshold, while the highest work rate was above this level.

Respiratory gas exchange ($\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$) and ventilation were monitored with a breath-by-breath system based on microcomputer (Microwat, Northern Digital,

TABLE 1
Characteristics of subjects

	Sex	Age	Height (cm)	Weight (kg)	$\dot{V}_{O_2}$max ($ml \cdot min^{-1}$)
1	M	22	183	65	3940
2	M	33	177	61	3870
3	M	26	180	80	4030
4	F	26	165	53	2550
5	F	25	169	61	2600

Waterloo, Canada), a respiratory mass spectrometer (Perkin Elmer MGA-1100), and a turbine volume meter (Alpha Technologies VMM-110). Calibration of the mass spectrometer with primary standard gases and of the volume turbine with a large calibrated syringe was checked prior to each test. The algorithm of Beaver *et al.* (1981) was used to calculate gas exchange at the alveolar level with corrections for changes in lung volume and lung gas composition. The breath-by-breath data were stored on diskette for later analysis.

A rebreathing technique (Jones and Campbell, 1981) was used to estimate the oxygenated mixed venous P_{CO_2} ($P\bar{v}_{CO_2}$) for each of the test conditions. In all cases, $P\bar{v}_{CO_2}$ was estimated prior to and following an experimental manipulation. For each rebreathe preceding a test, the respiratory exchange ratio was carefully monitored to ensure a return to the pre-rebreathe level before continuing the testing. This required up to 4–5 min in some subjects. The average value obtained from all rebreathes during the repetitions of a test was used in subsequent calculations.

Two models were studied to estimate the change in CO_2 storage capacity during exercise. One was based on the difference between predicted and measured CO_2 production at the onset of three levels of constant-load exercise. The second model was the hyperventilation technique applied by several previous investigators (e.g. Jones and Jurkowsi, 1979) during the steady state of constant-load exercise.

Onset of exercise studies. The change in CO_2 storage at the onset of exercise was determined in response to a square wave change in work rate. A steady state was established at a baseline of rest prior to the 70 W (male subjects) and 50 W (female subjects) tests, or at the preceding work rate for the higher power outputs. Without prior warning to the subject, the new higher power output was started with the change approximating a square wave. Each subject performed 4 repetitions of each of these transitions. The duration of the two lower work rates was 5 min; the higher work rate was continued for 8 min. The data from the repetitions were superimposed for analysis of individual subjects. In two of these square wave tests at each work rate, a catheter was placed in a dorsal hand vein. The hand was warmed in a heating pad and presumably arterialized blood samples ($P_{O_2} > 70$ torr) were obtained in the steady state for measurement of blood lactate by a fluorometric technique (Lowry and Passonneau, 1972), and for pH and P_{CO_2} by a Radiometer (PHM71 Mk2) acid–base analyzer.

Onset of exercise CO_2 storage was estimated from three models designed to include the probable range of metabolic respiratory quotient (RQ) responses at the initiation of a higher work rate. The respiratory exchange ratio (RER) during the final 2 min of each work rate was taken as equivalent to the RQ. Since the pattern of change for the increase in RQ is not known, it was necessary to propose three models. (1) To allow RQ to increase in an exponential manner from the pre-onset RER to the new steady level RER with a time constant of 45 sec (*i.e.* steady state in approximately 3–4 min). (2) To allow metabolic RQ to change as a square wave from the pre-onset RER to the steady level RER of exercise. (3) To allow RQ to increase instantly to 1.0 then decline with a time constant of 45 sec to the exercise steady level RER. The significance of these models

will be elaborated in the Discussion (see fig. 6). The predicted CO_2 production was obtained by multiplying the measured O_2 consumption by the time varying RQ. The sum of the difference between measured and predicted CO_2 production was obtained over the total exercise duration. The CO_2 production due to utilization of oxygen stores was not included in this calculation for reasons detailed in the Discussion. The absolute CO_2 storage (ml CO_2) was normalized by dividing by body weight and the change in rebreathing oxygenated $P\bar{v}_{CO_2}$ from pre-exercise to the end of the exercise period.

Hyperventilation studies. The hyperventilation technique described by Jones and Jurkowski (1979) was also used to estimate CO_2 storage. When the subject was in a steady state as judged by the constancy of the respiratory exchange ratio at each of the three exercise levels, hyperventilation was started. The subjects were instructed to achieve, as quickly as possible, an end tidal fractional CO_2 concentration of 0.36 (approximately equivalent to 3.4 kPa, or 25 torr). This value was displayed on a video screen at the end of each breath. Two repetitions were performed by each subject at the two lower work rates. At the high work rate, two repetitions were done by subjects 1 and 2 only. The repetitions were superimposed for data analysis. In one of the tests, arterialized venous blood was sampled as described above. Each hyperventilation session lasted 15 min.

Hyperventilation estimates of the change in CO_2 storage were obtained by subtracting the predicted V_{CO_2} calculated by multiplying the V_{O_2} by the RER at the end of hyperventilation, from the actual V_{CO_2} for each 10 sec period during the 15 min of hyperventilation. This absolute value of the change in CO_2 storage capacity was normalized as described above by dividing by body weight and the change in rebreathing oxygenated $P\bar{v}_{CO_2}$ from pre-hyperventilation to the value obtained immediately on cessation of 15 min hyperventilation.

Statistical analysis was performed by two way analysis of variance using the subject by treatment error term. Each model for the onset of exercise study was treated separately. *Post hoc* tests of significant *F* statistics were with Duncan's Multiple Range Test. The statistical level of significance accepted was $P < 0.05$.

Results

Onset of exercise studies. The response of subject 3 for $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ at the onset and the steady states of the three work rates is shown in fig. 1. The mean gas exchange values for all subjects based on the steady states following the step increase of work rate are shown in table 2. The $\dot{V}_{O_2}$ expressed as a percentage of $\dot{V}_{O_2}$max for work levels 1 to 3 were 33, 53 and 75%, respectively. The respiratory exchange ratio (RER) was significantly lower for exercise level 1 than 2 or 3.

Blood lactate response (table 3) reflected the $\%\dot{V}_{O_2}$max as a significant increase in concentration occurred between exercise levels 2 and 3. At the highest work rate, the blood lactate concentration was 3.7 mM (range 2.8–8.3 mM). No significant differ-

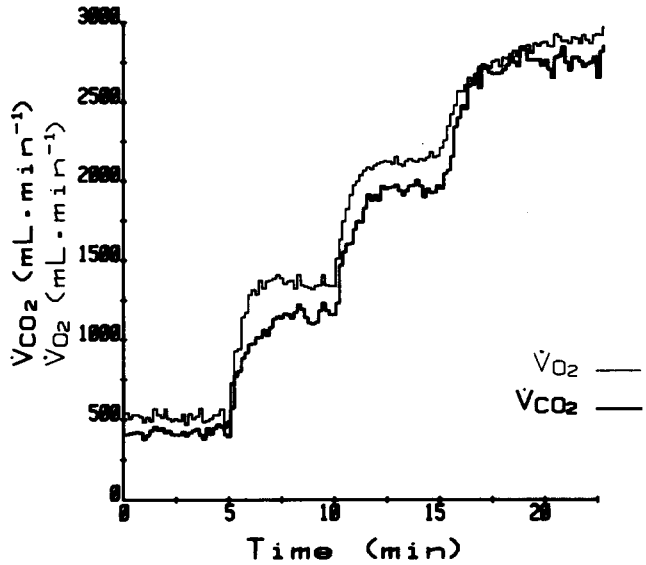

Fig. 1. The $\dot{V}_{O_2}$ (thin line) and $\dot{V}_{CO_2}$ (heavy line) are represented for each 10 sec interval in the transitions from rest to work rates 1, 2 and 3 for subject 3. The periods of CO_2 rebreathing have been removed to make the pattern more clear. Note that $\dot{V}_{CO_2}$ lags behind $\dot{V}_{O_2}$ adaptation in the rest to work rate 1 transition; but, the adaptation of $\dot{V}_{CO_2}$ is faster than that of $\dot{V}_{O_2}$ for the work rate 2 to 3 transition.

TABLE 2

Steady state values for respiratory gas exchange in each of the three exercise levels for the onset of exercise and the hyperventilation studies (values are means ± 1 SD, n = 5).

	Exercise 1		Exercise 2		Exercise 3	
	Ex. Onset	Hypervent.	Ex. Onset	Hypervent.	Ex. Onset	Hypervent.
$\dot{V}_{O_2}$ ($ml \cdot min^{-1}$)	1130 ± 170	1100 ± 250	1790 ± 300	1790 ± 280	2540 ± 390	2760 ± 360
$\dot{V}_{CO_2}$ ($ml \cdot min^{-1}$)	970 ± 160	1000 ± 230	1640 ± 260	1680 ± 260	2390 ± 360	2530 ± 370
RER	0.86* ± 0.02	0.91* ± 0.04	0.92 ± 0.01	0.93 ± 0.03	0.94 ± 0.01	0.92 ± 0.02

* Values of a pair are significantly different, $P < 0.05$.

ences were observed for arterialized blood P_{CO_2} and pH between any of the exercise levels.

The rebreathing estimate of $P\bar{v}_{CO_2}$ increased markedly from rest to work rate 1 and from work rate 1 to work rate 2 (table 3). The small increase in $P\bar{v}_{CO_2}$ from level 2 to 3 was not statistically significant.

The change in CO_2 storage during the onset of exercise studies is displayed in table 4.

TABLE 3

Arterialized venous blood values for lactate, pH and P_{CO_2} and rebreathing determination of $P\bar{v}_{CO_2}$ for rest and three work rates during the steady states for the onset of exercise (Ex. Onset) and hyperventilation studies (n = 5, mean + 1 SD).

	Rest	Exercise 1		Exercise 2		Exercise 3	
		Ex. Onset	Hypervent.	Ex. Onset	Hypervent.	Ex. Onset	Hypervent.
Lactate (mM)	0.81^a ± 0.39	0.81^a ± 0.19	1.13^a ± 0.40	1.33^a ± 0.47	1.80^a ± 0.76	3.67^b ± 1.86	5.22^c ± 2.07
pH	–	7.39^a ± 0.04	7.55^b ± 0.17	7.41^a ± 0.02	7.53^b ± 0.05	7.39^a ± 0.03	$7.44^{a,b}$ ± 0.06
P_{CO_2} (torr)	–	35.2^a ± 1.0	22.7^b ± 2.9	34.3^a ± 2.5	21.9^b ± 2.6	34.0^a ± 5.0	25.0^b ± 1.8
$P\bar{v}_{CO_2}$ (Torr)	53.1^a ± 1.3	62.1^b ± 1.9	47.1^c ± 1.9	70.9^d ± 3.9	53.1^a ± 2.8	72.5^d ± 6.5	61.1^b ± 2.9

[a,b] Statistical analysis by analysis of variance with *post-hoc* test by Duncan's Multiple Range test where means that do not have the same superscript letter are significantly different ($P < 0.05$).

TABLE 4

CO_2 storage for onset of exercise using three models of time varying RQ, and for hyperventilation in the steady state. Absolute and relative storage are given for each level (mean ± SD; n = 5 except for Exercise 3 hyperventilation where n = 4).

	Exercise 1		Exercise 2		Exercise 3	
	Absolute store (ml CO_2)	Relative store* (ml $CO_2 \cdot kg^{-1} \cdot torr^{-1}$)	Absolute store (ml CO_2)	Relative store (ml $CO_2 \cdot kg^{-1} \cdot torr^{-1}$)	Absolute store (ml CO_2)	Relative store (ml $CO_2 \cdot kg^{-1} \cdot torr^{-1}$)
Onset of Exercise						
Model 1	190^a ± 93	0.37^c ± 0.24	25^b ± 44	0.04^d ± 0.08	-99^b ± 146	-0.25^d ± 0.31
Model 2	200^a ± 87	0.38^c ± 0.22	$75^{a,b}$ ± 41	$0.14^{c,d}$ ± 0.07	-33^b ± 122	-0.06^d ± 0.29
Model 3	180^a ± 59	0.33^b ± 0.14	68^a ± 41	0.12^b ± 0.07	14^a ± 125	0.16^b ± 0.42
Hyperventilation						
	1650^a ± 690	1.63^b ± 0.51	1890^a ± 590	1.85^b ± 0.40	1380^a ± 440	1.68^b ± 0.78

[a,b] Statistical analysis across exercise levels by analysis of variance with *post-hoc* test by Ducan's Multiple Range test where means which do not have the same superscript letter are significantly different ($P < 0.05$).
* Relative CO_2 storage was determined by dividing the absolute storage value by body weight and the change in oxygenated $P\bar{v}_{CO_2}$ from the previous baseline to present condition.

It can be seen that the absolute change in CO_2 storage (ml CO_2) decreased at the higher work rates($P < 0.05$). All three models predicted similar storage for the rest to lowest work rate transition; but, there was a tendency at high work rates for the absolute storage to be greater for model 3 which predicted an abrupt increase of RQ to 1.0 followed by a decline to the steady exercise level of RER.

Change in CO_2 storage expressed relative to body weight and change in $P\bar{v}_{CO_2}$ decreased for models 1 and 2 (gradual increase and square wave increase in RQ respectively) from the lowest to highest work rates ($P < 0.05$). However, for model 3, the decline in estimated storage was not significantly different between work rates. Figure 2 shows the relationship between change in CO_2 storage for model 2 (the square wave change in RQ) and the measured $P\bar{v}_{CO_2}$ for each subject. The tendency to lower changes in CO_2 storage at the higher $P\bar{v}_{CO_2}$ values corresponded with an elevation of blood lactate for the higher work rates. This inverse relationship between the change in CO_2 storage and change in blood lactate is shown in figure 3 for model 2 data.

Hyperventilation studies: Figure 4 shows a typical example of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ during a hyperventilation study. The gas exchange values measured as the average of the 12 sample points between minutes 13 and 15 are shown in table 2. With the exception of $\dot{V}_{O_2}$ at the highest work rate, there were no significant differences in $\dot{V}_{O_2}$ or $\dot{V}_{CO_2}$ between the hyperventilation studies and the steady state values at the corresponding work rates for the onset of exercise studies. $\dot{V}_{O_2}$ was significantly higher during the hyperventilation study at work rate 3. The RER for work rate 1 during hyperventilation was significantly greater than the corresponding onset of exercise steady state.

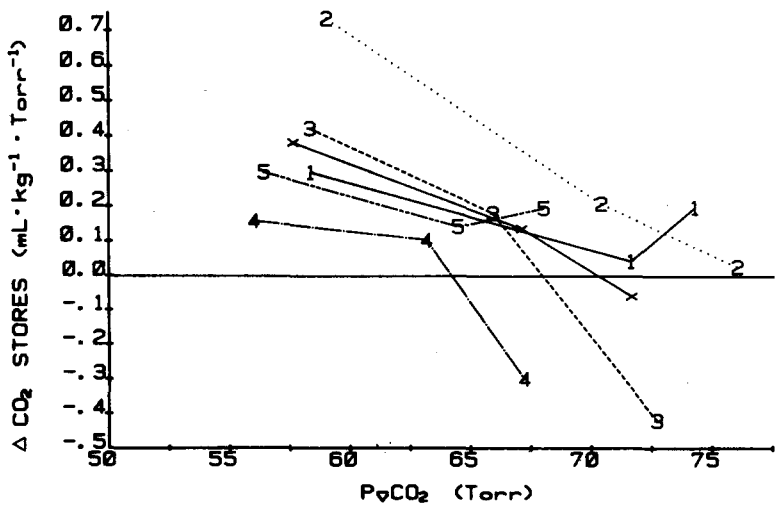

Fig. 2. The relationship between the change in relative CO_2 storage (ml $CO_2 \cdot kg^{-1} \cdot torr^{-1}$) using model 2 (square wave change in RQ, see text) from the onset of exercise studies and the average $P\bar{v}_{CO_2}$ obtained from pre-exercise and steady state measurements. Each subject is represented separately for each work rate, the mean values are shown by x————x.

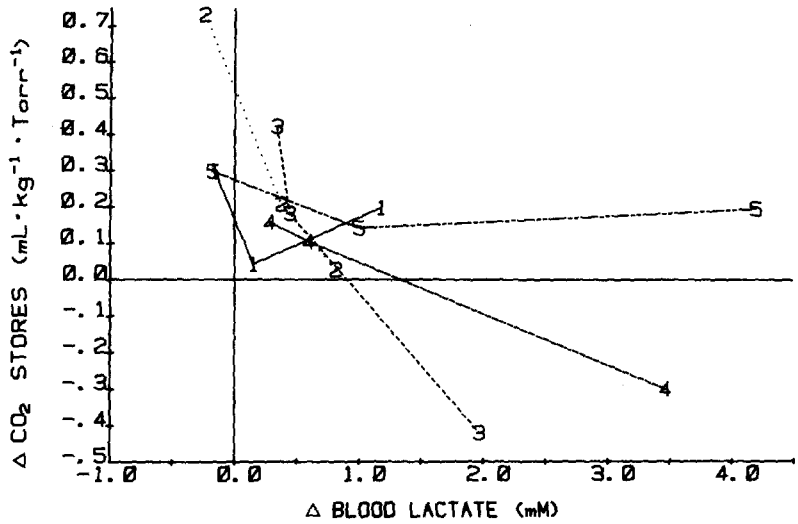

Fig. 3. The relationship between the change in relative CO_2 storage (ml $CO_2 \cdot kg^{-1} \cdot torr^{-1}$) using model 2 (square wave change in RQ) and the change in blood lactate concentration (mM) shown for subjects 1–5 for each of the onset of exercise studies.

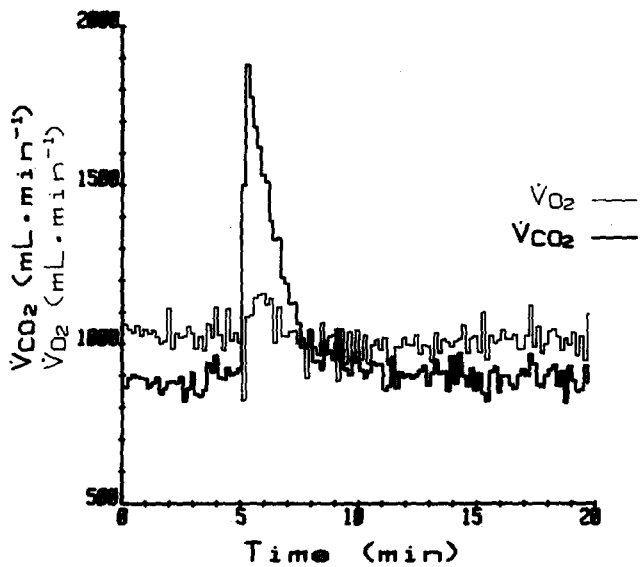

Fig. 4. An example of the $\dot{V}_{O_2}$ (thin line) and $\dot{V}_{CO_2}$ (heavy line) responses to the onset of hyperventilation at a work rate of 50 W for subject 5. Hyperventilation started at t = 5 min and continued to 20 min.

Blood lactate was slightly, but not significantly higher during the hyperventilation studies at work rates 1 and 2 than during the onset of exercise studies (table 3). At work rate 3, blood lactate was 5.22 mM during the hyperventilation as compared to 3.67 mM in the onset of exercise study ($P < 0.05$).

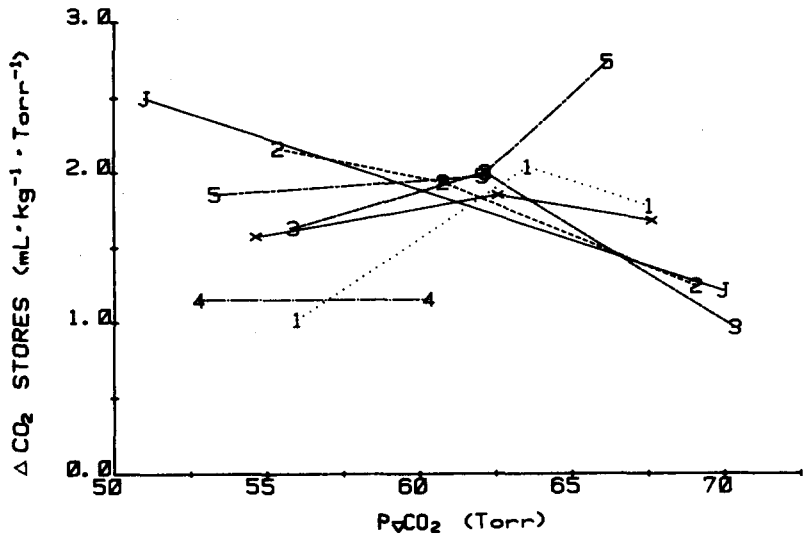

Fig. 5. The relationship between the change in relative storage of CO_2 (ml $CO_2 \cdot kg^{-1} \cdot torr^{-1}$) by the hyperventilation technique and the average $P\bar{v}_{CO_2}$ obtained from pre- and post-hyperventilation rebreathing. Each subject is represented separately for each work rate. Subject 4 was unable to successfully complete the high work rate. The dotted line connecting the "J" points is the regression determined from Jones and Jurkowski (1979).

Blood gases reflected the effect of hyperventilation (table 3). Arterialized blood P_{CO_2} was significantly reduced relative to the onset of exercise study steady states for each of the work rates. As a consequence of the hyperventilation, blood pH increased at each work rate. This increase was significant for work rates 1 and 2 only.

Rebreathing oxygenated $P\bar{v}_{CO_2}$ estimates were significantly lower for the hyperventilation studies than the corresponding value during steady state exercise at each of the three work rates (table 3).

CO_2 storage measured by hyperventilation expressed as either the absolute volume of CO_2 excreted or as the storage relative to body weight and change in $P\bar{v}_{CO_2}$ was not significantly different between any of the work rates (table 4, fig. 5).

Discussion

The major purpose of the present study was to obtain an estimate of changes in CO_2 storage which occur at the onset of exercise from gas exchange measures. To do this, it was necessary to make some major assumptions about what pattern the metabolic respiratory quotient (RQ) might follow in the transition from one steady state to the next. It was observed that regardless of model chosen, the onset of exercise estimate of CO_2 storage was markedly less than the hyperventilation estimates of CO_2 storage from either this study or Jones and Jurkowski (1979). Further, two of the three models

predicted a significant decrease in CO_2 storage at the onset of heavy exercise (75% $\dot{V}_{O_2}$max) relative to the onset of light exercise (33% $\dot{V}_{O_2}$max) in support of the hypothesis of Hughson and Morrissey (1982). This decrease in CO_2 storage was associated with a metabolic acidosis at the high work rate.

The metabolic RQ can be assumed to be equivalent to the respiratory exchange ratio (RER) when the RER is unchanging in exercise. Thus, the constant RER in the pre-exercise condition and in the steady state of exercise reflect the CO_2 production for a given O_2 consumption. Metabolic substrate (carbohydrate *vs* fat) determines the RQ. It has been well established that RQ increases with greater work rates as shown in table 2. Also, RQ is highest at the start of exercise and declines progressively with time during prolonged steady state exercise (Bergström *et al.*, 1967). It has not been possible to date to estimate the relative proportion of carbohydrate and fat metabolized at the onset of exercise. To account for a realistic range of possibilities, the RQ was allowed to vary with time according to three models (fig. 6). Model 1 was selected to increase RQ from the pre-onset RER to the steady state RER according to an exponential pattern. The time constant (45 sec) was selected so that the steady RER observed by 3–4 min of exercise would be duplicated in the model. This model should give the lowest estimate of predicted CO_2 production and CO_2 storage.

Model 2 was a square wave change in RQ from the pre-onset to the exercise RER. Although it is unlikely that metabolism changes in this manner, this model provides an alternative to the two extremes of models 1 and 3.

Model 3 was an immediate increase in RQ to 1.0 at the onset of exercise. While the observation of a higher RQ at the beginning of long duration exercise (Bergström *et al.*, 1967) supports the concept of this model, it is unlikely that RQ actually approaches 1.0. This would imply turning off the pathway for fat metabolism, then gradually allowing

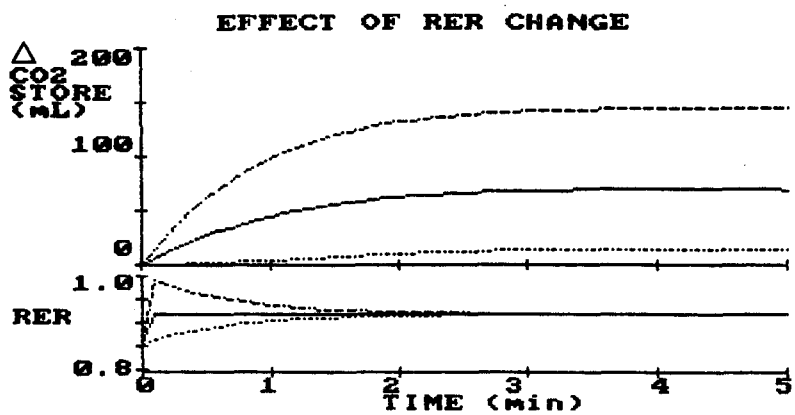

Fig. 6. A schematic of the three models used for time varying RQ (lower graph) and the calculated change in CO_2 storage (upper graph). Data used to set conditions are the mean values of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ from table 2 for the work rate 1 to work rate 2 transition. Time constants for $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ are from Hughson and Morrissey (1982). Model 1 is represented by the lower dotted line, model 2 by the solid line and model 3 by the upper dashed line (see text for model description).

it to be turned on again. A more realistic model would be to increase RQ to some level between 1.0 and steady state RER at the onset of exercise. This would be followed by a decline in RQ within 3–4 min to the steady state RER. Model 3 provides an estimate of the upper limit for CO_2 storage capacity at the onset of exercise.

The present study has not included the metabolic production of CO_2 due to utilization of oxygen stores. While the change in oxygen stores is quite marked in the transitions from one work rate to the next, the time course of the change is not known. Thus, it is impossible to assign a time varying O_2 consumption to the models of time varying RQ to yield estimates of additional metabolic CO_2 production. For model 2 (step change in RQ), it is not necessary to know the time course of change. With some assumptions, the change in oxygen stores can be estimated. The arterial – venous oxygen content differences can be obtained from the Fick equation using measured cardiac output by CO_2 rebreathing and $\dot{V}_{O_2}$. If arterial oxygen content remained constant, mixed venous oxygen content change from one work rate to the next is then calculated. This value is multiplied by an estimated venous blood volume to yield the change in oxygen stores. Based on the estimate of change in oxygen stores, the predicted absolute CO_2 production could be underpredicted by approximately 40–70 ml CO_2 at each of the exercise levels. To obtain estimates of tissue $\dot{V}_{O_2}$, it is necessary to know simultaneously the transitions in both $\dot{V}_{O_2}$ and $\dot{Q}$ at the onset of exercise. The algorithm used in our breath-by-breath system calculates $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ (Beaver *et al.*, 1981) as suggested in the modelling approach of Gilbert *et al.* (1966), but does not give adequate information about tissue $\dot{V}_{O_2}$.

It was anticipated that the changes in CO_2 storage which occur at the onset of exercise would be smaller than the hyperventilation estimate because hyperventilation must lower the P_{CO_2} in all tissues of the body. In table 3, it can be seen that hyperventilation resulted in a significant reduction of both Pa_{CO_2} and $P\bar{v}_{CO_2}$. In contrast, Pa_{CO_2} remained relatively constant while $P\bar{v}_{CO_2}$ increased with the three steady state exercise levels. Various body tissues such as heart muscle, brain, blood and skeletal muscle have different buffer values (Bettice *et al.*, 1976; Francis *et al.*, 1980; Gamble and Bettice, 1977; Lai *et al.*, 1973a,b), and tissues such as bone do not take part in the CO_2 storage within the first hour (Bettice and Gamble, 1975).

Exercise provides a unique model in which natural respiratory acidosis could be studied essentially free of metabolic acidosis at low work rates (*e.g.* 33% $\dot{V}_{O_2}$max); or, combined respiratory and metabolic acidosis can be studied at higher work rates (above 75% $\dot{V}_{O_2}$max). The majority of studies to date which have examined body buffer values have utilized hypercapnia or hyperventilation to alter the respiratory acid load, or exogenous administration of an acid to simulate metabolic acidosis. Since CO_2 freely passes through the cell membrane, there should be no difference between the artificial respiratory acidosis and exercise induced respiratory acidosis. All studies have shown the body to respond to increased P_{CO_2} by increasing the concentration of HCO_3^- in both blood and tissue (Bettice and Gamble, 1975; Gamble and Bettice, 1977; Heisler and Piiper, 1972; Lai *et al.*, 1973a,b). The resultant pH of blood and tissues decreased with this respiratory acidosis. In a comparison of metabolic acidosis of intracellular or

extracellular origin, Brown *et al.* (1967) concluded that there was no difference in the way the cell responded. Therefore, a metabolic acidosis as caused by exogenous acid administration or by exercise would be expected to utilize the non-carbonic intracellular buffers and to decrease the intracellular and extracellular HCO_3^- (Brown *et al.*, 1967; Gamble and Bettice, 1977). Some HCO_3^- is probably transferred into the muscle cells by the HCO_3^-/Cl^- exchange (Aickin and Thomas, 1977); however, this is unlikely to add to intracellular CO_2 stores as buffering of H^+ is taking place.

Hyperventilation estimates of CO_2 storage capacity have been conducted at rest (Cherniack *et al.*, 1974; Farhi and Rahn, 1955; Khambatta and Sullivan, 1974) and in exercise (Clode *et al.*, 1967; Jones and Jurkowski, 1979). At rest, the low perfusion of skeletal muscle requires that the test duration be at least 60 min (Farhi and Rahn, 1955; Khambatta and Sullivan, 1974). In exercise, the higher blood flow rate means that a new steady state occurs sooner (Jones and Jurkowski, 1979). The estimates of CO_2 storage at rest are approximately 2–3 $ml \cdot kg^{-1} \cdot torr^{-1}$. The value of approximately 1.7 $ml \cdot kg^{-1} \cdot torr^{-1}$ in the present study is similar to that of Jones and Jurkowski (1979) in exercise. The most likely explanation for the difference between rest and exercise studies is that the very low P_{CO_2} reached in resting studies (as low as 15 torr) is on the steep portion of the CO_2 dissociation curve (Jones and Jurkowski, 1979). In the present study, the lowest $P\bar{v}_{CO_2}$ was 47 torr at work rate 1.

Extreme levels of hyperventilation at rest have been associated with an increase in $\dot{V}_{O_2}$ (Khambatta and Sullivan, 1974). Neither the present study at work rates 1 or 2, nor Jones and Jurkowski (1979) measured a significant effect of hyperventilation on $\dot{V}_{O_2}$. At work rate 3, the very high levels of ventilation (130–150 $L \cdot min^{-1}$ BTPS in subjects 1–3) probably accounted for the significant increase in $\dot{V}_{O_2}$.

The trend to increased blood lactate during hyperventilation at the low work rates and the significant increase at work rate 3 was probably accounted for by two mechanisms. First, a pH-sensitive regulation of phosphofructokinase probably increased glycolysis with relative respiratory alkalosis (Sutton *et al.*, 1981). Second, efflux of lactate from muscle to blood is slightly higher under alkalotic conditions for example when blood HCO_3^- is artificially elevated (Sutton *et al.*, 1981).

The hyperventilation estimate of CO_2 storage was expected to decrease at the highest work rate because of a metabolic acidosis. It did not, in spite of finding a significant decrease in storage determined at the onset of exercise at this same work rate. At the highest work rate, $P\bar{v}_{CO_2}$ increased by only 2 torr above the previous work rate. Hyperventilation brought about a similar reduction in Pa_{CO_2} and $P\bar{v}_{CO_2}$ as seen at lower work rates. Therefore, the contribution of CO_2 excretion from other sites as well as the working muscle still accounted for similar calculated CO_2 storage. It is possible that CO_2 storage might decrease if an additional work rate was studied.

A possible explanation for the absence of a decrease in CO_2 storage measured by hyperventilation in this study compared to Jones and Jurkowski (1979) could be the method used to predict V_{CO_2}. These latter investigators used the pre-hyperventilation RER to calculate predicted V_{CO_2} from the product RER × V_{O_2}. We chose to use the RER from the last 2 min of hyperventilation. Although the mean values of RER in the

hyperventilation to pre-hyperventilation comparison (table 2) were not different for work rates 2 and 3, small individual differences sometimes resulted in calculation of a negative CO_2 storage if pre-hyperventilation RER was used; this in spite of clear evidence of change in both Pa_{CO_2} and $P\bar{v}_{CO_2}$. At the highest work rate, use of the pre-hyperventilation RER would have yielded a mean CO_2 storage capacity similar to that of Jones and Jurkowski (1979); however, the scatter would have been considerably greater.

Estimation of the change in CO_2 storage at the onset of exercise would appear to be of greater value than estimation by hyperventilation. The former method determines only that storage which takes place, while the latter includes storage in tissues such as non-working muscle, brain and splanchnic organs which have no real impact on buffering during exercise. The immediate significance of these findings is with respect to the relationship between $\dot{V}_{CO_2}$ and expired ventilation in exercise. At low work rates, below 60–70% $\dot{V}_{O_2}$max, a significant portion of metabolic CO_2 production will be stored for every increment in work rate. Above these work rates, $\dot{V}_{CO_2}$ will reflect the reduced capacity for additional CO_2 storage with either no further increment or an actual release of some stored CO_2 as a consequence of metabolic acidosis. This change in CO_2 storage capacity appears to occur at approximately the same work rate as the so-called ventilatory "anaerobic" threshold. Jones and Jurkowski (1979) had previously indicated the coincidence of the ventilatory threshold and a decrease in total body CO_2 storage capacity.

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