

# The Sources of Muscular Energy

*The immediate source is adenosine triphosphate (ATP). The ultimate sources are the combustion of food and the breakdown of glycogen. The time relations of these processes offer some practical hints*

by Rodolfo Margaria

A muscle can be regarded as an engine, and like any engine it obtains its energy essentially from the "burning" of fuel. Its performance, or capacity for work, depends on the nature and availability of the source of energy. In the case of an artificial engine the energy input is easily identified and measured: it is simply the rate of consumption of the supplied fuel. The muscle engine, however, is much more complex. It uses several different fuels, and it regenerates some of them itself. As a result the evaluation of the factors involved in muscle performance is far from a simple matter. It requires detailed, quantitative analysis of each of the sources of energy and their relative timing and collaboration. Through systematic investigations over the past few years a reasonably comprehensive picture of the operation of the energy sources in muscular exercise has been obtained, and it has become possible to suggest rational regimes for employing muscles most efficiently. The new knowledge should be widely applicable in athletics and in physical work, thus improving the productive capacity, comfort and health of people engaged in such activities.

The direct source of energy for a muscle's activity is adenosine triphosphate (ATP); the release of energy from the splitting of ATP into adenosine diphosphate (ADP) and phosphoric acid is what powers muscle contractions. The ATP must be synthesized continuously, as there is no appreciable store of it in the muscle. It is actually resynthesized from its products as soon as it is broken down. The energy needed for the recombination of ADP and phosphoric acid into ATP is supplied by another energy-yielding reaction in the cells: the splitting of creatine phosphate. This

auxiliary "phosphagen" is likewise in short supply in the muscle and needs to be resynthesized continuously. There are, in turn, two ultimate sources of energy for the resynthesis of the phosphagens: (1) combustion of food, measured by the consumption of oxygen, and (2) glycolysis, the breakdown of glycogen resulting in the formation of lactic acid. The second of these processes is reversible: with an input of energy from food combustion, lactic acid is reconstituted to glycogen.

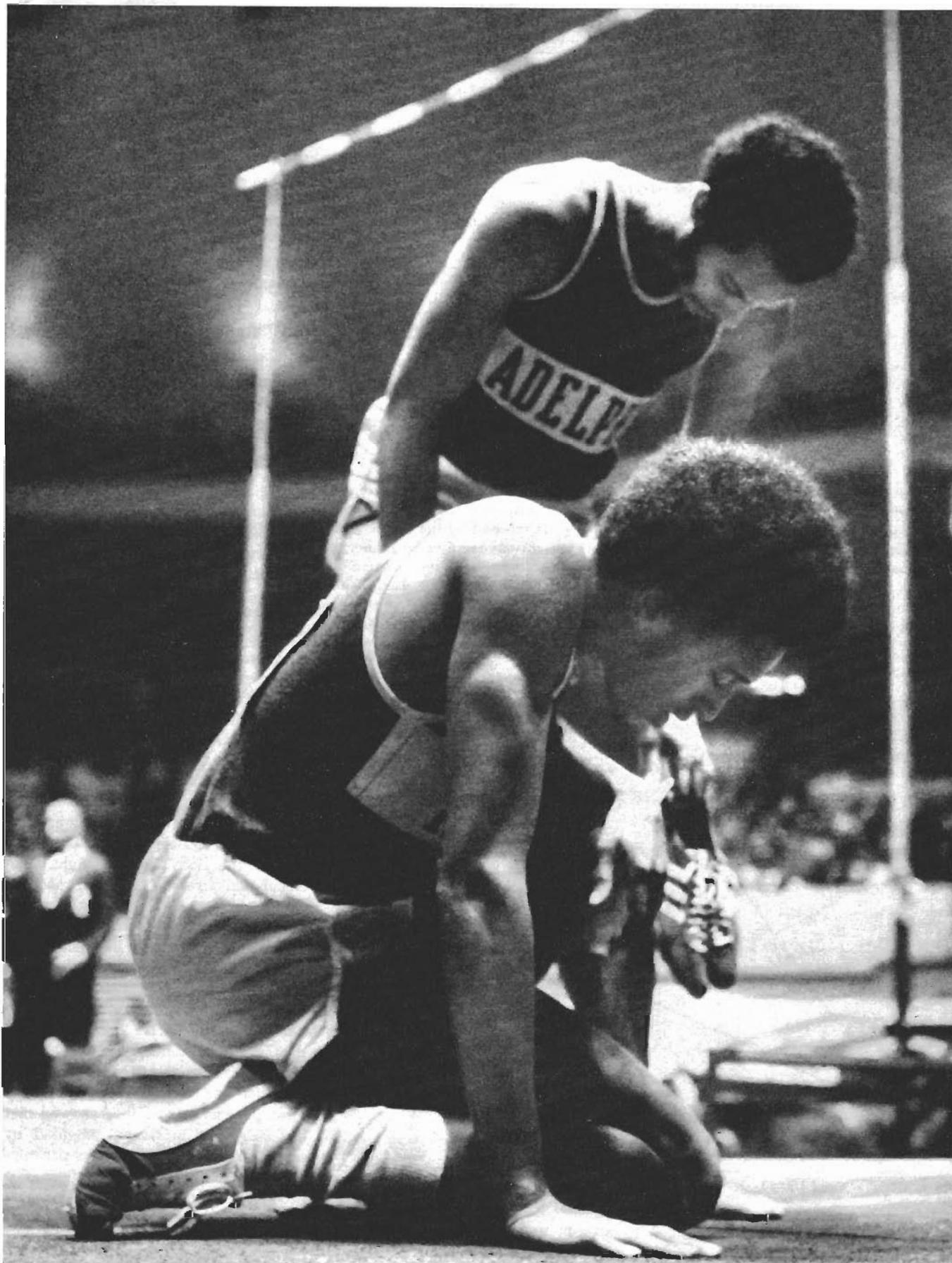
The system, then, consists of five reactions, three of which (phosphagen-splitting, food combustion and glycolysis) yield energy and two of which (phosphagen and glycogen resynthesis) absorb energy [see top illustration on page 86]. We need to obtain a measure of each of these five quantities in order to compute the net total of energy and power (energy per unit of time) available to the muscle for given levels of performance.

How can we disentangle the factors for separate measurement? Fortunately we can set up experimental conditions in which some of the factors can be disregarded. For example, it is known that during moderate exercise (that is, below a certain level of exertion) the muscles do not produce lactic acid; therefore glycolysis and the reverse do not enter into the equation. Furthermore, if the exercise is maintained at a constant level of energy consumption, the splitting and resynthesis of the phosphagens soon balance out in energy terms, so that we can disregard those quantities also. In exercise under these conditions the net expenditure of energy can be calculated simply from the consumption of oxygen. It has been known for some time that the energy yield from food combustion in the muscles is five

calories per milliliter of oxygen consumed. Hence it is easy to calculate that during exercise at a constant, submaximal level the energy employed for the given work load is a number of calories amounting to five times the number of milliliters of oxygen consumed. This formula has been known and employed in physiological studies for many years. In such studies the work load is commonly measured on an ergometer such as a treadmill or a bicycle.

When exercise is raised to a strenuous level at which energy can no longer be provided in sufficient quantity through oxidation (because of the limit on the rate of delivery of oxygenated blood to the tissues), the muscles begin to supplement the energy supply by means of glycolysis. The quantitative details of this process are difficult to get at and have only recently been determined.

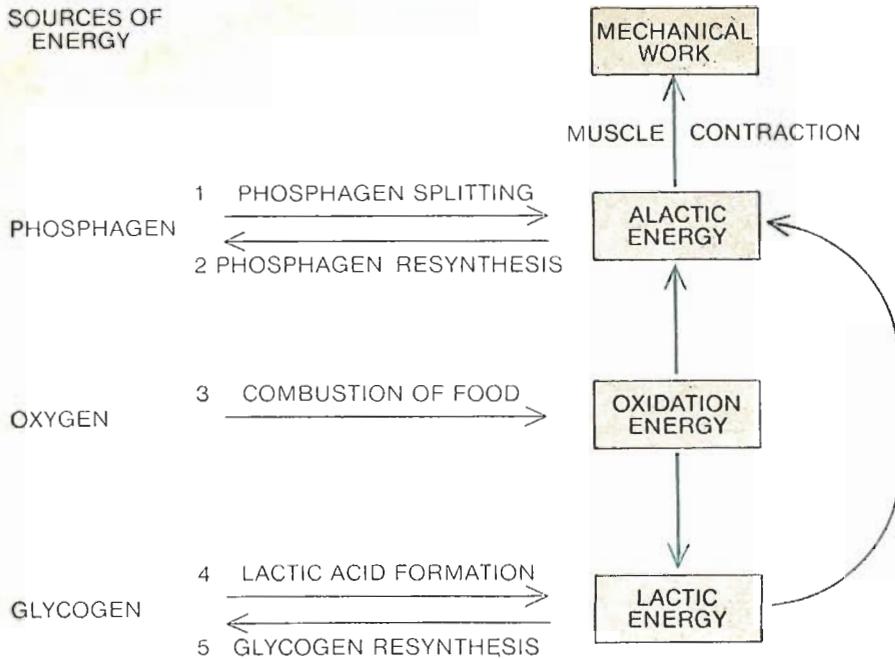
Let us consider a maximal effort such as a runner's sprint of 100 or 400 meters at top speed. Within a few seconds his muscles' energy requirement has established an equilibrium between the splitting and the resynthesis of phosphagen and also has passed the limit of production of energy by oxidation. The only variable, then, is the amount of energy generated by glycolysis. Can this be estimated from measurement of the amount of lactic acid (the breakdown product) in the blood? If glycogen were resynthesized from lactic acid about as rapidly as it is broken down, such a measurement would be meaningless. Actually, however, the resynthesis is very slow; it takes about 15 minutes, by exponential increase, to reach half its maximal rate. Therefore in a test of strenuous exercise lasting only a few seconds or a few minutes the amount of resynthesis is so small it can be disregarded and the concentration of lactic acid in the blood can be



AFTER A HARD RUN an athlete may be near exhaustion because his muscles have depleted their supply of ATP, and oxidation and glycolysis have not yet been able to replenish the muscles with their primary source of energy. Here the kneeling runner, com-

ported by one of his Adelphi University teammates, has just finished running the fourth half-mile leg of a two-mile relay at the Wanamaker Millrose Games, which were held at Madison Square Garden in New York on January 28. His team finished fourth.

**SOURCES OF ENERGY**



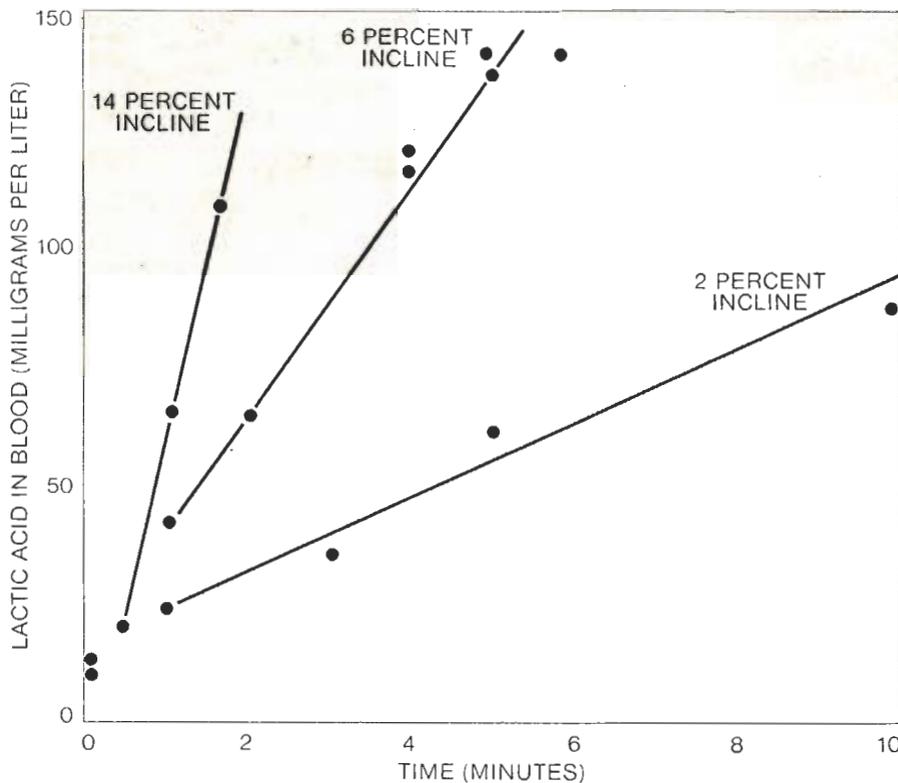
taken as a good indication of the energy contribution of glycolysis beyond what is supplied by oxidation. For a given subject the production of lactic acid per minute should vary directly with the magnitude of the energy requirement or with the length of time a given requirement is imposed on the muscles.

Of course, the subject's blood cannot be sampled while he is running. Furthermore, a sample taken during the exercise would be misleading, because it takes time for the lactic acid to diffuse from the muscles into the body fluids. As a result the drawing of the blood samples can conveniently be postponed until two or three minutes after the run, and the lactic acid concentration in the blood at that time can be considered a reasonably accurate representation of the total quantity of lactic acid formed as a result of the exercise.

RELATIONS OF SOURCES of muscular energy are outlined. "Phosphagen," the direct source of energy, is a general term for the high-energy phosphates such as ATP and creatine phosphate (CP) that are found in cells. Energy is released by the splitting of phosphagen molecules. The split phosphagen is almost immediately resynthesized. Energy for the recombination is supplied by the two secondary energy sources: the combustion of food and the breakdown of glycogen, a carbohydrate stored in the muscle, into lactic acid. Glycogen in turn is resynthesized from lactic acid with energy from oxidation. The overall cycle consists of five reactions, three of which release energy and two of which absorb it.

Experiments have proved these assumptions to be correct. Subjects were tested in runs on a treadmill, tilted at different inclinations to call for different intensities of exercise, and the exercise levels were strenuous enough to lead to exhaustion in one minute to 10 minutes. Measurement of the lactic acid concentration in the blood after the run indicated that the amount of glycolysis for a given work load did indeed increase linearly with time, as the premises predicted [see bottom illustration at left]. On the basis of assumptions about the diffusion of lactic acid to the various tissues and organs of the body it was possible to calculate how much lactic acid the muscles produced in relation to the body's total weight. This calculation likewise showed that the amount of lactic acid produced per minute per kilogram of body weight varied in direct proportion to the energy requirement [see illustration on opposite page].

The measurements established several interesting facts. They confirmed that in steady exercise the body meets its energy needs exclusively by means of oxidation up to a certain level of requirement for energy, and they showed that ordinarily the maximum provided by oxidation is about 220 calories per minute per kilogram of body weight. The production of lactic acid usually began when the energy requirement passed that level. Furthermore, the amount of lactic acid produced in relation to the energy need indicated that the energy yield from glycolysis is about 230 calories per gram of lactic acid produced. This determination of the energy yield



HEAVY EXERCISE leads to the formation of lactic acid. For a given work load the concentration of lactic acid in the blood increases linearly with the duration of the exercise. The exercise consisted in running to exhaustion at a constant speed of 12 kilometers per hour on a treadmill tilted at inclines of 2, 6 or 14 percent. At these work loads the rate of increase of lactic acid, indicated by the slope of the curves on the graph, is proportional to the intensity of the exercise. Blood samples were taken a few minutes after the exercise to allow the lactic acid from the muscles to become uniformly distributed throughout the body.

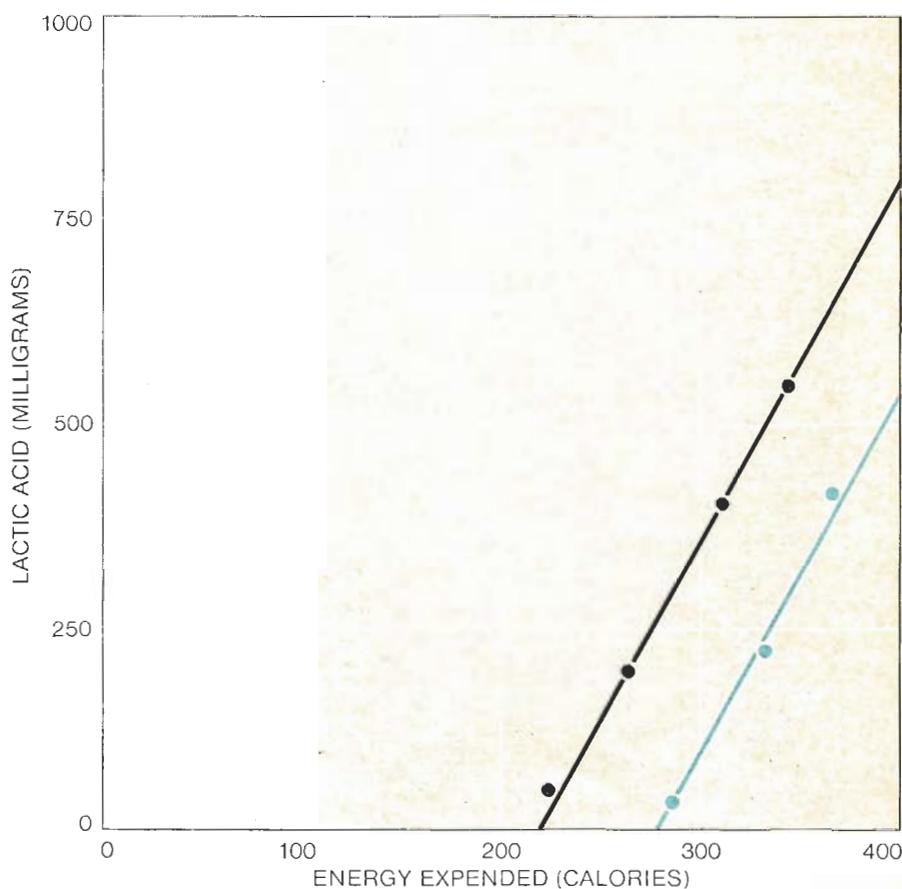
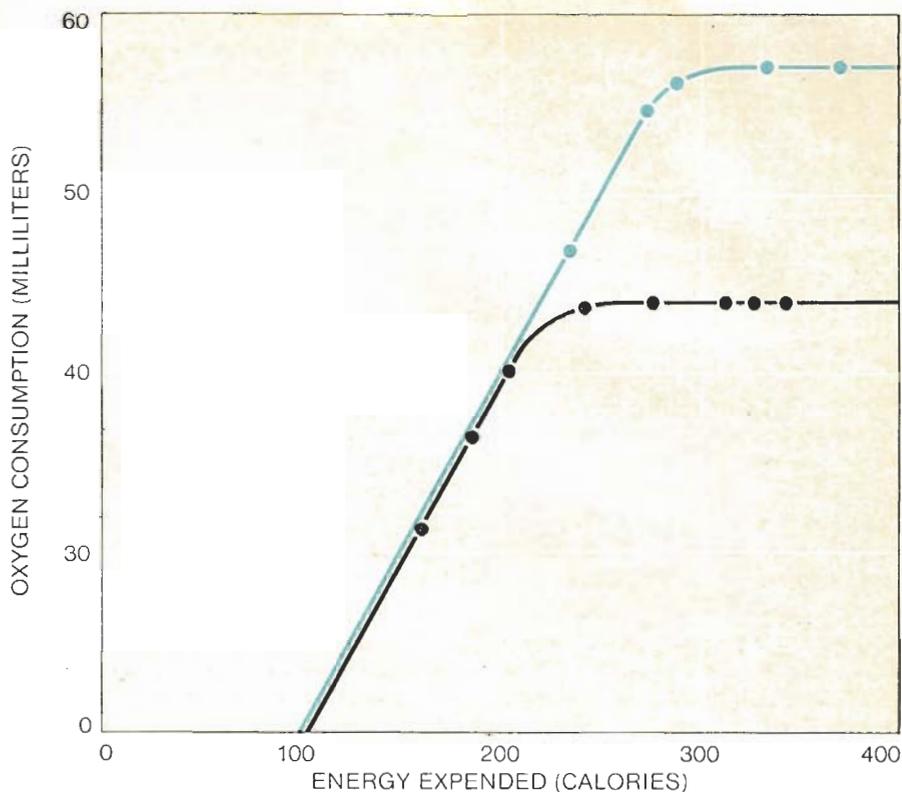
could be considered a close approximation of the true value, since it was obtained in vivo with the subjects showing an entirely normal physiological state in terms of their body temperature and the physical characteristics of their body fluids. Moreover, the energy yield was the same in trained athletes as it was in other persons.

Another significant finding is that trained athletes (middle-distance runners) were able to obtain an unusually large share of their energy need from oxygen consumption, so that lactic acid production began at a somewhat higher level of exertion than it does in non-athletes. The same effect was obtained by nonathletes by their breathing oxygen during exercise. Breathing oxygen before the performance, however, apparently is not helpful, and there is no physiological basis for believing it should be (although it is sometimes resorted to by athletes). Oxygen respiration during a performance is useful because it provides an extra current supply for the continuing need for chemical energy; by the same token, air with a subnormal content of oxygen, such as the athletes had to contend with at the high altitude of Mexico City in the Olympic Games of 1968, understandably must reduce performance.

As the trained athletes' performances in our tests indicated, people differ in their capacity for performing work without resorting to glycolysis. When we tested subjects with different capacities in this respect on the same work load, we found that individuals differ in the rate of lactic acid production. A person with a low capacity for oxygen consumption produces considerably more lactic acid.

What, then, is the total contribution glycolysis can make to the muscle machine? Measurements of the lactic acid concentration in the blood after strenuous exercise have shown that the maximum increase in this content is about 1.5 grams per liter, or about 1.12 grams per kilogram of body weight. Putting the yield per gram at about 230 calories, we can compute that the maximum amount of energy obtainable from the formation of lactic acid is about 260 calories per kilogram of body weight.

Obviously the rate at which lactic acid can be produced must have an upper limit, just as there is a limit on the rate of oxygen consumption by the tissues. In the case of lactic acid the limit is imposed by the rate of the chemical processes involved in its production. We find that increasing the intensity of ex-



**ENERGY CONTRIBUTIONS** of oxygen (*upper graph*) and a glycolysis (*lower graph*) during exercise are plotted. In moderate exercise the oxidation of food, as measured by increased oxygen consumption (in milliliters per minute per kilogram of body weight), provides virtually all of the energy requirement (shown on the abscissa in calories per minute per kilogram of body weight). When the energy requirement surpasses the upper limit of oxygen consumption, the additional energy is provided by formation of lactic acid (in milligrams per minute per kilogram of body weight) from glycogen. Athletes (*colored curves*) have a higher oxygen-consumption capacity, which delays the formation of lactic acid.

ercise raises the rate of lactic acid production only to a certain level; beyond that the speed of its production cannot be pushed further. The maximal rate is about 1.7 grams per kilogram of body weight per minute, which corresponds to a power output of 390 calories per kilogram per minute. Thus the power available from glycolysis turns out to be about 50 percent higher than the power from oxidation (220 calories per kilogram per minute).

Consider now the physiological debts the body contracts in strenuous exercise that leads quickly to exhaustion, say within 35 seconds, when lactic acid production has reached its maximal rate. We know that in exercise of such intensity there is for the first 15 seconds or so no energy contribution from glycolysis. The oxidative mechanism also is rather sluggish and in the first 15 seconds it contributes only a small portion of the energy, although its contribution rises at an exponential rate. On the basis of these known facts we can calculate the energy contributions made in exhausting exercise by each of the three

energy-yielding mechanisms: oxygen consumption, lactic acid production and phosphagen-splitting, the last called the "alactic" mechanism [see illustration on opposite page].

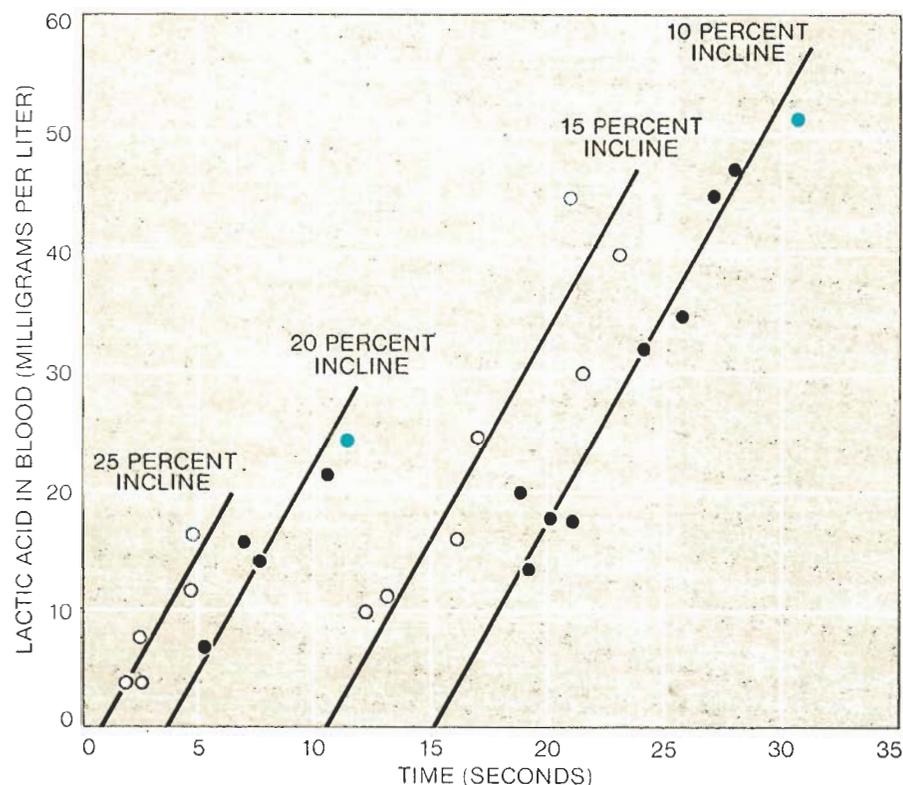
The calculation on this basis indicates that theoretically the maximal contribution of phosphagen-splitting itself (the alactic source) would be about 200 calories per kilogram of body weight, which would amount to the splitting of almost all the available phosphagen. We find in experiments that the amount of split phosphagen at the end of a maximal aerobic exercise (exercise that can be supported by energy from oxidations only) is only about half this theoretical quantity; the amount corresponds to an energy yield of about 100 calories per kilogram of body weight instead of 200 calories. At the end of supramaximal exercise that involves energy from anaerobic sources and leads to exhaustion in a short time, the energy yield from phosphagen breakdown may go up to 150 calories per kilogram of body weight; this has been found recently by Pietro di Prampero and others in my laboratory in measurements of the alactic oxy-

gen debt. Under no conditions, however, did they find that the energy yield from phosphagen reaches 200 calories per kilogram of body weight, which would be the case if all the phosphagen in the muscle had been broken down.

In spite of this experimental finding in strenuous supramaximal exercise to exhaustion, I believe practically all the available phosphagen has actually been split. The reason the experiments show otherwise probably lies in the fact that the theoretical estimate of the energy balance overstates the amount of contribution by glycolysis during the exercise. It overlooks the fact that some of the lactic acid is produced afterward during the early period of the muscles' recovery. This production of lactic acid represents an energy debt that is used to pay a corresponding amount of the alactic debt. In other words, a fraction of the alactic debt is shifted into a lactacid debt. That such a process of anaerobic recovery (contributing energy for phosphagen resynthesis by a means other than oxidation) takes place after exercise was observed many years ago in studies of the isolated frog muscle by the author and Gianni Moruzzi and more recently in our laboratory at the University of Milan by Paolo Cerretelli. It is estimated now that during recovery from very strenuous exercise the delayed production of lactic acid may contribute about 50 calories per kilogram of body weight to the resynthesis of phosphagen, which would explain why Prampero did not find complete breakdown of phosphagen at exhaustion.

In short, the "oxygen debt" that the British physiologist A. V. Hill first described in the 1920's has two aspects: oxygen is needed for the dual functions of (1) reconstituting glycogen from lactic acid (as Hill observed) and (2) providing energy directly on its own account for the resynthesis of phosphagen (as H. T. Edwards, D. B. Dill and I found later in studies at the Harvard Fatigue Laboratory). We call these aspects the lactacid oxygen debt and the alactic oxygen debt.

From the standpoint of provision of energy we can distinguish three phases in the operation of the muscle engine in strenuous exercise. During the first phase, lasting only a few seconds, all the energy is provided solely by the splitting of phosphagen, as the oxidative and glycolytic reactions have not yet got under way. How much power can be provided by this alactic mechanism? We can obtain a measure of the maxi-

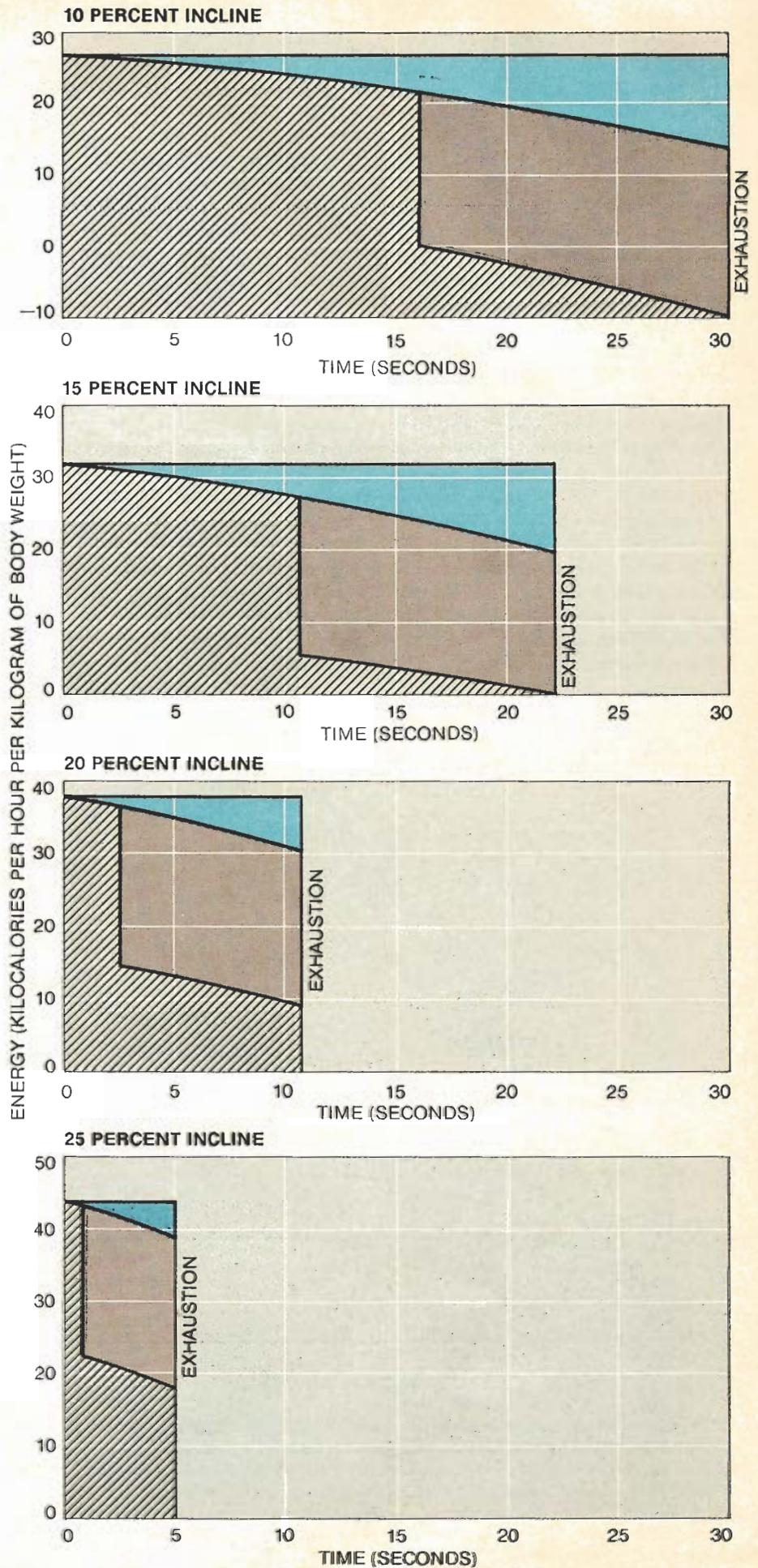


**SUPEREXERTION** pushes the rate of lactic acid formation to its upper limit, after which increasing the intensity of the exercise no longer affects the rate, as is indicated by the parallel slope of the curves in the graph. The work load consisted in running to exhaustion at a constant speed of 18 kilometers per hour on a treadmill tilted at inclines of 10, 15, 20 or 25 percent. The point of exhaustion (colored dots and colored circles) is reached more rapidly as the exercise becomes more strenuous. Although rate of lactic acid production does not change, the more strenuous the exercise, the more quickly formation of lactic acid begins.

imum output by using an exercise in which the subject climbs stairs two steps at a time at top speed. The maximum speed is reached within three seconds and is maintained for one or two seconds after that. Since the work consists almost entirely in lifting the body, it can be calculated as the kilogram-meters of rise per second per kilogram of body weight. The maximum efficiency in the use of muscle energy by a man running uphill has been found to be about 25 percent. Dividing the work performed in the tests by this figure, we calculate that the maximum of muscular power obtainable from the splitting of phosphagen is about 800 calories per minute per kilogram of body weight. (Of course, this test tells us only about the power in the muscles of the lower limbs; work involving mainly the arms might give a different figure.)

The second phase in the energy economy, chronologically speaking, is the arrival of oxidation as a source of energy for resynthesizing phosphagen. The maximum power available from this contribution too can conveniently be measured experimentally. The rate of the heartbeat gives a sufficiently accurate measure of the rate of oxygen consumption by the body, and it has been found that there is a maximum for the heart rate during exercise, depending on the person's age. A convenient and well-accepted exercise for this test is stepping up on and down from a stool of a given height at a given frequency dictated by a metronome. The subject's heart rate is measured after three or four minutes, when the rate has reached a constant level. The test shows that this rate in an average young man indicates a maximum oxygen consumption of about 40 to 45 milliliters per minute per kilogram of body weight, providing a power contribution of about 220 calories per minute

**CONTRIBUTIONS** of the three energy sources during exercises calling for superexertion are plotted in the four graphs at the right. The exercises consisted in running to exhaustion at 18 kilometers per hour on a treadmill inclined at 10, 15, 20 or 25 percent. Alactic energy (*hatched areas*), released by the splitting of phosphagen, is both the initial and the major source of energy during superexertion. Energy from the oxidation of food (*colored area*) increases exponentially from the onset of strenuous exercise, but the mechanism is sluggish and provides only a small portion of the required energy during the first few seconds. The remaining energy is provided by breakdown of glycogen into lactic acid (*gray area*).



per kilogram, as we have already noted.

The third energy contribution for exercise, which enters only after oxidation is no longer able to keep up with the muscles' needs, is glycolysis. I have already mentioned that the maximum quantity of lactic acid produced in strenuous exercise is about 1.12 grams per kilogram of body weight, corresponding to an energy production of about 260 calories per kilogram. In recent studies Jan Karlsson and Bengt Saltin of the Gymnastic School in Stockholm found that on the average human muscle contains about 10 grams of glycogen per kilogram of muscle tissue, which suggests that only about a third of the glycogen in the muscles is broken down to lactic acid to furnish energy for work. These general characteristics are not very significant for judging an individual's capacity for exercise, however, because people vary greatly in the glycogen content of their muscles. The glycogen content depends on the state of the individual's nutrition; obviously, then, an athlete or anyone engaging in strenuous exercise should pay careful attention to nutrition.

The measurements I have described give us a balance sheet showing the capacity and power of each of the three contributing mechanisms and some information about the contraction and repayment of the alactic and lactacid oxygen debts. We are interested, however, not just in the overall balance sheet but, more important, in the timing of the respective processes for supplying energy. From the various experiments and analyses we can now sketch a rough, well-confirmed picture of the energy events that take place during exercise and the following recovery period.

In exercise that calls for maximal consumption of oxygen but no glycolysis, the oxygen consumption rises exponentially to its limit (40 milliliters per minute per kilogram of body weight) and then, at the end of the exercise, falls back exponentially to the rate of a resting muscle. The oxygen debt contracted is entirely alactic; it amounts to about 20 milliliters and is quickly paid off. Only half of the phosphagen content of the muscle is split during the peak period of activity, and all of this is resyn-

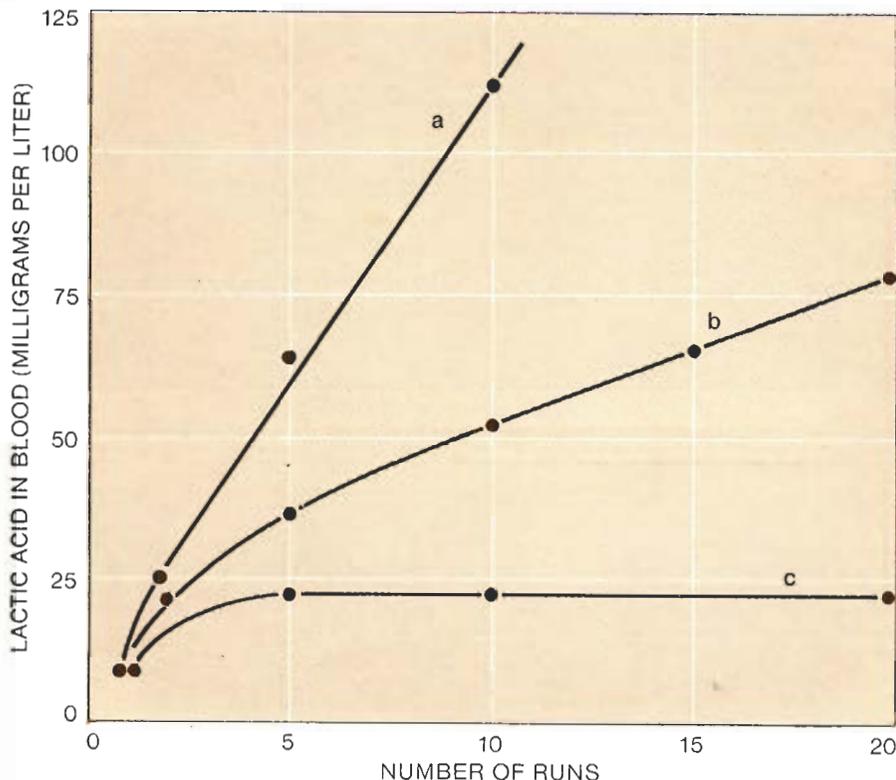
thesized by means of energy from oxidation in the brief recovery period [see top illustration on opposite page].

The picture in exercise that requires the additional input of energy from glycolysis is considerably more complex and has only recently been traced out. When the energy requirement is twice as great as what can be furnished by oxidation (that is, when the requirement is equivalent to an oxygen consumption of 80 milliliters per minute per kilogram of body weight), oxygen consumption rises to its maximum rate in half the time, and the formation of lactic acid, apparently triggered by the splitting of 50 percent of the muscle phosphagen, begins at that point. If the exercise proceeds to exhaustion, presumably the remaining 50 percent of the muscle phosphagen is split. The alactic oxygen debt at the onset of the recovery period after exhaustion amounts to about 40 milliliters per kilogram of body weight, the lactacid oxygen debt depends on the amount of lactic acid built up during the exercise. In the recovery period of the alactic energy debt 30 milliliters are paid by energy from oxidation and about 10 milliliters by energy from the delayed production of lactic acid through glycolysis [see bottom illustration on opposite page].

What does all of this tell us about how to make efficient use of the muscle engine? Obviously it is advisable to avoid, if possible, driving the muscle to the pitch of incurring a lactacid debt. The payment of that debt is a very slow process, taking more than an hour after the exercise has been concluded, and the lactic acid in the body induces a state of acidosis that hampers muscle performance, causes great discomfort and produces other disagreeable symptoms. On the other hand, if the oxygen debt is only alactic, there is no acidosis and the debt is paid off in a few minutes.

Because there is always a certain period of delay in the onset of lactic acid production, even in highly strenuous exercise, one can avoid this production by limiting the activity period to a short enough time. This suggests that, in the case of exercise or work that may push the energy requirements beyond what can be furnished by oxidation, the muscles can be used most effectively by adopting a schedule of intermittent activity and rest, each activity period being short enough to forestall lactic acid production and each rest period long enough to pay off the alactic oxygen debt contracted during the period of strenuous activity.

We have conducted experiments that



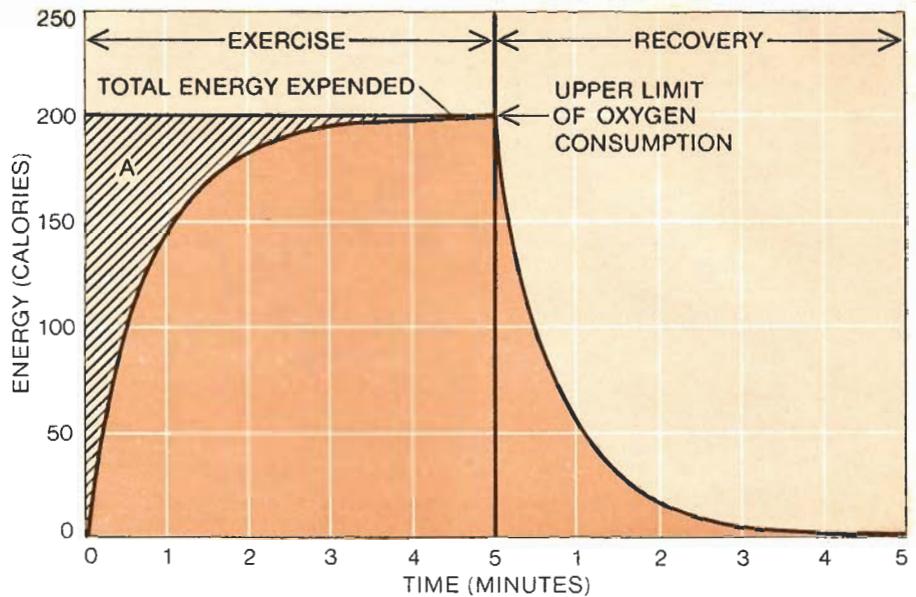
REST INTERVALS between sessions of strenuous running can greatly reduce the production of lactic acid and increase the total distance that can be run. The exercise consisted in running on a treadmill at 18 kilometers per hour for 10 seconds followed by a rest period. When the rest period was 10 seconds (a), the runner could complete 10 cycles before exhaustion. When the rest period was 20 seconds (b), exhaustion occurred after 20 cycles. With a rest period of 30 seconds between runs (c) the lactic acid level remained constant and the exercise could be continued indefinitely. Athletes in training can increase the amount of strenuous exercise they can perform by judicious timing of rest periods.

strikingly demonstrate the value of this tactic. The test consisted in running on a treadmill at a speed and incline that would lead to exhaustion in about 35 seconds if it were continued without rest. We limited the run to 10 seconds at a time and varied the experiment by trying rest periods of different lengths between the runs. The object of the test was to find out how many 10-second runs could be accomplished (in effect, how much distance could be covered in total) before exhaustion.

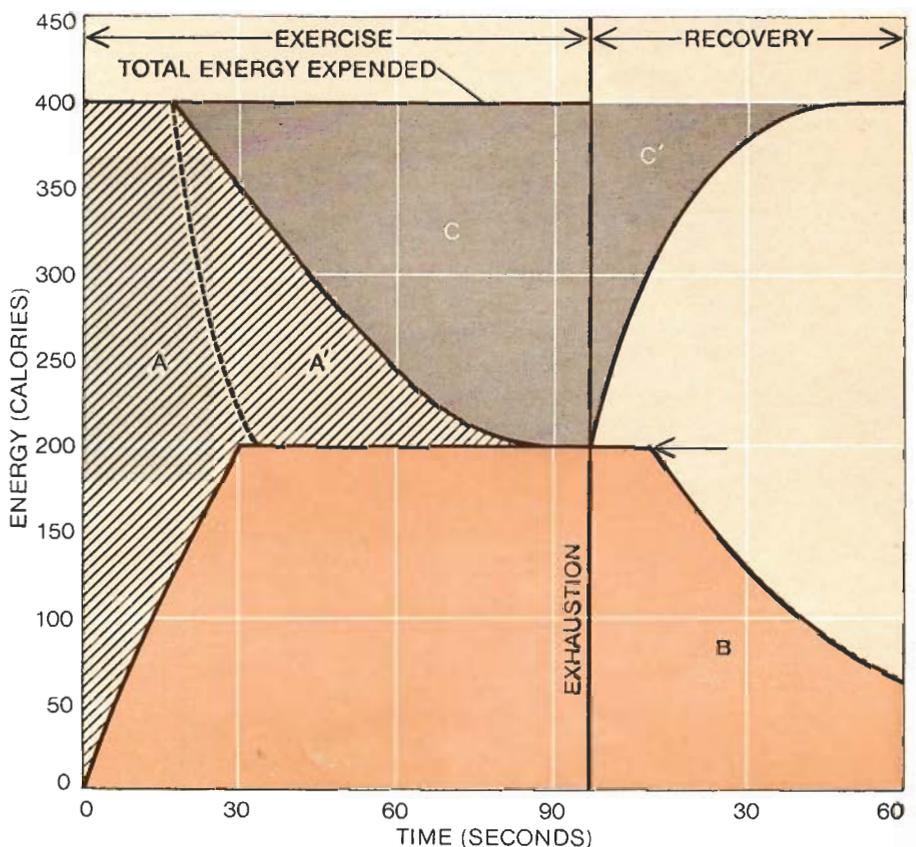
When the rest period was 10 seconds, the subjects could run about 10 cycles (totaling 100 seconds of exercise) and cover a distance corresponding to 500 meters. The lactic acid in the blood at the end of the performance amounted to 1.15 grams per liter. When the rest period was increased to 20 seconds, the subjects accumulated less lactic acid and covered a considerably greater distance. With a rest period of 30 seconds between runs the subjects were able to go on with runs indefinitely and showed a lactic acid content in the blood of only about .2 gram per liter; this content could be attributed to the fact that leg muscles usually generate a little lactic acid at the beginning of exercise because of sluggishness of the oxidative mechanism [see illustration on opposite page].

These findings can be projected to predict potential performances in sports events on a track. For example, a trained runner sprinting 400 meters at top speed will finish the race with a state of acidosis that will require a rest of at least an hour and a half for recovery; thus in four hours he could make only three such runs at most, covering a total distance of 1,200 meters. If instead the runner cut the runs to shorter ones, sprinting only 100 meters each time (at the same speed) and resting for 30 seconds, he would not accumulate any lactic acid and in four hours could make 360 runs, covering a total distance of 36,000 meters. In other words, by limiting the individual runs to 100 meters with the short resting intervals he could accomplish 30 times more work than with 400-meter runs. Thus a program of intermittent 100-meter sprints could be more effective as training for a 400-meter runner than 400-meter sprints.

The same principle very probably applies to any kind of muscular work that can be taxing for the worker. By proper pacing of the work and the intervals of rest a person can produce more work than by driving himself relentlessly.



ALACTIC OXYGEN DEBT is created by muscles drawing energy from phosphagen-splitting (*hatched area A*) while the oxidation mechanism is being activated. In moderate exercise that does not lead to the formation of lactic acid, oxygen consumption quickly rises to its upper limit of about 40 milliliters (equivalent to 200 calories) per minute per kilogram of body weight and provides all of the energy required by the muscles. At the end of the exercise additional oxygen is consumed (*colored area B*) to repay the alactic oxygen debt (*A*). The repayment energy is used to resynthesize the phosphagens that were split.



ALACTIC AND LACTACID DEBTS are incurred when the exercise calls for superexertion to exhaustion. The alactic oxygen debt (*hatched areas A and A'*) is formed by the muscles obtaining energy from phosphagen-splitting while energy from oxygen consumption (*colored area B*) is rising to its upper limit (*arrow*). The lactacid oxygen debt (*gray area C and C'*) is the result of energy obtained from the formation of lactic acid. During recovery from superexertion oxygen consumption remains at a high level for 15 to 20 seconds and then begins to drop. Energy from the delayed oxygen consumption (*colored area B*) pays the greater part (*area A*) of the alactic oxygen debt. Continued production of lactic acid (*C'*) after the exercise is over provides energy to pay the fraction *A'* of the alactic debt.

