

Symposium: Nutrition and Exercise

Carbohydrate Supplementation during Exercise¹

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ABSTRACT Muscle glycogen and plasma glucose are oxidized by skeletal muscle to supply the carbohydrate energy needed to exercise strenuously for several hours (i.e., 70% maximal O₂ consumption). With increasing exercise duration there is a progressive shift from muscle glycogen to blood glucose. Blood glucose concentration declines to hypoglycemic levels (i.e., 2.5 mmol/L) in well-trained cyclists after ~3 h of exercise and this appears to cause muscle fatigue by reducing the contribution of blood glucose to oxidative metabolism. Carbohydrate feeding throughout exercise delays fatigue by 30–60 min, apparently by maintaining blood glucose concentration and the rate of carbohydrate oxidation necessary to exercise strenuously. Carbohydrate feedings do not spare muscle glycogen utilization. Very little muscle glycogen is used for energy during the 3–4-h period of prolonged exercise when fed carbohydrate, suggesting that blood glucose is the predominant carbohydrate source. At this time, exogenous glucose disposal exceeds 1 g/min (i.e., 16 mg · kg⁻¹ · min⁻¹) as evidenced by the observation that intravenous glucose infusion at this rate is required to maintain blood glucose at 5 mmol/L. However, at this time these cyclist cannot exercise more intensely than 74% of maximal O₂ consumption, suggesting a limit to the rate at which blood glucose can be used for energy. It is important to realize that carbohydrate supplementation during exercise delays fatigue by 30–60 min, but does not prevent fatigue. In conclusion, fatigue during prolonged strenuous exercise is often due to inadequate carbohydrate oxidation. This is partly a result of hypoglycemia, which limits carbohydrate oxidation and causes muscle fatigue. Carbohydrate feedings during strenuous exercise maintain blood glucose oxidation and delay fatigue by 30–60 min, but do not prevent fatigue, which eventually results from other yet unknown factors. *J. Nutr.* 122: 788–795, 1992.

INDEXING KEY WORDS:

- exercise • carbohydrate • fatigue • glycogen
- hypoglycemia

Early in this century it was established that both fat and carbohydrate are oxidized for energy during exercise (1). Further work demonstrated that the relative contribution of carbohydrate and fat to energy depends

upon the intensity and duration of exercise as well as upon the preexercise diet and the state of physical training (2–4).

Early studies relied upon the measurement of blood glucose concentration and/or the respiratory exchange ratio (R) to assess carbohydrate metabolism during exercise and its relation to fatigue. Carbohydrate metabolism during exercise was typically manipulated by altering diet either before or during exercise. Dill et al. (5), for example, examined the effects of carbohydrate ingestion on running performance in a dog trained to run at a set intensity on a laboratory treadmill. After an overnight fast, the dog was able to run for 3–6 h before fatiguing, which coincided with a marked decrease in blood glucose concentration. When fed carbohydrate before and during exercise, however, the dog was able to run for ≥ 13 h before fatiguing. In another experiment performed after an overnight fast, the dog ran for > 4 h before fatiguing at a time when blood glucose concentration was 2.6 mmol/L. At this point, the dog was given 40 g of sugar to eat. Subsequently, blood glucose increased to > 6 mmol/L and the dog was able to exercise for another 1.5 h. These observations led Dill et al. (5) to conclude that the limiting factor in the performance of prolonged exercise "seems to be merely the quantity of easily available fuel" in the form of blood-borne glucose. They implied that carbohydrate ingestion during exercise delayed fatigue by maintaining the supply of carbohydrate for oxidation by muscle.

In contrast to these observations in the dog, early studies of humans focused upon the effects of altering blood glucose concentration upon the central nervous

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system. In 1924, Levine et al. (6) observed that some runners who were hypoglycemic at the end of the Boston Marathon "showed muscular twitching, extreme pallor, cold moist skin, nervous irritability and even collapse and unconsciousness." These symptoms were prevented and running performance was reported to improve when these same men consumed additional carbohydrate on the days before as well as during the race of the following year (7). Carbohydrate ingestion during exercise was therefore thought to improve performance primarily by preventing such symptoms of neuroglucopenia.

This concept was reinforced by the classic studies of Christensen and Hansen (8-10). In a series of experiments on three subjects, they observed that consuming a high fat diet markedly impaired performance during exercise at 60% maximal oxygen uptake ($\dot{V}O_{2\max}$). They also observed that fatigue during exercise after the high fat diet was associated with a low R during exercise and hypoglycemia severe enough to result in symptoms of neuroglucopenia (8-10). In an attempt to differentiate the possible causes of fatigue, two of these men were fed 200 g of glucose "at almost complete exhaustion." This resulted in a rapid increase in blood glucose concentration and relief of the neuroglucopenic symptoms. Fatigue was reversed and the men exercised for an additional 60 min. However, R, which was lower than normal during exercise because of the preceding high fat diet, did not change significantly either before or after glucose ingestion. Christensen and Hansen (8-10) implied that the development and reversal of fatigue under these conditions of exercise after a high fat diet was not due to changes in the rate of carbohydrate oxidation, although they felt these results did not completely rule out this possibility. These observations have been the basis for the idea that carbohydrate ingestion during exercise primarily delays fatigue by preventing symptoms of neuroglucopenia. As discussed below, based upon recent findings, we think that symptoms of neuroglucopenia do not usually cause fatigue. Instead, it appears that hypoglycemia usually causes muscular fatigue, probably because it deprives the exercising muscles of carbohydrate energy.

CARBOHYDRATE ENERGY AND STRENUOUS EXERCISE: IMPORTANCE OF MUSCLE GLYCOGEN

It had become clear from these early observations that strenuous exercise at intensities requiring $> 60\% \dot{V}O_{2\max}$ was impaired when dietary carbohydrate was lacking and that this was usually associated with an inadequate rate of carbohydrate oxidation. The introduction of the muscle biopsy technique in the 1960s demonstrated that muscle glycogen levels become depleted after intense

exercise performed to fatigue (11). Furthermore, the duration that strenuous exercise could be maintained was altered by raising and lowering preexercise muscle glycogen levels through manipulation of diet and exercise (12). This has led to the concept that muscle glycogen is the primary carbohydrate source during exercise. Although this is not incorrect, this oversimplified concept indirectly minimizes the potential of blood glucose to serve as a fuel for carbohydrate oxidation during exercise at 60-80% $\dot{V}O_{2\max}$. This concept that muscle glycogen is the primary source of carbohydrate energy did not appear to conflict with the conclusions of Christensen and Hansen (8-10) that low blood glucose causes fatigue due to neuroglucopenia and that the elevation of blood glucose by carbohydrate feedings reverses fatigue by eliminating neuroglucopenia. Therefore, during the period of the 1960s and 1970s, there was little support for the idea that blood glucose serves as a primary source of carbohydrate energy or that fatigue during exercise is related to the availability of blood glucose as a fuel.

CARBOHYDRATE ENERGY AND STRENUOUS EXERCISE: CONTRIBUTION OF BLOOD GLUCOSE

Data from studies conducted during the 1970s, which directly measured muscle glucose uptake, indicated that blood glucose could make substantial contributions to energy metabolism. Wahren et al. (13) observed that leg glucose uptake increases during exercise of increasing duration and intensity. Ahlborg et al. (14) also reported that the progressive increase in leg glucose uptake with increasing exercise duration was halted due to a decline in blood glucose concentration secondary to reduced liver glucose output. This was assumed to result from a depletion of liver glycogen stores. Ahlborg and Felig (15) subsequently demonstrated that, when blood glucose concentration was maintained throughout exercise by glucose ingestion, leg glucose uptake was maintained at high levels. Additionally, Gollnick et al. (16) observed that the continued increase in leg glucose uptake was related to the number of muscle fibers low in muscle glycogen. These findings suggest that there appears to be a shift in the source of carbohydrate energy from muscle glycogen to blood glucose with exercise of increasing duration and that blood glucose has the potential to contribute significantly to energy metabolism, provided that glucose concentration in the blood is maintained. These studies of leg glucose uptake did not employ exercise of sufficient intensity or duration to cause fatigue, and therefore the association between blood glucose concentration, oxidation and endurance was not established.

CARBOHYDRATE FEEDINGS AND ENDURANCE PERFORMANCE: RECENT PERSPECTIVES

As discussed below, it has become increasingly apparent during the past decade that carbohydrate feeding during exercise has the potential to delay fatigue. It is our interpretation that carbohydrate feedings maintain blood glucose concentration and oxidation and thus become the major source of carbohydrate energy during the latter stages of prolonged exercise when muscle glycogen concentration is low. Therefore, a purpose of this paper is to identify the exercise conditions that result in fatigue due to an inadequate availability of blood glucose as a fuel. An additional purpose is to discuss the possible mechanisms by which carbohydrate feedings delay fatigue.

EVIDENCE THAT CARBOHYDRATE FEEDINGS DELAY FATIGUE

During the 1970s, it was also generally believed that glucose ingestion in humans contributes little to the total energy utilized during prolonged exercise (17). Although it was recognized that muscle glucose uptake can increase to high levels, especially when ingesting carbohydrate (15), in 1982 Felig et al. (18) concluded that glucose feedings do not delay fatigue during bicycle ergometer exercise at 60–65% of $\dot{V}O_{2\max}$. However, the subjects in this study were not experienced cyclists and there was a large amount of variability in response due to motivation and learning. This was apparent in that 13 and 19 subjects increased their endurance on the second trial when provided with a monetary incentive. However, in each of the comparisons, the exercise times were longer with glucose feedings; the average increases in exercise time ranged from 7 to 13 min. Because of the tremendous variability in response, it is not surprising that these differences were not statistically significant.

An indication that carbohydrate ingestion may improve endurance performance in people was provided by Ivy et al. (19). Carbohydrate ingestion did not increase 2-h total work output compared with control, and thus actual performance was not significantly improved. However, during the last 30 min of exercise, the subjects were able to maintain or even increase their initial work rate when fed carbohydrate, yet they began to fatigue during this period while consuming only water. These observations suggested that carbohydrate feedings begin to exert a beneficial influence upon endurance after about 2 h of exercise and prompted Coyle et al. (20) to study subjects for longer periods.

Coyle et al. (20) asked experienced cyclists to exercise at 74% of $\dot{V}O_{2\max}$ for as long as possible on two occasions. When they were no longer able to maintain

this work rate, they were permitted to reduce the work rate to the highest intensity they could maintain for at least another 10-min period. Fatigue was defined as the time when work rate declined by 10% of $\dot{V}O_{2\max}$ below the initial intensity. All trials were performed after an overnight fast. During one trial they drank a placebo solution (flavored and colored water) whereas during the carbohydrate trial they ingested ~70 g of maltodextrin in a 500 g/L solution after 20 min of exercise and an additional 18 g of maltodextrin in a 60 g/L solution after 60, 90 and 120 min. In the entire group of 10 subjects, fatigue was significantly delayed by 23 min (i.e., 134 ± 6 to 157 ± 5 min; $P < 0.01$) when fed carbohydrate. Additionally, 6.6% more work was completed after 150 min of exercise. However, fatigue was delayed (i.e., 33 min; from 126 ± 3 to 159 ± 6 min) only in the seven subjects who experienced a decline in blood glucose to levels < 3 mmol/L during the placebo trial (Fig. 1). Fatigue during the placebo trial was associated with central nervous system symptoms of hypoglycemia in only two of these subject whereas the remainder complained primarily of severe weariness in the exercising muscles as the cause of fatigue. Fatigue was not delayed in the three subjects whose blood glucose concentration did not decline during the placebo trial, as shown in Figure 1. This study demonstrated that carbohydrate feedings delay fatigue and improve endurance in people by preventing blood glucose from declining to levels that, in most of the subjects, causes local muscle fatigue during the latter stages of prolonged exercise.

CARBOHYDRATE FEEDINGS DO NOT AFFECT MUSCLE GLYCOGEN USE DURING CONTINUOUS STRENUOUS EXERCISE

In a subsequent study we measured the pattern of decline in muscle glycogen concentration in the vastus lateralis during exercise to fatigue at 74% $\dot{V}O_{2\max}$ on two occasions, with and without carbohydrate feedings (21). Fatigue occurred after 3.0 ± 0.2 h when fed a placebo, whereas fatigue was delayed until 4.0 ± 0.3 h when fed carbohydrate (i.e., ~70 g of maltodextrin in a 500 g/L solution at 20 min followed by 28 g of maltodextrin in a 100 g/L solution every 20 min thereafter). As shown in Figure 2C, the pattern of decline in muscle glycogen concentration was similar during the first three hours of exercise with and without carbohydrate feeding. Remarkably, the additional hour of exercise made possible by carbohydrate feedings occurred without a further decline in muscle glycogen concentration.

The following interpretation of these observations forms the basis for our model regarding the mechanism by which carbohydrate feedings improve performance during prolonged intense exercise. During the first 2

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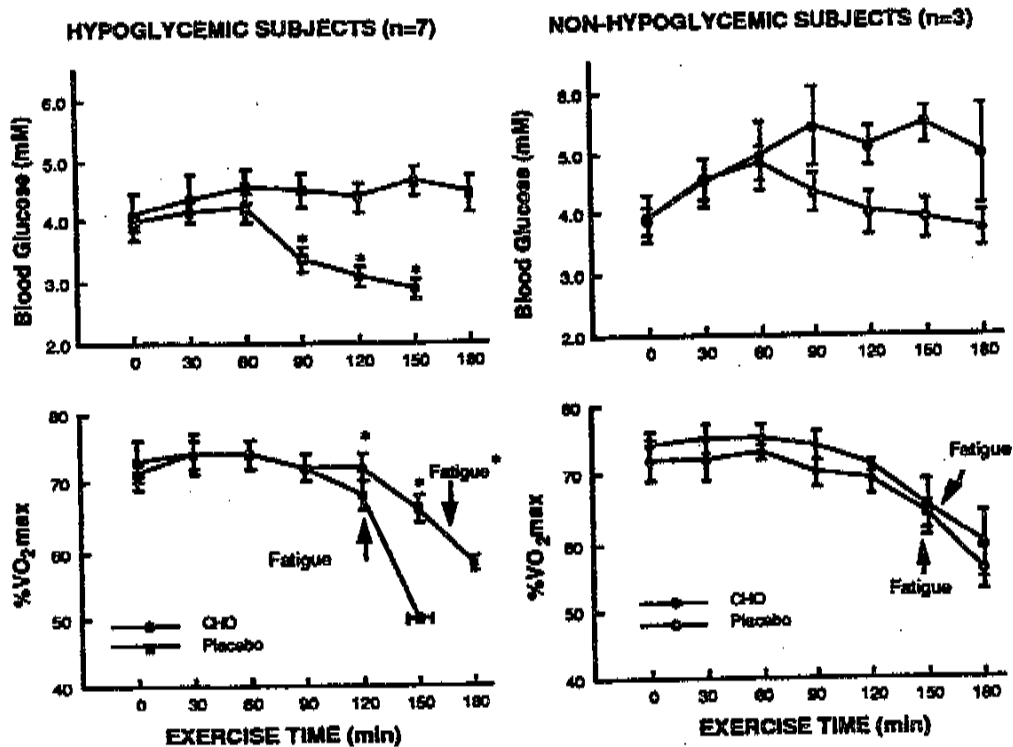


FIGURE 1. Work rate responses during exercise to fatigue in subjects who become hypoglycemic compared with those who do not become hypoglycemic. *denotes significant difference from the other trial at that time; $P < 0.05$.

h of exercise, the rate of carbohydrate oxidation was similar during both trials (Fig. 2B). However, carbohydrate oxidation began declining during the third hour of the placebo trial, a time when muscle glycogen was low and plasma glucose concentration declined significantly to 2.5 mmol/L at the point of fatigue. We interpret these observations to indicate that the lowering of blood glucose during the latter stages of prolonged strenuous exercise (Fig. 2A) plays a major role in the development of muscular fatigue by not allowing leg glucose uptake to increase sufficiently to offset reduced muscle glycogen availability. Fatigue under these conditions is clearly preceded by a decline in carbohydrate oxidation, which is preceded by a decline in plasma glucose to ~2.5–3.0 mmol/L.

When plasma glucose was maintained at 4–5 mmol/L, through carbohydrate ingestion, the high rate of carbohydrate oxidation required by exercise at 70% $VO_{2\max}$ was held constant and the subjects were able to exercise strenuously for 1 h longer (i.e., from 3–4 h) than when fasted (Fig. 2A, B). As mentioned, muscle glycogen concentration was already low after 3 h and it contributed little to the maintenance of carbohydrate oxidation and exercise tolerance. Instead, it appears that other carbohydrate sources, presumably blood glucose, can largely replace muscle glycogen in providing carbohydrate for oxidation during the latter stages of prolonged strenuous exercise.

These concepts are summarized in Figure 3 which depicts the percentage of energy derived from the oxidation of fat and carbohydrates, calculated from R. The energy derived from muscle glycogen was also calculated with the assumption that 10 kg of muscle were active and using glycogen at an average rate reflected by the decline in glycogen within the vastus lateralis. The difference between the rate of total carbohydrate oxidation and muscle glycogen utilization presumably reflects the oxidation of blood glucose.

During the first 2 h of exercise, the energy sources are similar with and without carbohydrate feedings, although it should be realized that the ingested glucose probably replaces liver glycogen as the source of blood glucose oxidation. Carbohydrate availability appears to become limiting during the third hour of the placebo trial because of a decline in blood glucose concentration at a time when muscle glycogen is low. This prevents blood glucose oxidation from increasing sufficiently to offset the reduced contribution of muscle glycogen. As a result, muscle fatigue occurs after 3 h. Carbohydrate feedings that maintain blood glucose at 4–5 mmol/L during the latter stages of strenuous exercise appear to allow for a progressive increase in blood glucose oxidation to the point where it appears to supply all of the carbohydrate energy.

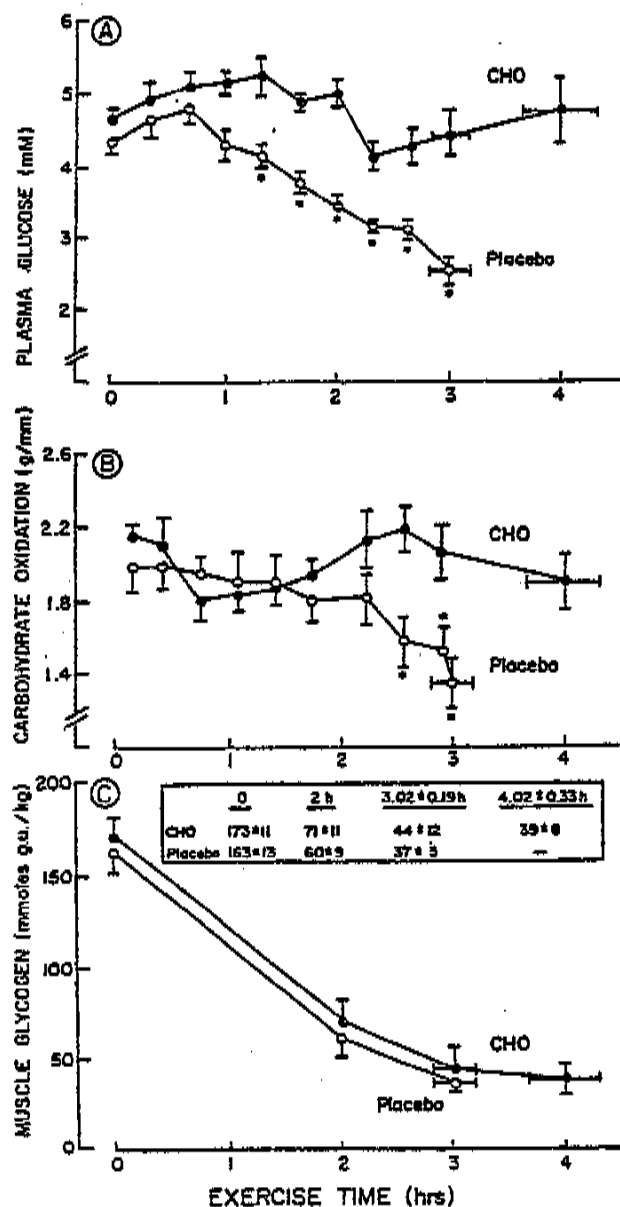


FIGURE 2 Responses when cycling at 74% $\dot{V}O_{2\max}$ with a placebo or when ingesting carbohydrate every 20 min (CHO). *Placebo different from carbohydrate, $P < 0.05$. (from ref. 21 with permission).

WHAT CAUSES FATIGUE DURING EXERCISE WITH CARBOHYDRATE FEEDINGS?

An interesting question regards the cause of fatigue during exercise with the carbohydrate feedings. There was no indication that the rate of carbohydrate oxidation was declining before fatigue when receiving carbohydrate supplementation, although it was low (Fig. 2B). Therefore, it might be expected that the subjects should be able to continue for even longer than

4 h (Fig. 2, 3). These observations could also be interpreted to suggest that fatigue under these conditions is caused by factors other than carbohydrate depletion per se. If carbohydrate availability is not as limited, other subsequent causes of fatigue may emerge. Many possibilities exist, including muscular metabolic disturbances as well as neurological alterations. Figure 3 also raises the possibility that fatigue during exercise with carbohydrate feeding occurs at the general time that the contribution of muscle glycogen to energy production becomes zero, although its relative contribution is small during the hour before fatigue. The point is that this experimental model may be helpful in designing future studies of the causes of fatigue during prolonged intense exercise.

CARBOHYDRATE SUPPLEMENTATION AT FATIGUE

To more directly test the hypothesis that carbohydrate feedings improve exercise performance by preventing the decline in blood glucose concentration and oxidation late in exercise, we reasoned that it should be possible to reverse the decline in carbohydrate oxidation, as well as fatigue during exercise when fasted, by restoring euglycemia (22). Therefore, the study described in Figure 4 was performed. On three separate occasions subjects first exercised at 70% $\dot{V}O_{2\max}$ to the point of fatigue when fasted (exercise bout 1, Fig. 4), displaying a decline in plasma glucose concentration (i.e., to 3.1 mmol/L) and R (i.e., to 0.81) before fatigue. After a 20-min rest, the subjects were encouraged to perform further exercise (i.e., exercise bout 2, Fig. 4) with three different treatments. In one trial, they re-

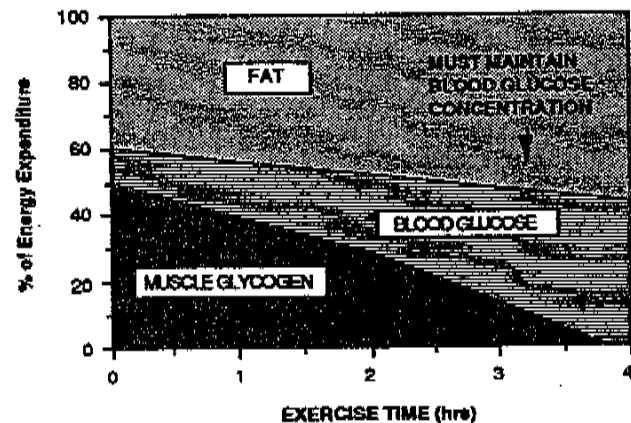


FIGURE 3 Various sources of energy during prolonged exercise at 70% $\dot{V}O_{2\max}$. Note that blood glucose becomes the predominant source of carbohydrate energy during the latter stages of exercise and thus it is important to maintain blood glucose concentration by eating carbohydrate.

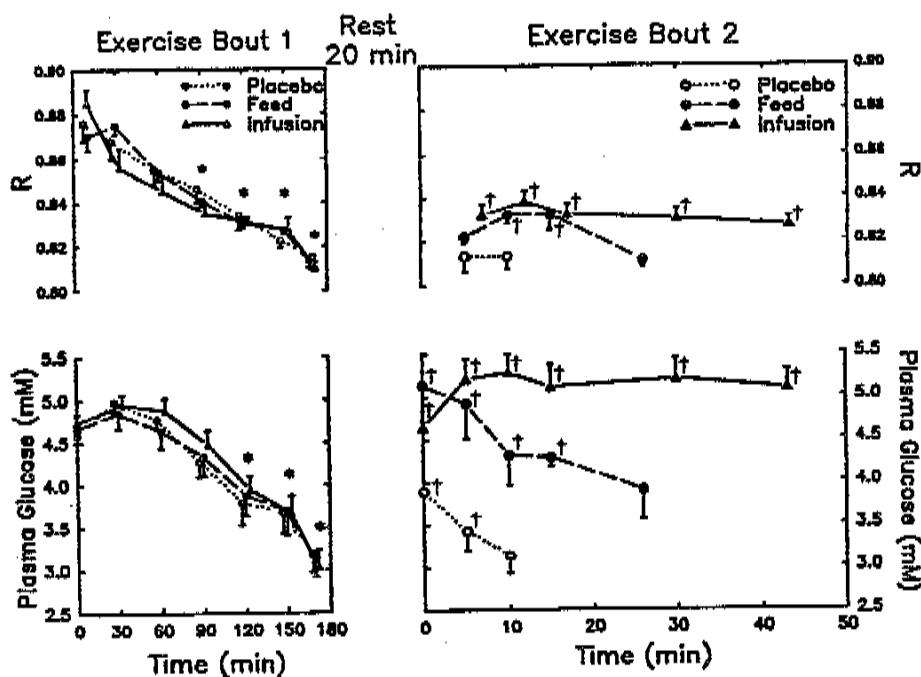


FIGURE 4. During Exercise Bout 1, the subjects cycled at 74% $\dot{V}O_{2\max}$ until fatigued. After a 20-min rest, they continued to exercise (bout 2) with three different treatments: placebo, after drinking flavored water and being infused with saline; infusion, receiving intravenous glucose infusion at a rate that maintained plasma glucose at 5 mmol/L; and feeding, ingestion of 200 g of a 500 g/L maltodextrin solution. †denotes a significant decline during Exercise Bout 1, $P < 0.05$; *denotes values during Exercise Bout 2 that were significantly higher than at the end of Exercise Bout 1, $P < 0.05$ (from ref. 22 with permission).

ceived a placebo solution to drink during the rest. When they attempted further exercise, plasma glucose concentration and R were not maintained above the levels observed at fatigue of exercise bout 1, and thus the subjects tolerated only an additional 10 ± 1 min of exercise. During another trial, glucose was infused (via a pump) intravenously at the beginning of exercise bout 2 at the rate required to maintain plasma glucose concentration at 5 mmol/L. The maintenance of euglycemia under these conditions raised and maintained R above the levels observed at fatigue during exercise bout 1 (i.e., 0.83 vs 0.81), although R was still lower than observed at the beginning of exercise bout 1, when muscle glycogen was high. The maintenance of euglycemia allowed the subjects to complete an additional 43 ± 5 min of exercise (Fig. 4). It was also observed that muscle glycogen use was minimal during this additional exercise, suggesting that blood glucose was the primary energy source for carbohydrate oxidation, which was occurring at 1.6 g/min.

An important finding of this study was that a glucose infusion rate of over 1.1 g/min was required to maintain euglycemia, suggesting that this exogenous glucose was being oxidized at a high rate under these conditions (i.e., low muscle glycogen, hypoinsulinemic). Because muscle glycogen contributed little to energy, it is likely that endogenous glucose production supplemented the exogenous glucose infusion in pro-

viding the carbohydrate needs of exercise at this intensity.

During a third trial, 200 g of a 500 g/L maltodextrin solution was ingested during the rest period. As a result, during exercise bout 2, plasma glucose concentration and R were initially increased above levels at fatigue of exercise bout 1, but they could not be maintained, declining progressively to the point of fatigue, which occurred after 26 ± 4 min. This suggests that the ingested carbohydrate was not able to empty from the stomach and to be absorbed by the intestines into the blood rapidly enough to match the rate at which glucose was being removed from the circulation. Therefore, it generally appears that people should not wait until they are fatigued before consuming carbohydrate. However, individual subjects differed widely in the extent to which the ingested glucose was able to maintain blood glucose concentration and extend performance.

FEED BEFORE FATIGUE

We thought it practically important to also determine how long before the point of fatigue a cyclist should begin ingesting carbohydrate to restore and maintain blood glucose throughout exercise while im-

proving performance ability (23). Cyclists ingested ~200 g of carbohydrate (i.e., 3 g/kg body weight in a 500 g/L solution of maltodextrin) after 135 min of exercise, which was on the average ~35 min before the point of fatigue when ingesting a placebo solution. Figure 5 compares these responses to exercise with a placebo. Fatigue occurred after 170 ± 10 min during placebo and a delay by 35 min occurred (205 ± 14 min; $P < 0.05$) when carbohydrate was ingested ($P < 0.05$). As shown in Figure 5, carbohydrate feeding after 135 min reversed the decline in plasma glucose and successfully restored and maintained euglycemia throughout the remainder of exercise. The decline in R was also halted. These findings indicate that fatigue can be effectively delayed by 35 min in cyclists when carbohydrate feeding is not begun until 35 min before the time that fatigue would occur without feeding. This delay of fatigue when fed before fatigue was of similar magnitude to the 43 min of further exercise that was permitted by intravenous glucose infusion.

TIMING OF CARBOHYDRATE FEEDING DURING EXERCISE

We have shown that fatigue can be delayed 30–60 min both when feedings are taken throughout exercise (20, 21) and when they are initiated 35 min before the point of fatigue when fasted (23). Therefore we have no reason to recommend that one feeding schedule is superior. The important aspect is that the ingested carbohydrate be capable of supplementing blood glucose stores at a rate of > 1 g/min late in exercise (22).

MUSCLE GLYCOGEN RESYNTHESIS DURING EXERCISE

These recommendations pertain to continuous exercise at ~70% $\dot{V}O_{2\max}$. The net decline in muscle glycogen concentration during exercise when ingesting carbohydrate will be determined by the balance between glycogenolysis and glycogen resynthesis. It does not appear that carbohydrate feedings alter the net rate of decline in muscle glycogen concentration during prolonged exercise maintained at a constant high intensity (21). However, it has been demonstrated in rats and in man that carbohydrate feedings given during low intensity exercise, which followed prolonged high intensity exercise, can promote glycogen resynthesis within nonactive muscle fibers with low glycogen concentration (24, 25). Therefore, it is possible that carbohydrate feedings given during prolonged exercise that varies from high to low intensity or that includes rest periods may result in less of a net reduction in muscle glycogen concentration (26). Presumably this is due to glycogen resynthesis in fibers that are non-

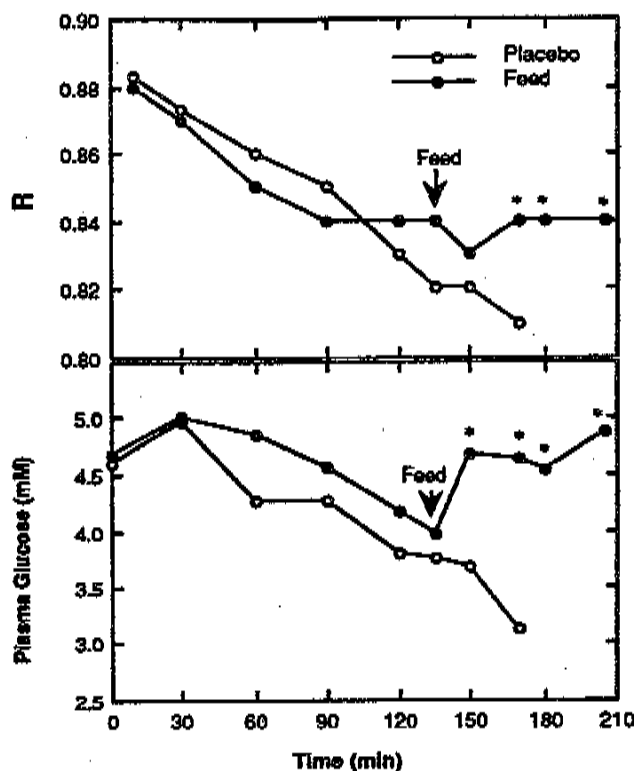


FIGURE 5. Respiratory exchange ratio (R) and plasma glucose responses to exercise when ingesting a placebo compared with when ingesting a 200 g of maltodextrin (Feed) 35 min before the estimated point of fatigue. *Feed significantly higher than Placebo ($P < 0.05$). (from ref. 23 with permission).

active during the low intensity bouts of exercise. Therefore, when there is potential for glycogen resynthesis during exercise, it would seem that carbohydrate feeding throughout exercise is potentially more beneficial than withholding carbohydrate feeding until late in exercise.

EXERCISE INTENSITY LIMITATIONS

Because it is our concept that blood glucose is the major carbohydrate source during the latter stages of prolonged exercise when fed carbohydrate, thus requiring a high rate of blood glucose uptake by muscle, we wondered if there was a limit to the exercise intensity that could be maintained. Therefore, as shown in Figure 6, we determined the highest steady-state intensity that could be maintained by well-trained cyclists after 2–3 h of exercise (27). Exercise consisted of alternating 15 min bouts of moderate intensity (i.e., 60% $\dot{V}O_{2\max}$) and high intensity (i.e., initially 80–85% $\dot{V}O_{2\max}$) cycling performed to exhaustion. As shown in Figure 6, the work tolerance of the subjects was

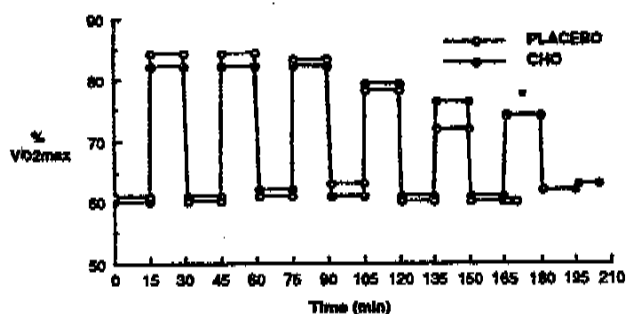


FIGURE 6. Exercise intensity (% $\dot{V}O_{2max}$) maintained during exercise with PLACEBO and when fed carbohydrate (CHO). Values are mean \pm SE for seven subjects. *Denotes carbohydrate feeding significantly different from placebo.

identical during the first 2 h of exercise. Interestingly, during the 105–120-min period, the subjects had to lower their exercise intensity below 80% $\dot{V}O_{2max}$ during both the placebo and carbohydrate feeding trial. However, during the placebo trial the subjects' work rate progressively declined to 60% $\dot{V}O_{2max}$ and they fatigued after 174 min. When fed carbohydrate, their fatigue was significantly delayed to 205 min ($P < 0.05$). Additionally, when fed, the subjects were able to tolerate exercise at 74–76% $\dot{V}O_{2max}$ during the high intensity periods. It is interesting to speculate that the inability of the cyclists to exercise more intensely than $\sim 75\%$ $\dot{V}O_{2max}$ is due to a limitation in their ability to transport blood glucose into the exercising muscle fibers for oxidation.

Fatigue during prolonged strenuous exercise is often due to inadequate carbohydrate oxidation. This is sometimes a result of hypoglycemia, which limits carbohydrate oxidation and causes muscle fatigue. Carbohydrate feedings during strenuous exercise maintain blood glucose oxidation and delay fatigue by 30–60 min, but do not prevent fatigue, which eventually results from other yet unknown factors. During the latter stages of prolonged cycling, when muscle glycogen is low, it appears that blood glucose can supply carbohydrate energy at rates necessary to exercise at $\sim 75\%$ $\dot{V}O_{2max}$ in well-trained cyclists.

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