MODEL SIMULATION OF BLOOD FLOW AND OXYGEN UPTAKE DURING EXERCISE

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ABSTRACT We developed a dynamic model to account for blood flow in the working muscle during step changes in work rate. The model contains a proportional controller based on oxygen tension in the muscle and a description of the various oxygen-equivalent energy stores. Because of nonlinearities only particular solutions can be obtained. Such solutions were obtained via the finite difference method for various work levels and regimens. Model predictions are presented in comparisons with new experimental data, and with data reported in the literature. The changes in oxygen-equivalent energy stores and in muscle blood flow occur very rapidly after onset of exercise, with at least 90% of the steady-state response being reached within 90 sec.

INTRODUCTION

During the transition from rest to a steady state of exercise, many metabolic and circulatory adjustments occur. Increased muscular work requires an increase in oxygen uptake, in turn requiring increased muscle blood flow. The increase in blood flow is made possible by an increase in heart rate and stroke volume and a consequent increase in cardiac output. Increased pulmonary ventilation serves to keep arterial oxygen tension essentially constant. Venous oxygen tension decreases because of increased oxygen extraction in the working muscle. The energy necessary for muscular contraction is derived from sources such as depletion of phosphagen stores, increased glycolytic activity, and enhanced mitochondrial activity. All of these adjustments are interrelated, and together constitute the homeokinetic response to exercise. The relationships between many of these quantities have been determined experimentally and are rather well established in the steady state of exercise, and, to a much smaller extent, in the transient; however, at present there is no general theory available to relate these terms quantitatively, particularly in the transient.

Various investigators have attempted to describe the time-course of oxygen

uptake and heart rate during exercise transients in terms of exponential and similar functions. Henry (1951) postulated that the increase in oxygen uptake in working muscle tissue proceeds as a first-order reaction. This leads to an exponential rise in oxygen uptake with time and a single characteristic time constant for a given muscle. The experimental results for whole body oxygen uptake have been analyzed using curve-fitting techniques to determine these time constants (Broman and Wigertz, 1971; Di Prampero et al., 1970; Henry, 1951). Cardus and Ziegler (1968) have arbitrarily postulated weighted first-order reactions and stochastic processes for oxygen uptake and developed complex exponential relationships for the response. None of these models have been based on known physiological mechanisms.

Gilbert et al. (1966, 1967) formulated a model in which the inflow, outflow, and storage of oxygen in a working muscle were related by the conservation of matter principle. The energy contributions in terms of phosphagen depletion and anaerobic glycolysis were not included, and there were no control or feedback equations relating blood flow or local vascular resistance to oxygen uptake. Consequently, the variation in blood flow with time must be specified before oxygen uptake can be computed. While their model is not complete in many ways, it represents the first attempt to model working muscle. In this paper, a more complete model is developed for predicting circulatory and metabolic responses during exercise.

MODEL FORMULATION

In the development of the present model for a working muscle, a "standard" man is assumed, and the anthropomorphic and physiological data are given in Table I.

TABLE I
ANTHROPOMETRIC DATA FOR MODEL MAN

	Upright rest	Upright maximal exercise
Whole body		
$\dot{V}_{O_2}$ (liters/min)	0.3	4.0
CO (liters/min)	5.0	22.9
HR (beats/min)	60	200
SV (ml/beat)	83	114
x_a (vol %)	20	20
Blood flow to body excluding muscle (liters/min)	4.4	4.4
Muscle mass		
$\dot{V}_{O_2}$ (ml/min-100 g)	0.1	14.7
Muscle blood flow rate (ml/min-100 g)	2.5	74

Total body mass = 74 kg; working muscle mass = 25 kg.

These values are consistent with the model developed by Stolwijk and Hardy (1966), with additions, as needed, to include cardiovascular variables.

The model for muscle is based on the conservation of matter principle applied to the oxygen in a unit mass of working muscle under transient exercise. This principle relates the inflow of oxygen carried with the blood to the outflow, rate of change in storage, and uptake by the muscle.

$$dx_m/dt = \dot{m}_{bl}(x_a - x_v) - \dot{V}_{O_2,m}, \tag{1}$$

where $\dot{m}_{bl}$ is the blood flow rate per 100 g of muscle (milliliters per minute × 100 g muscle), x_a and x_v are the arterial and venous oxygen concentrations in the blood flowing through the muscle (milliliters O_2 per milliliter blood), x_m is the oxygen stored in the muscle myoglobin (milliliters O_2 per 100 g muscle), $\dot{V}_{O_2,m}$ is the rate of oxygen uptake by the muscle (milliliters O_2 per minute × 100 g muscle), and the subscript m denotes muscle.

The conservation of energy principle applied to the same muscle mass is

$$k de_m/dt = k\dot{V}_{O_2,m} - (M_0 + M), \tag{2}$$

where k is a constant relating the conversion of oxygen to heat and work (assumed to be 4.85 cal/ml O_2), e_m is the oxygen equivalent of the chemical energy equivalent stored in the muscle in milliliters O_2 per 100 g muscle, M_0 is the basal metabolic rate (calories per minute × 100 g muscle), and M is the increase in metabolism due to work which is converted to heat and mechanical work during exercise.

Equations 1 and 2 can be combined to eliminate $\dot{V}_{O_2,m}$ and yield the controlling equation for the muscle process

$$\dot{m}_{bl}(x_a - x_v) = dx_m/dt + (1/k)de_m/dt + (M_0 + M)/k. \tag{3}$$

Equation 3 describes the processes occurring in the working muscle mass. The whole body cardiovascular response to the changes in muscle blood flow and oxygen uptake during work is given by the following equation:

$$CO = 4.4 + \dot{m}_{bl}(0.25), \tag{4}$$

where CO is the cardiac output (liters per minute), 4.4 is the blood flow to the body excluding working muscle (liters per minute), $\dot{m}_{bl}$ is the muscle blood flow (milliliters per minute × 100 g muscle), and the constant 0.25 accounts for the working muscle mass (25 kg, see Table I) and the consistency in terms. Since the blood flow to the splanchnic region may decrease by as much as 1.2 liters/min under heavy exercise (Rowell, 1969), and since after the first few minutes of exercise skin blood flow increases in response to thermal demands by 1 to 2 liters/min (Harris and Porter, 1958;

Marx et al., 1967; Rowell, 1969), and since these changes are small relative to the cardiac output during exercise, it was assumed that the blood flow to the rest of the body excluding the muscles stays essentially constant at 4.4 liters/min.

The whole body oxygen uptake $\dot{V}_{O_2}$ (liters per minute) is given by

$$\dot{V}_{O_2} = 0.3 + \dot{m}_{bl}(x_a - x_v)\ (0.25), \tag{5}$$

where 0.3 is the basal oxygen uptake for the rest of the body excluding the muscle mass (liters per minute). The over-all arteriovenous oxygen concentration difference (A-V difference or $x_a - x_v$) is related to $\dot{V}_{O_2}$ and CO by

$$CO = \dot{V}_{O_2}/(x_a - x_v). \tag{6}$$

The heart rate HR is related to CO and the stroke volume SV (milliliters) by

$$SV = 0.001\ CO/HR. \tag{7}$$

For the standard man the stroke volume at rest is taken as 83 ml, and it is assumed to increase to 114 ml for all levels of exercise (Asmussen and Nielsen, 1955; Jones et al., 1970; Rowell, 1969; Rushmer, 1961).

Additional relationships among the variables in equation 3 are needed before solutions may be obtained. The oxygen concentrations in the hemoglobin and myoglobin are dependent on the oxygen tension P_{O_2} (millimeters mercury), and these oxygen dissociation curves for standard conditions (Johnson, 1966) are given in Fig. 1. Since the shifts in these curves with pH and P_{CO_2} would be relatively small in the present formulation, the effects of the shifts were ignored. It is assumed that in the capillaries blood flow is slow enough to allow complete equilibration of oxygen tension in the blood and the tissue so that the oxygen tension in the venous

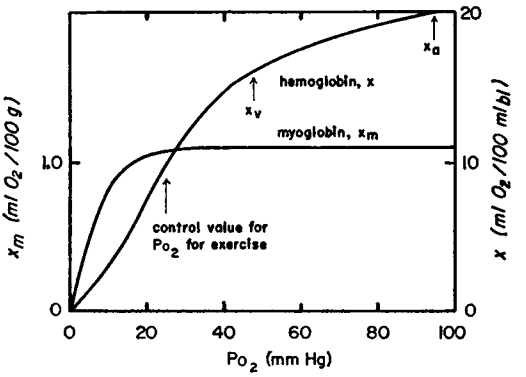

FIGURE 1 Oxygen dissociation curves for hemoglobin and myoglobin at pH = 7.4, P_{CO_2} = 40 mm Hg, and temperature = 37°C.

blood equals that in the muscle. This assumption relates both the blood and muscle oxygen content to venous oxygen tension. The arterial oxygen tension is assumed to remain constant at all work levels at a value of 95 mm Hg (Wasserman et al., 1967).

Based on physiological observations (Rowell, 1969; Rushmer, 1961; Wasserman et al., 1967), a control equation for the regulation of blood flow during exercise can be postulated as follows. During rest, the over-all arteriovenous difference is about 4 ml/100 ml, and the corresponding mixed venous oxygen tension is about 50 mm Hg as indicated in Fig. 1. The over-all A-V difference for steady-state exercise increases rather rapidly to 8–10 ml/100 ml at low levels of exercise, and then rather slowly increases as the exercise level increases (Rowell, 1969; Rushmer, 1961; Wasserman et al., 1967). At the level of exercise at which the over-all A-V difference reaches 8–10 ml/100 ml, approximately two-thirds of the cardiac output is through the working muscles. The local muscle A-V difference is then approximately 10 ml/100 ml and the corresponding venous oxygen tension is about 25 mm Hg. It can be assumed that blood flow control (control over local vascular resistance) initiates at a value of P_{O_2} of about 25 mm Hg in the muscle (B. Saltin, personal communication).

The exact mechanisms by which vascular resistance and blood flow rate in the working muscle are regulated during the transient of exercise are not known at present; however, it is known that the levels of lactate, P_{CO_2}, pH, $[K^+]$, and P_{O_2} can each affect local blood flow (Karlsson, 1971; Skinner and Powell, 1967). Since all of these levels are related through the chemical reaction equations for metabolism, and all are correlated during exercise (Wasserman et al., 1967), there is justification for using any one of these as the control variable in a model. In this model, $P_{O_{2,m}}$ is a convenient measure of the chemical state of the muscle and is chosen as the control variable.

Based on these considerations, a proportional control equation for blood flow rate is assumed in which the blood flow rate increases in direct proportion to the decrease of $P_{O_{2,m}}$ below the control value of 25 mm Hg

$$\dot{m}_{bl} = \dot{m}_{bl,0} + A(25 - P_{O_{2,m}}), \tag{8}$$

with the condition that $\dot{m}_{bl} = \dot{m}_{bl,0}$ for $P_{O_{2,m}} > 25$ and where $\dot{m}_{bl,0}$ is the blood flow rate in the resting muscle (milliliters per minute $\times$ 100 g muscle) and A is the proportional control constant. The metabolic rate for resting muscle is taken to be 0.5 cal/min-100 g_m, which corresponds to an oxygen uptake of 0.1 ml O_2/min-100 g_m (Johnson, 1966; Stolwijk and Hardy, 1966). The blood flow rate in the resting muscle needed to sustain this metabolic rate at an A-V difference of 4 ml/100 ml is $\dot{m}_{bl,0} = 2.5$ ml/100 g_m.

It is assumed that the maximum oxygen uptake for the whole man is 4 liters/min, and that at this maximum, the oxygen tension in the venous blood leaving the muscle is 0 mm Hg. The maximum blood flow rate in the working muscles is then

calculated from equation 5 to be 74 ml/100 g_m , and the relationship between blood flow rate and $P_{O_2,m}$ given by equation 8 becomes

$$\dot{m}_{bl} = 2.5 + 2.86\ (25 - P_{O_2,m}). \tag{9}$$

This relation between $\dot{m}_{bl}$ and $P_{O_2,m}$ is shown in Fig. 2.

The amount of chemical energy equivalent stored in the muscle e_m is deduced from experimental measurements of the oxygen deficit in man during the transition from rest to exercise. The values of oxygen deficit at various work loads as determined by several investigators (Karlsson, 1971; Karlsson and Saltin, 1970; Knuttgen, 1970; Thomas et al., 1964; Wasserman et al., 1967; Whipp et al., 1970) and by the present authors are given in Fig. 3. The original data were converted from a total deficit measured as liters of oxygen to a per 100 g_m basis by assuming that the oxygen deficit was distributed uniformly over the working muscle mass (25 kg) of the subject. A smooth curve was then drawn through these data as shown in Fig. 3.

The total oxygen deficit involves the depletion of oxygen stored in the venous blood, muscle myoglobin, plasma, and tissue water, as well as the O_2 equivalent of the depletion of phosphagen stores and anaerobic glycolysis. The separate contributions of the myoglobin, plasma, tissue water, and hemoglobin oxygen stores were determined using the following relations:

$$(\text{Myoglobin deficit}) = (1.2 - x_m), \tag{10}$$

where 1.2 ml/100 g_m is the saturated oxygen content for myoglobin (Fig. 1), and

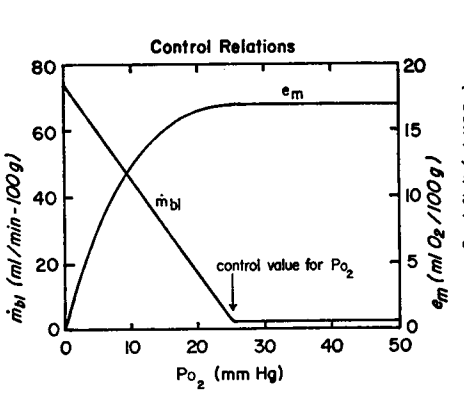

FIGURE 2

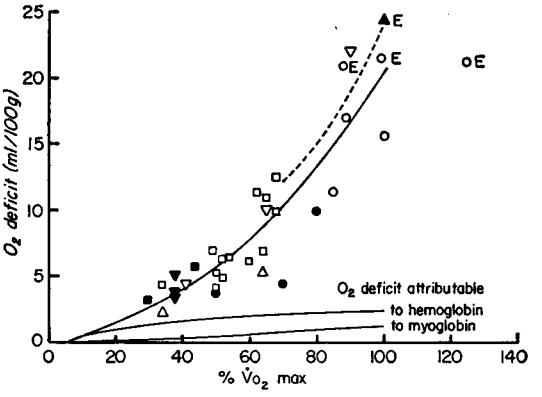

FIGURE 3

FIGURE 2 Muscle blood flow rate and chemical energy stores as functions of oxygen tension.

FIGURE 3 Total, venous, hemoglobin, and myoglobin oxygen deficits as functions of relative oxygen uptake. △, Di Prampero et al., 1970; --- ▲, Karlsson, 1971; ○, Karlsson and Saltin, 1970; ●, Knuttgen, 1970; □, this study; ■, Thomas et al., 1964; ▽, Wasserman et al., 1965; ▼, Whipp et al., 1970. E, exhaustive test.

x_m (milliliters per 100 g muscle) is a function of $P_{O_2,m}$, which in turn is a function of blood flow rate and oxygen uptake as given by equations 5 and 9. The computed myoglobin deficit is shown in Fig. 3.

The oxygen depletion in the venous hemoglobin during exercise was computed assuming a systemic venous blood volume excluding the pulmonary circuit of 3.5 iters. This deficit is then

$$(\text{Venous deficit}) = (3.5/0.25)\ (16 - x_v), \tag{11}$$

where 16 (milliliters per 100 ml blood) is the concentration of venous oxyhemoglobin at rest and x_v (milliliters per 100 ml blood) is a function of $P_{O_2,m}$ (Fig. 1), blood flow rate, and oxygen uptake. This relation is also shown in Fig. 3.

The solubility of oxygen in aqueous solutions is about 2.4 ml O_2/(100 ml $\times$ 760 mm Hg) (Johnson, 1966). At an arterial P_{O_2} of 95 mm Hg, the O_2 dissolved in plasma amounts to 0.3 ml/100 ml. This is approximately 2% of the oxyhemoglobin store, and is neglected in this model. The oxygen dissolved in the tissue water is about 0.2 ml/100 ml, which is small relative to the muscle myoglobin store, and is also neglected.

The energy obtained from anaerobic processes was computed as the difference between the total oxygen deficit and the sum of the deficits from myoglobin and hemoglobin. This difference, which is e_m, is plotted in Fig. 2 as a function of $P_{O_2,m}$. In the model, it is assumed that for submaximal exercise, the anaerobic energy release occurs so rapidly that the instantaneous energy level e_m is given by the instantaneous value of $P_{O_2,m}$; the relation in Fig. 2 is assumed to be valid at any instant of time. This is consistent with observations of rapidly increasing lactate levels at the start of moderate and heavy exercise (Karlsson, 1971; Karlsson and Saltin, 1970; Wasserman et al., 1967). The calculations by Wasserman et al. (1967) also support the assumption that lactate production contributes directly to the deficit during the early phases of moderate exercise.

In summary, equations 3 and 9 represent the governing equations for the local muscle processes during exercise. It is assumed that blood flow rate, oxygen concentration in the hemoglobin and myoglobin, and the oxygen equivalent stored in the muscle are functions of the instantaneous oxygen tension as presented graphically in Figs. 1 and 2. For convenience, oxygen tension has been chosen as the indicator of the chemical state of the muscle. The whole body cardiovascular and metabolic responses to exercise are given by equations 4–7.

Equations 3 and 9 cannot be solved analytically because of the nature of the relations between $\dot{m}_{bl}$, x_m, e_m, and oxygen tension. Solutions for various work levels were obtained by rewriting equation 3 in finite difference form and rearranging

$$\bar{m}_{bl}(x_a - \bar{x}_v) = [(x'_m - x_m) + (e'_m - e_m)/k]/\Delta t + (M_0 + M)/k, \tag{12}$$

where the primes denote the future values for the time step and the bars denote the average value over the time step. To determine the future values, equation 12 was written as

$$R = (x'_m - x_m) + (e'_m - e_m)/k + \Delta t(M_0 + M)/k - \Delta t\, \bar{m}_{bl}(x_a - x_v), \quad (13)$$

where R is the residual and must be equal to zero for each time step. A computer program was written to solve equation 13 by iteration for each time step.

RESULTS

Steady-State Results

The general model equations developed in the previous section are first solved for the steady state by setting the derivatives in equation 3 equal to zero. Equation 3 becomes the steady-state energy balance equation

$$\dot{m}_{bl}(x_a - x_v) = (M_0 + M)/k\,. \quad (14)$$

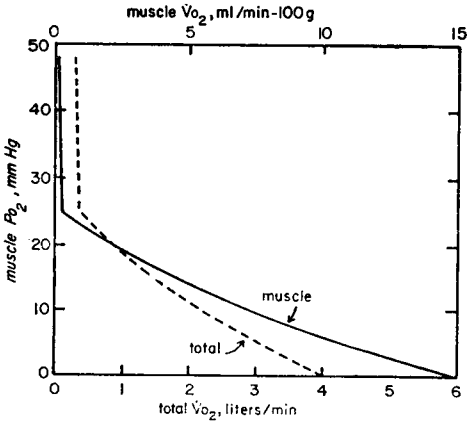

FIGURE 4

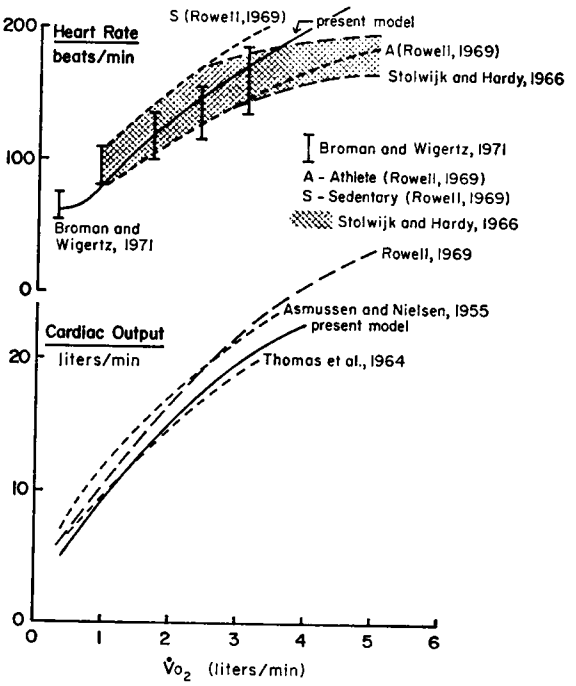

FIGURE 5

FIGURE 4 Steady-state muscle and total oxygen consumption as a function of oxygen tension.

FIGURE 5 Steady-state cardiac output and heart rate as a function of oxygen uptake.

Equation 9 for blood flow rate control and Fig. 1 for the oxygen concentrations are employed to solve equation 14 for different metabolic rates. Equations 4, 5, and 7 are used to compute the total CO, $\dot{V}_{O_2}$, and HR. The muscle and total oxygen uptakes are shown in Fig. 4 as functions of P_{O_2}. These results, together with the relations in Figs. 1 and 2, show that increased blood flow is the major factor in facilitating the increase in oxygen uptake. The over-all A-V difference can only increase by a factor of 5 at most over resting values, while flow can increase by up to a factor of 20. The total oxygen uptake reflects the increase in muscle oxygen uptake.

The steady-state cardiac output and heart rate predicted by the model are compared in Fig. 5 with the experimental results of several investigators. The measured cardiac outputs include not only increased muscle blood flow, but increased skin blood flow over resting levels due to the increased body temperatures in exercise and reduced flow to internal organs as discussed earlier. The skin blood flow is probably on the order of up to 10% of the total cardiac output, while the other circulatory shifts are small compared with the total cardiac output. The present model results do not take the increased skin blood flow into account, but only predict the increased flow to the working muscles. The model predictions agree with the observations within this difference.

Transient Results

The model results for the time-course of blood flow rate and oxygen tension at several metabolic rates are presented in Figs. 6 and 7. Blood flow rate and $P_{O_{2,m}}$

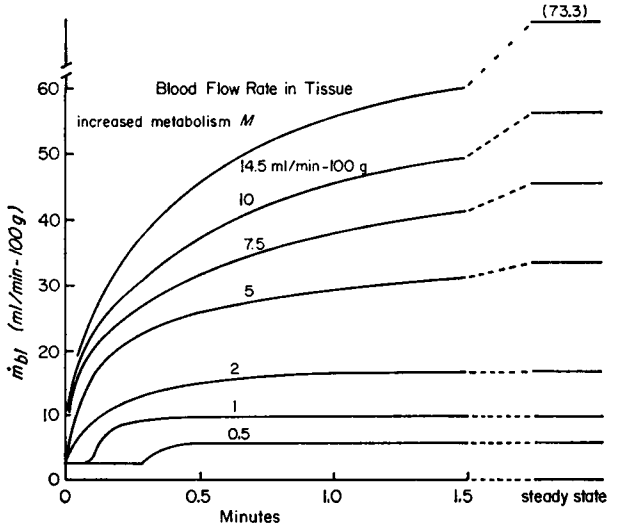

FIGURE 6 Model predictions for muscle blood flow rate as a function of time.

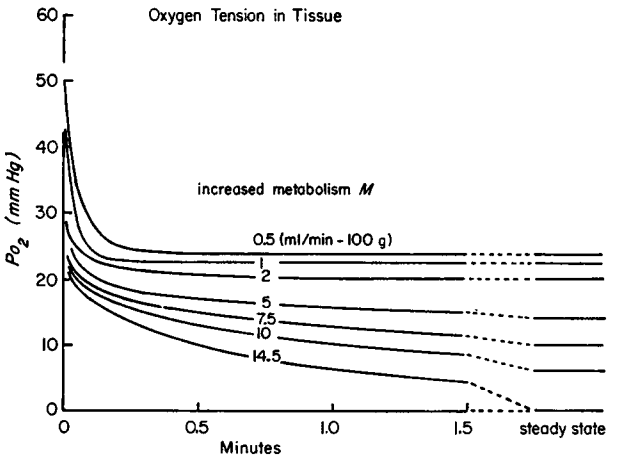

FIGURE 7 Model predictions for muscle oxygen tension as a function of time.

change very rapidly during the transient. For low work levels (M less than about 2 ml/min-100 g_m or 20 M_0), equilibrium values are reached in less than 1 min. At higher work levels, most of the transient is over in 1.5 min, with steady state reached in 3–5 min. The metabolic rate of 14.5 ml/min-100 g_m represents the maximum steady-state level for the muscle in the model formulated here.

There are no explicit data available for a comparison with the predicted results of Figs. 6 and 7. The predicted responses have therefore been extended to predict heart rates, and these are compared in Fig. 8 with measurements made during the transient onset of exercise at two exercise levels. The measured heart rate values were obtained from an electrocardiogram and represent average values over a 6 sec time period. Predicted rates were also computed using a higher stroke volume (140 ml) than given in Table I. This higher value is representative of athletes (Rowell, 1969) and appears to be more appropriate for subjects J. M., E. N., and B. S. than the lower value. The model and experimental results agree within about 10% during the first minute of exercise.

In Fig. 9, the model results are compared with the cardiac output measurements of Jones et al. (1970) at two exercise levels. Their cardiac outputs were calculated from instantaneous arterial pressure measurements. The model results predict a slightly faster response than measured; however, their experimental values for rest appear to be high (7.5–9 liters/min) which suggests that some artifact has been introduced by the experimental technique. The model and data disagree by less than 10%, which is about one standard deviation for the data.

The model was used to predict the response during the transient from one exercise level to another. The experiments of Broman and Wigertz (1971) were simulated using the model, and these results are presented in Fig. 10. The difference between the model and the data is about 8% during the transient from a lower to a higher level of exercise.

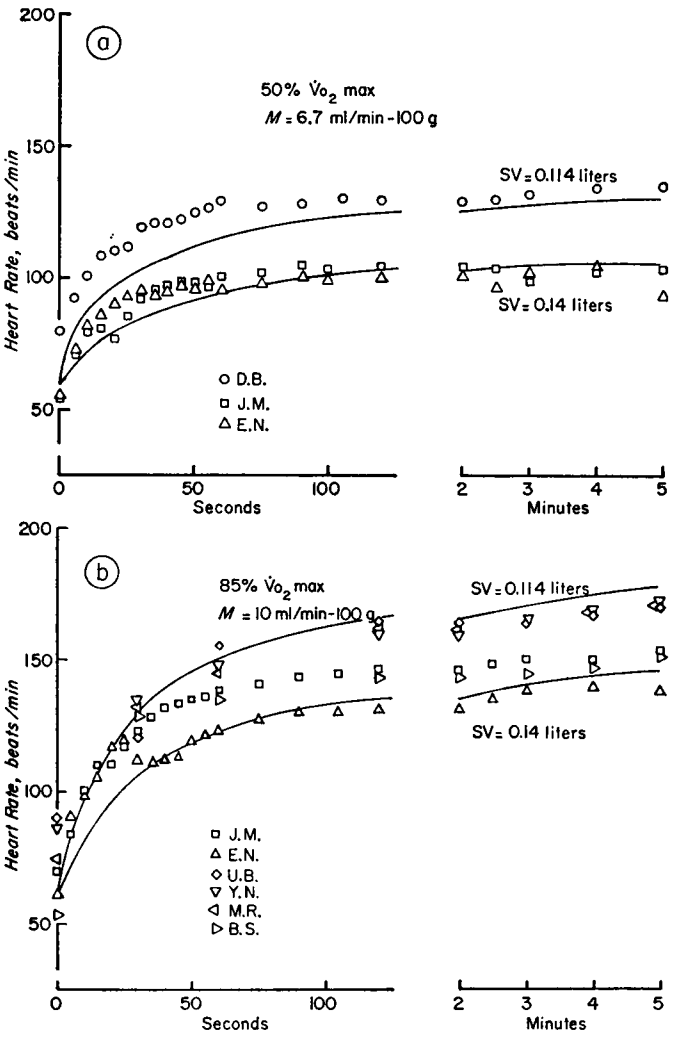

FIGURE 8 Comparison between experimental and model results. (*a*) Heart rate as a function of time at 50% $\dot{V}o_2$ max. (*b*) Heart rate as a function of time at 85% $\dot{V}o_2$ max.

In addition to predictions for the increase in work level, predictions were made for the decrease in level of work using two different assumptions. In the first simulation, it was assumed that there was a continuous repayment of the myoglobin, lactate, and phosphagen deficits; the control relations for both x_m and e_m as given in Figs. 1 and 2 were employed. In the second, it was assumed that only the myoglobin deficit was repayed. As shown in Fig. 10, it appears that neither of these assumptions accurately models the results, and that the repayment during recovery proceeds more slowly than does the release during exercise.

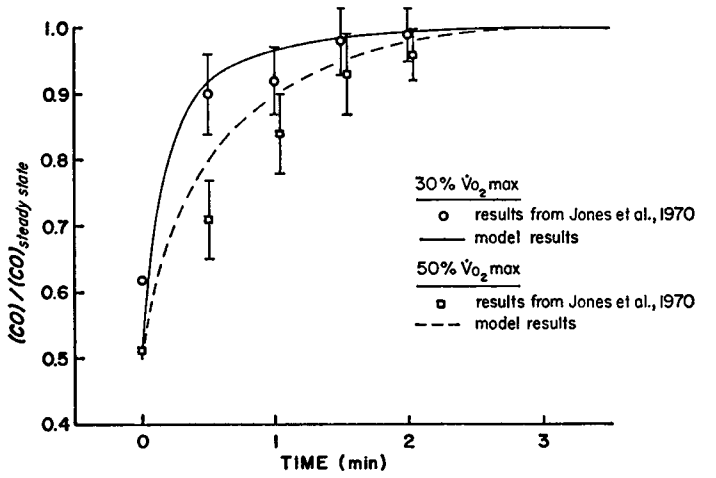

FIGURE 9 Comparison between experimental and model results for cardiac output response as a function of time at 30 and 50% $\dot{V}_{O_2}$ max.

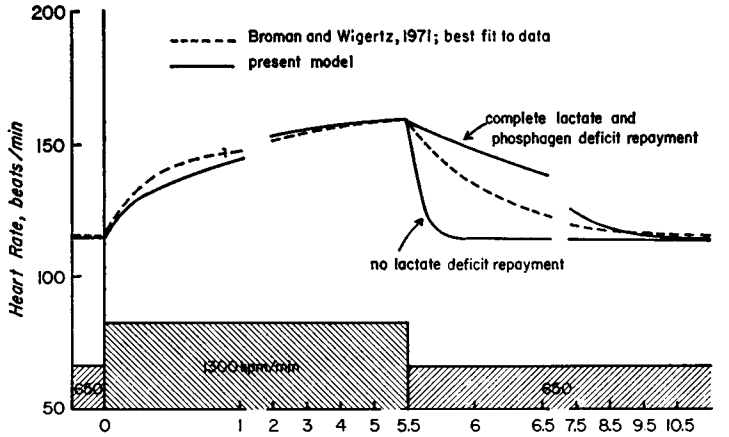

FIGURE 10 Comparison between experimental and model results for heart rate as a function of time for step changes in work level.

DISCUSSION

The control value of $P_{O_{2,m}}$ of 25 mm Hg chosen here is the oxygen tension at which myoglobin begins to desaturate and the release of chemical oxygen equivalent tores begins (Figs. 1 and 2). The error signal initiates control mechanisms which reduce resistance in the vascular bed and increase blood flow. Concomitant alterations in levels of many variables occur during the initial transient, such as $P_{O_{2,m}}$, pH, $P_{CO_{2,m}}$, bicarbonate, and lactate. These changes in level are all correlated with the intensity of exercise (Thomas et al., 1964), and thus each variable is correlated with all others. The use here of $P_{O_{2,m}}$ as the controlling variable does not

imply that the oxygen tension alone acts to signal the need for increased oxygen. Oxygen tension is chosen as a convenient measure of the physicochemical state of the muscle during exercise.

The model results aid interpretation of experimental observations. Previous investigators have reported that metabolism is essentially aerobic at low work levels (up to about four times resting values) (Wasserman et al., 1965, 1967). The model results show that the muscle P_{O_2} would be less than 17 mm Hg at these low $\dot{V}_{O_2}$ levels (less than about 1.2 liters/min) (Fig. 4). From Fig. 2, it can be seen that the anaerobic contributions (the change in e_m) at these tensions are negligible. Thus, the calculations presented here show that the major components of the oxygen deficit at low work levels are the depletion of oxygen in myoglobin and hemoglobin and reduction in phosphagen stores.

Using the model results, two phases of transient metabolism may be identified. There is initially an increased $x_a - x_v$ difference due to greater extraction of oxygen from the blood and some O_2 extraction from myoglobin. This phase occurs rapidly because of the relatively small amount of oxygen stored in the myoglobin. The second phase consists of the release of potential energy via anaerobic glycolysis, and occurs slowly. The values of e_m are approximately 10 times those of x_m .

The heart rate, blood flow rate, and $P_{O_{2,m}}$ curves presented in Figs. 6–11 are not exponential with time. The nonlinear relations between $\dot{m}_{bl}$, e_m , x_m , x, and $P_{O_{2,m}}$ imply that the response cannot be represented by exponentials in this model, or even in terms of known analytic functions. Steady-state blood flow during light exercise is reached in very short times, while higher work loads require a longer period (Fig. 6). In the absence of thermoregulatory requirements, steady state is essentially reached in about 1 min for 25% $\dot{V}_{O_2}$ max, 2–3 min for 50% $\dot{V}_{O_2}$ max, and 3–5 min for 75% $\dot{V}_{O_2}$ max.

As shown in Fig. 8, the measured heart rates increase slightly more rapidly than the predicted values. This may be because of an increased sympathetic nervous system activity and reduced vagal tone at the start of exercise that is not accounted for in the model. It is also probable that stroke volume does not increase instantaneously from its resting to its exercise value as assumed in the model. The measurements of Jones et al. (1970) show, in general, a constant stroke volume from the start of exercise, with any increase being moderate; however, the high resting cardiac outputs in their work (7.5–9 liters/min) may mask any change at the start of exercise. The heart rate measurements in Fig. 8 show a slight decrease between 10 and 50 sec after the start. This drop may reflect the increasing stroke volume from the lower resting volume.

The relative contributions of the different forms of stored energy to the blood flow response during the transient were evaluated, and representative results are presented in Fig. 11. These results were obtained by solving equation 3 with x_m constant (no myoglobin stores), e_m constant, (no potential energy stores), and e_m

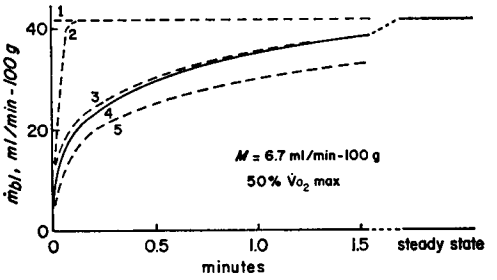

FIGURE 11 Effect of different energy stores on predicted muscle blood flow rate response at 50% $\dot{V}_{O_2}$ max. (1) Predicted response with no stored forms of energy equivalents. (2) No storage of energy equivalents in terms of phosphagens or anaerobic glycolysis. (3) No O_2 available from myoglobin. (4) Prediction from present model. (5) Prediction with e_m doubled.

doubled (equivalent to allocating the total deficit to 12.5 kg of working muscle). With no forms of storage of adenosine triphosphate (ATP) equivalents, the blood flow response is instantaneous. The presence of myoglobin stores can significantly affect the blood flow response only at low work levels, or only briefly at high work levels. Conversely, phosphagen depletion and anaerobic glycolysis affect the transient only at high work levels; however, if myoglobin oxygen were the only energy store, steady state would be reached in about 15 sec regardless of level of the work. Thus, the time to reach steady state is longer at the higher work levels because of phosphagen depletion and anaerobic glycolysis.

The calculations for values of e_m twice that of Fig. 2 were performed to evaluate the assumption of distributing the deficit over the muscle mass of 25 kg. In bicycle exercise, the leg muscles (about 16 kg) are primarily involved rather than the entire musculature, and the previously measured oxygen deficits (Fig. 3) might be distributed over these muscles only. At higher work loads, the response with the higher e_m is considerably slower (Fig. 11). The corresponding heart rates for this case would show a greater discrepancy between the experimental and model results (Fig. 8) but the discrepancy in cardiac output (Fig. 8) would be reduced. At present, it is not known whether energy stores from nonworking muscles may be utilized by working muscles and further research into the sites of the anaerobic stores in different forms of exercise is needed.

The comparison between the predicted and calculated heart rates during the increase and decrease of work levels (Fig. 10) illustrates the difference that must exist between the mechanisms for the release and repayment of potential energy. The agreement between model prediction and data during the step increase in work rate implies that the energy is readily available, and that thermal effects are not significant. During the step decrease in work level, the implication is that the chemical processes for repayment do not occur as rapidly as for release as indicated by the difference between the experimental results and the curve computed for complete repayment; however, some repayment must occur, or the heart rate would

drop rapidly to the new level as shown by the lower curve. This difference between the onset and recovery is consistent with the observation that the oxygen deficit occurs in the first 2–4 min, while the debt must be determined over 20–30 min (Knuttgen, 1970).

The implication of this analysis is that the initial transient response to exercise is very rapid, with most of the changes that occur taking place in the first minutes. Blood flow rate and vascular resistance in the working muscles are possibly controlled by a combination of neural signals via the sympathetic nervous system and local effects via the direct chemical action of lactate, phosphagen, bicarbonate, potassium, pH, P_{CO_2} and P_{O_2} on the capillary vasculature. The presence of chemical buffers (HCO_3^-, $HPO_4^=$, Hb) probably mitigates the effects of lowered pH minimizing potentially greater effects on blood flow. The metabolic processes produce changes in all of these chemicals and make identification of the controlling substances difficult in the transient. Utilization of the model presented above should provide a framework from which to investigate the circulatory response to exercise, particularly as it pertains to muscle blood flow and the control mechanisms involved.

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