SESSION III: Paper 5

Lactate and Related Acid Base and Blood Gas Changes During Constant Load and Graded Exercise

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SINCE the work of A. V. Hill and his associates,[1] it has been recognized that the concentration of blood lactate increases as a consequence of anaerobic oxidation during exercise. They postulated and obtained convincing evidence that the Pasteur effect (pyruvate → lactate mechanism) was the creditor for the O_2 debt that occurs during exercise, and that this was the mechanism repaid during the recovery period.[2] Margaria, Edwards and Dill[3] subsequently obtained evidence that the pyruvate-lactate mechanism was not an important creditor of the O_2 debt until work became heavy. At moderate and low work rates, other mechanisms provided most of oxidative energy and it was to these that the O_2 debt was paid.

It had also been recognized that changes in acid-base balance might occur during work.[4, 5] When it occurs, a non-respiratory acidosis exists. We find that the changes in acid-base balance and blood gases are interrelated with lactic acid production and anaerobic oxidation. Therefore these changes in the blood are best understood in this context. It is the purpose of this presentation to review the relationship between the changes in blood lactate and associated changes in acid-base balance and blood gases during constant work-rate exercise done at three different work intensities.

METHODS

All the subjects were exercised on a Lanooy Cycle Ergometer (Instrumentation Associates Ltd., New York). The calibration of this ergometer was checked in our laboratory.[5] During these studies, the subjects breathed through a modified Otis-McKerrow two-way valve with a dead space of 175 ml. The mixed expired gas was collected in meteorological balloons and analyzed with a Beckman C-2 (expanded scale) oxygen analyzer within a minute after collection. Inspired and expired nitrogen and carbon-dioxide concentrations were recorded continuously using zero supressed nitrogen and carbon-dioxide gas analyzers, as previously described.[5] Minute ventilation was obtained by integrating the expired air flow as measured with a Fleisch-type pneumotachograph. The respiratory quotient (R) was determined from a nomogram which relates end tidal nitrogen and carbon-dioxide gas tensions and R, as previously reported.[6] The true oxygen difference was determined from the oxygen concentration, the mixed expired air, and R, using the nomogram of Dill and Fölling.[7]

Arterial blood was sampled through a polyethylene catheter (PE 160) inserted percutaneously into a brachial artery under local anesthesia. At the time of the oxygen consumption measurements, arterial blood was drawn for determination of pH, $PaCO_2$ and bicarbonate by the Astrup technique, PaO_2 with a Clark-Severinghaus electrode, and lactate concentrations by an enzymatic technique as previously reported.[8] The micro-Scholander technique[9] was employed to analyze the Astrup equilibrating gases and all gases necessary to calibrate the respiratory gas analyzers and oxygen electrode.

Most of the studies reported here were done on 10 medical students whose performance was well characterized by duplicate graded work tests. During these tests, heart rate, oxygen consumption ($\dot{V}o_2$) and respiratory quotient (R) were measured at graded work rates as previously described.[6] A titration curve consisting of the respiratory quotient (R) at each work rate ($\dot{V}o_2$) was plotted for each subject. From these data the work rate at which R increased most abruptly (the anaerobic threshold[10]) was determined. This usually occurred in these subjects at work rates associated with heart rates of about 120 beats/min. From these studies, three work rates were selected for study on a second day (several days later). The lowest work rate was just below the "anaerobic threshold" (moderate exercise). A second and third work rate, referred to as heavy and very heavy work intensities,* were approximately 700 and 1500 ml./min. oxygen consumption ($\dot{V}o_2$) above the moderate, respectively. This work rate classification is the same as that of Wells, Balke and Van Fossan.[11]

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*Work rate is used in the absolute sense (kg-m/min). Work intensity refers to the severity of work for a given subject based on the titration study, i.e. moderate, heavy, very heavy.

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RESULTS AND DISCUSSION

Arterial Blood Lactate and Bicarbonate Concentration as Affected by Work Intensity and Duration

Ten medical students performed three constant work rate exercise tests for 50 minutes or to exhaustion. The three work rates selected for each subject were based on the criteria described above, and were considered to be of moderate, heavy and very heavy work intensities. At the moderate work intensity (mean $\dot{V}_{O_2}$ = 1240 ml./min), arterial blood-lactate concentration usually changed very little, or rose initially and then decreased back to control values (Fig. 1).

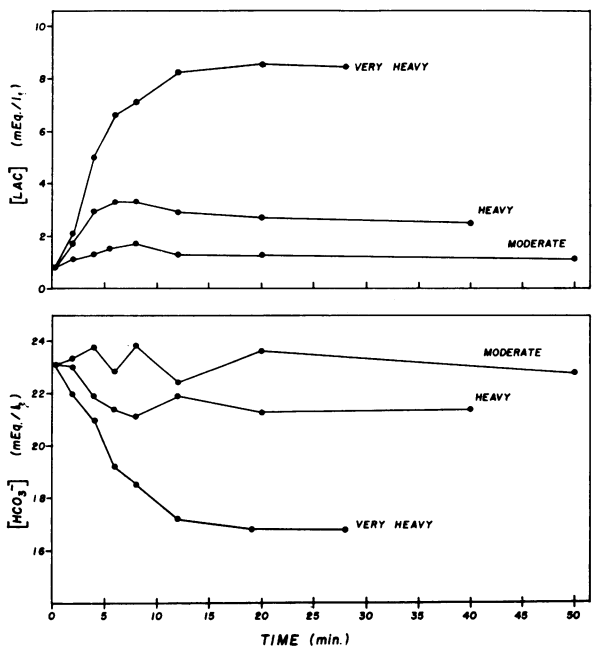

Fig. 1.—Average arterial lactate and bicarbonate concentrations for 10 male subjects during constant work rate exercise tests of moderate, heavy and very heavy intensity.

During heavy exercise (mean $\dot{V}_{O_2}$ = 1940 ml./min), the arterial blood lactate concentration increased by 2 to 4 mEq./l. Again after the initial increase, there was a decrease. However, the decrease did not continue. The arterial lactate concentration levelled off at a value that was well above the control value. Very heavy work (mean $\dot{V}_{O_2}$ = 2720 ml./min) resulted in peak lactate values which were about four times those achieved during heavy work. Furthermore, the maximum values occurred at a later time than the lesser work intensities. Some subjects did not reach a peak lactate value at the time they had to stop, while others had reached peak values which then started to decline. These differences in response probably reflect differences in the relative severity of the work for individual subjects.

The changes in arterial plasma bicarbonate concentration are reciprocally related to the lactate concentration at each work intensity (Fig. 1). This is to be expected, since lactic acid is almost completely dissociated at the pH of arterial blood. Because of the effectiveness of the respiratory system in keeping the arterial pH within a very narrow range by elimination of CO_2, the bicarbonate buffer system is the principal buffer affected when lactic acid is added to the blood during exercise. Thus the measurement of bicarbonate becomes an additional method for quantitating the anaerobic response to exercise.

It has been reported that lactate or "'excess lactate" continues to increase during exercise.[12] Apparently, a continual increase or a decrease after an initial increase might be observed during constant load exercise, depending on the duration of the exercise. However, our studies indicate that the arterial lactate concentration does not increase or decrease after the initial changes. Instead, it appears to achieve a new steady state value if the exercise is continued and is not too severe. This value depends on the work intensity.

Regulation of Acid-Base Balance During Exercise

At moderate work intensities, the respiratory system appears to do a remarkable job in handling the large acid load in the form of CO_2. The respiratory system does not function more than or less than is required to keep the pH within normal range (Fig. 2). It appears that with the production of additional lactic acid, it might fall behind in the regulation of pH at heavy work intensity. However, this failure to compensate completely does not persist; the pH returns to control values following respiratory compensation as the exercise continues, and this is evidenced by the simultaneous reduction in arterial CO_2 tension (Fig. 2). Our subjects could only partially compensate for the metabolic acidosis of very heavy exercise.

Alveolar ventilation must increase and remain increased if respiratory compensation of metabolic acidosis is to eliminate the CO_2 produced at a reduced mean alveolar (arterial) CO_2 tension. This is apparently very difficult or impossible at the high rate of CO_2 production found in very heavy exercise. The amount of ventilation required for complete compensation in most of our subjects would have been in excess of their maximum breathing capacities.

Arterial O_2 tension averaged 93 mm. Hg and did not decrease at any of the work loads tested. In fact it must have actually increased, since we did not correct the O_2 tensions for the increased

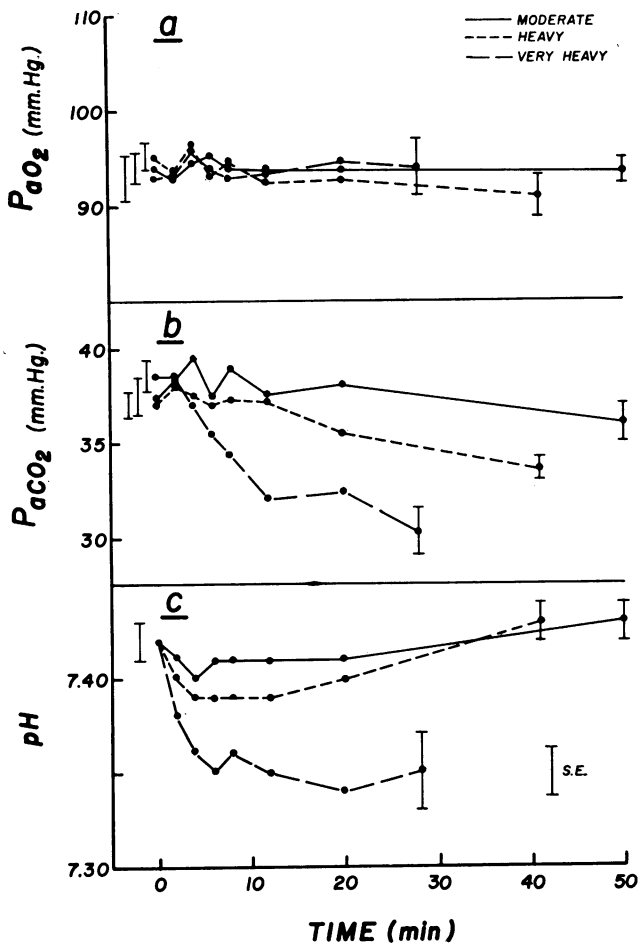

Fig. 2.—Average arterial O_2 and CO_2 tensions and pH for 10 normal male subjects during constant work rate exercise tests of moderate, heavy and very heavy intensity.

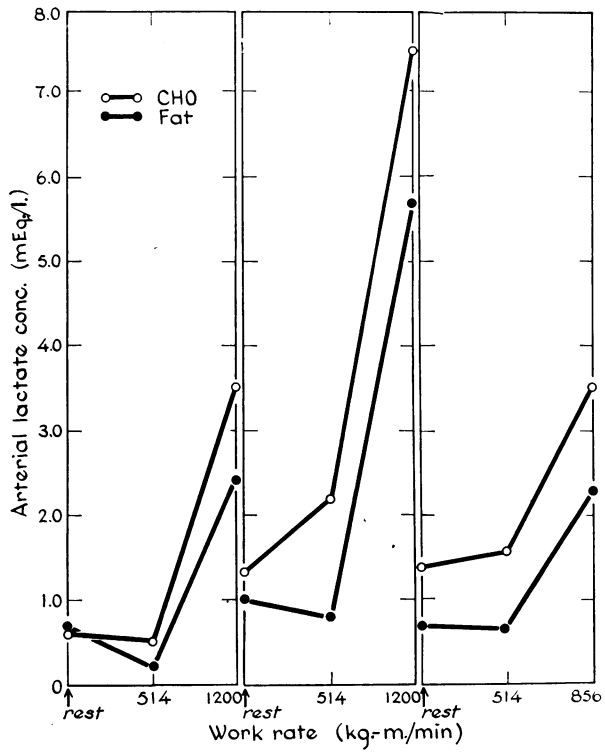

Fig. 3.—Effect of diet on arterial blood lactate during exercise in three subjects. The measurement was made between the 9th and 10th minute of each work rate.

body temperature that our subjects undoubtedly developed during exercise. From the work of others[13] and recent work of our own, we estimate that the increase in P_{aO_2} would be of the same order of magnitude as the decrease in P_{aCO_2}. Thus it appears that diffusion does not limit oxygen uptake in normal subjects at sea level even at very heavy work rates. These same conclusions were reached by Holmgren and McIlroy.[14]

Effect of Diet on Lactate Concentration During Exercise

The level of arterial blood lactate during exercise is apparently dependent on diet. Arterial blood lactate was measured at two work rates after three days on a high-carbohydrate diet, and after one day of fast and three days on a high-fat diet (Fig. 3). The changes tend to parallel each other, although the absolute concentrations of lactate were uniformly higher when the subject was on the carbohydrate diet than when on the fat diet. The respiratory quotient was about 0.2 higher on the carbohydrate diet than on the fat diet. Mechanical efficiency was greater while on the carbohydrate diet than while on the fat diet. This is expected, since there is a greater caloric yield from the oxidation of carbohydrate than from the oxidation of fats.

Lactate Production and the Oxygen Deficit

As reported above, the lactate concentration achieved at the end of constant work rate exercise of long duration was dependent on the work intensity. Since to the pyruvate-lactate mechanism has been ascribed the role of providing anaerobic oxidation at a time when aerobic oxidation is not readily available,[1, 3,15] a relationship should exist between the size of the oxygen deficit* and lactate concentration late in exercise. This correlation is shown for the 30 exercise studies on our 10 subjects (Fig. 4). A positive correlation exists for each subject.

Role of the Pasteur Effect in the Total Energy Requirement During Exercise

Oxidative energy is obtained from the Pasteur effect when pyruvate accepts two protons and

*"Oxygen deficit" is the difference between the steady-state oxygen consumption and the actual oxygen consumption.

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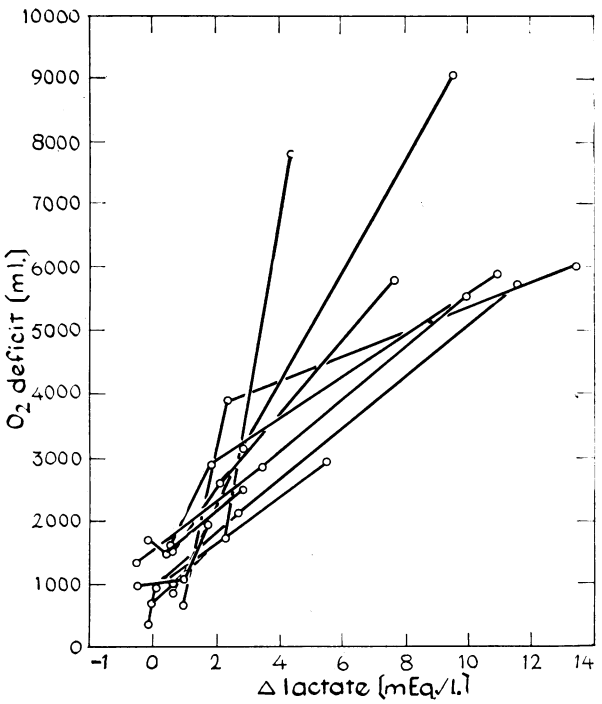

Fig. 4.—Correlation between arterial blood-lactate change and oxygen deficit. Ten normal subjects exercised to steady state $\dot{V}O_2$ during moderate, heavy and very heavy exercise. Each point represents a different exercise study. The values for the same subject are joined.

is converted to lactate. Therefore, the amount of oxidative energy obtained from this mechanism must be calculated from the rate of increase in lactate rather than the lactate concentration itself.

After lactate reaches a constant value, no net oxidative energy is obtained from this mechanism. The oxygen equivalent of the increase in total body lactate* per minute (11 ml. O_2/mEq. lactate) was added to the oxygen consumption during moderate, heavy and very heavy exercise in the studies on the 10 subjects described above (Fig. 5). The time when the pyruvate-lactate mechanism stops providing anaerobic oxidation is about the time when the oxygen consumption from atmospheric oxygen reaches a steady state. While there is an overshoot at four minutes, followed by an undershoot in the case of the heavy and very heavy exercises, the total area of the oxidative energy supplied by the pyruvate-lactate mechanism closely approximates the oxygen deficit after the first two minutes of exercise. The overshoot and subsequent undershoot are likely due to the fact that newly formed lactate requires more than four minutes to equilibrate throughout the body water. The total area would be unaffected if the studies were carried out over a sufficiently long period to permit lactate to reach its final volume of distribution. The oxygen deficit during the first two minutes of exercise not accounted for by lactate production is probably accounted for by the other oxygen creditors which are known to be present during exercise.[3, 8]

*Total body lactate is calculated by multiplying the concentration of lactate × litres of body water (assumed to be 60% of the body weight).

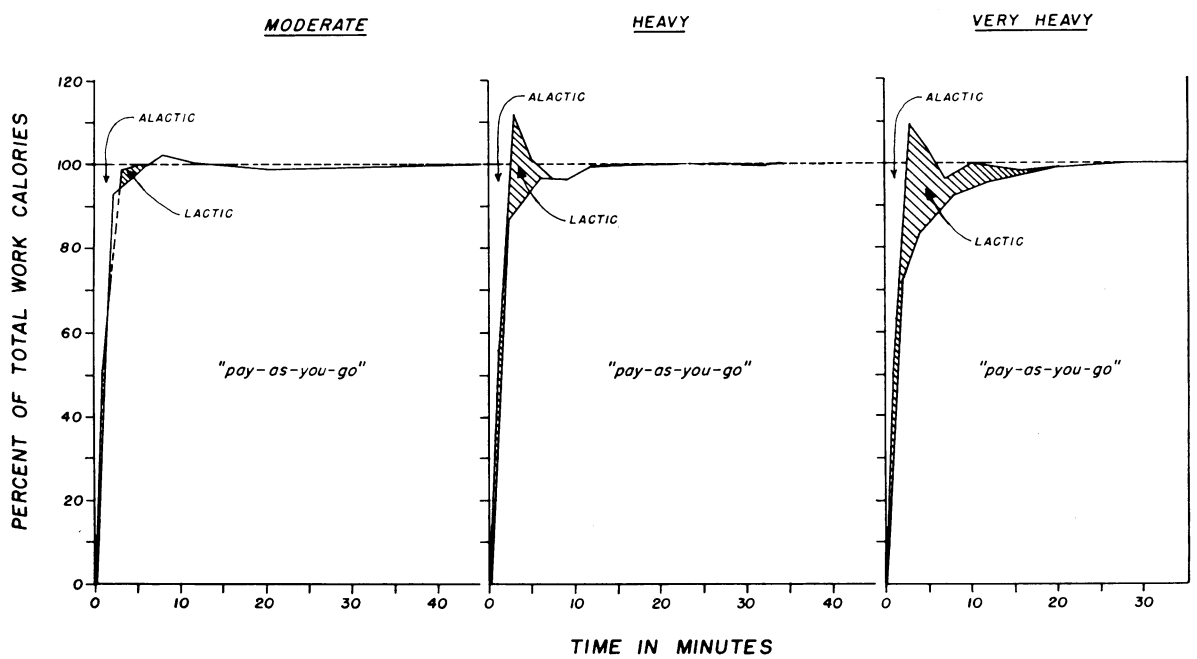

Fig. 5.—Sources of oxidation during constant work rate exercise. Work calories were calculated from $\dot{V}O_2$ and O_2 equivalent of lactate, equating 1 mEq. of lactate to 11 ml. O_2.

Besides the correlation between "steady state" lactate concentration during constant work rate and the oxygen deficit, there is a positive correlation between work intensity and the time $\dot{V}O_2$ reaches a steady state. Thus the time to a steady state $\dot{V}O_2$ and oxygen deficit as well as acid-base and blood gas changes help quantitate the anaerobic mechanism during work.

SUMMARY

Normal male subjects were exercised at three different work intensities for prolonged periods—to exhaustion or 50 minutes. The changes in acid-base balance and blood gases during these constant load exercise periods were interrelated with lactate production and anaerobic oxidation. The magnitude of the changes in arterial lactate, blood gas and pH, and the time at which these values reached a new steady state were dependent on the work intensity. Diet was also shown to affect the lactate concentration, but it had little effect on the increment in lactate concentration in response to a given work stress.

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Commentaries

Commentary: E. R. BUSKIRK, *University Park, Pennsylvania*

DEFINITION of the mechanisms involved in the oxygen debt and of the extent to which lactate is involved is complicated. An adequate explanation must take into account the many factors that affect the production, movement, and utilization of pyruvate, lactate, and perhaps other metabolic intermediates. There is some evidence, for example, that working muscle may utilize lactate as an energy source; thus there may be lactate turnover in the mitochondria. This utilization apparently is associated with the reversibility of the pyruvate-lactate, NADH-NAD relationship. If the lactate and/or pyruvate moves from the mitochondria by diffusion or active transport, one is then faced with the consideration of pools of different sizes, such as the vascular, extravascular and intracellular fluid pools. Thus various concentrations of the substrate materials are presented to different tissues and cellular matrices, at different places, and at widely separated times. When these facts are coupled with the view that the rates of formation and probably local turnover are different in the various cells of the body, interpretation becomes difficult indeed. The heart, kidney and liver are known to utilize lactate, and hypoxic conditions are apparently not necessary for this utilization. In addition, there is some evidence that utilization of lactate in a tissue is dependent on regional blood flow. Apparently an adequate amount of NAD must be available if oxidation is to proceed, even in the presence of adequate oxygen. Other factors also complicate the picture, because hemoglobin and myoglobin become desaturated during hypoxia and are resaturated under conditions of normoxia. This resaturation may account for 100 ml. or more of the post-exercise excess oxygen consumption. Elevated body temperatures, together with the release of adrenaline and noradrenaline during and after exercise, also complicate interpretation because they change metabolic events—presumably via rate alteration. Recent investigations indicate that free-fatty acids comprise a major metabolic substrate under both normoxic and moderate hypoxic conditions. After consideration of the above, one is tempted to view the relationship between the blood lactate disappearance curve and excess oxygen utilization as an oversimpli-