# Glucose Turnover During Recovery from Intensive Exercise

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**SUMMARY**

**This study was undertaken to examine glucose turnover during a 30-min recovery period following an acute bout of intensive exercise (85% $\dot{V}O_2$ max) performed to exhaustion (11.7 ± 1.4 min). Plasma glucose (basal 85 ± 2 mg/dl) rose by 10 mg/dl at exhaustion and increased further during the initial phase of recovery, reaching a peak value of 35 mg/dl above basal at 5 min of recovery. Thereafter, there was a gradual decline, but the values remained 15–20 mg/dl above basal at 30 min. The early rise in plasma glucose during recovery was due to an imbalance between glucose production and utilization caused by a more rapid decline in utilization than production. At 5 min of recovery, glucose production was fivefold greater than in the basal state and comparable to peak values observed at exhaustion, while glucose utilization was 33% lower than observed at exhaustion and only 75% higher than in the basal state. Beyond 5 min of recovery glucose utilization and production again differed in the direction of response. Glucose production fell to basal values while glucose utilization remained 70–80% above baseline. The maintenance of basal rates of glucose production and increased rates of glucose utilization occurred in a setting in which plasma insulin levels were increased by 25–50%. Plasma catecholamines, which rose 5–10-fold during exercise, fell rapidly during the initial 3 min of recovery.**

**We conclude that recovery from exhaustive exercise is characterized by a biphasic imbalance between glucose production and utilization in which production exceeds utilization for the initial 5 min and utilization exceeds production at 10–30 min. The hormone-substrate milieu (modest increments in plasma insulin and glucose) accompanying the changes in glucose kinetics observed beyond 5 min suggests that the recovery period from acute exercise may be characterized by an increase in peripheral sensitivity to insulin, which could provide a mechanism for facilitating muscle glycogen repletion during recovery from intensive exercise. DIABETES 32:734–738, August 1983.**

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The plasma glucose response to exercise is determined by the intensity and duration of the exercise performed. With moderate to high intensity exercise (65% of $\dot{V}O_2$ max) lasting up to 60 min, unchanged plasma glucose levels or small increments (5–10 mg/dl) are observed.[1,2] With lower-intensity prolonged exercise (90 min) a decline in glucose concentration even to frank levels of hypoglycemia has been documented.[3,4] Exercise-associated increments in plasma glucose in excess of 15–20 mg/dl in normal subjects have previously been reported only with intensive, intermittent exercise.[5,6] The latter observations suggest that the hyperglycemic effects of such exercise may largely depend on alterations in glucose kinetics that occur during recovery.

To meet the increased needs of muscle for glucose during exercise, hepatic glucose production rises and values as high as two- to fourfold the basal rate have been reported with intensive exercise.[1,2,7,8] This change in endogenous glucose supply is mediated by increases in counterregulatory hormones[9–13] and a decrease in plasma insulin.[1,2,14] Muscle consumption of blood-borne glucose can rise as high as 20–40-fold above baseline during intensive exercise[1,2] and generally parallels the rise in hepatic glucose production.[1,2]

The metabolic adaptations in the recovery period following exercise have received less attention. A rapid decrease in glucose output by the liver and an increase in glucose uptake by previously exercising muscle have been observed after exercise of mild to moderate intensity.[4,15] Data, however, are not available on the changes in glucose kinetics during recovery from intensive exercise of the type associated with a rise in plasma glucose concentration. Such data are of particular interest since previous reports have emphasized the role of in situ conversion of lactate to glucose in muscle



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tissue rather than increased glucose uptake as the prime mechanism for glycogen repletion during recovery from intensive exercise.[16,17] Furthermore, studies examining arteriovenous differences for glucose during recovery after intensive exercise have been interpreted as showing "almost no uptake of glucose by muscle."[16] In addition, an increase in muscle sensitivity to insulin has been observed during recovery after prolonged low-intensity exercise.[4,18] Such changes in insulin sensitivity have been attributed to the depletion of muscle glycogen that occurs with prolonged exercise.[18] Whether a short burst of maximal exercise in which substantially less glycogen depletion occurs (as compared with prolonged exercise) also alters muscle sensitivity to insulin has not been determined.

The present study was consequently undertaken to evaluate the changes in glucose turnover and hormone secretion that occur in the first 30 min of recovery from an acute bout of intensive exercise (>85% $\dot{V}O_2$ max).

## MATERIALS AND METHODS

Eleven normal, well-trained subjects were studied 15 times (4 subjects were studied twice). Eight were male and 3 female; mean age was 31 yr (range 18–55). All subjects gave written informed consent before their participation.

The maximal aerobic power ($\dot{V}O_2$ max) of each volunteer was determined on a cycle ergometer as described previously.[19] On the day of the study, after an overnight fast of 12 h, an antecubital vein was cannulated and a slow drip of saline solution (0.9%) was infused to maintain patency of the catheter. No heparin was used. In the studies using [3-$^3$H]glucose a second i.v. line was placed for the infusion of the tracer.

After two baseline blood samples were obtained at 10-min intervals, the subjects exercised at a load corresponding to 85% of the $\dot{V}O_2$ max. The exercise was maintained until exhaustion. Exhaustion was defined as the inability of the subject to maintain a speed of 50 rpm on the cycle ergometer. At that moment, the exercise was completely stopped and the subjects remained seated or recumbent on a bed for 45 min. In six studies [3-$^3$H]glucose was administered as a prime-continuous infusion (loading dose 30 μCi; continuous infusion 0.25 μCi/min). The infusion was initiated 2 h before the exercise (equilibration period) and continued for the remainder of the study. Blood samples were taken at intervals of 1–3 min during the exercise and at 1, 3, 5, 10, 20, and 30 min during the recovery period.

Plasma glucose was determined with a Beckman Glucose Analyzer I (Beckman Instruments, Fullerton, California) in duplicate. Plasma insulin was measured with a radioimmunoassay as previously described.[20] The glucagon assay was performed with antibody K-30 (from R. Unger, Dallas, Texas).[21] Plasma catecholamines were determined with a radioenzymatic method.[22] Lactate was measured with an enzymatic technique.[23] Methods for the determination of glucose specific activity in plasma have been described previously.[24]

In the resting state glucose appearance (Ra) and disappearance (Rd) rates were computed using the isotope dilution method. During non-steady-state conditions (exercise and recovery), glucose kinetics were calculated using the equations of Steele[25] as modified by DeBodo et al.[26] In applying these equations we used a polynomial fitting procedure[27] and a two-compartment analysis in an Olivetti P6060 computer, as described by Radziuk et al.[28] In this model, time-dependent glucose loss is assumed to occur from both compartments at an equal rate. It is further assumed that the volumes of the two compartments as well as the transfer rate between the two are constant over time. The values for the initial distribution volume (65 ml/kg), the total distribution volume (200 ml/kg), and the total exit rate of glucose from the initial mixing compartment (0.445 mg/min) were taken from published data.[29] This approach has been shown to be superior to the classic monocompartmental method in predicting rapid changes in the rate of glucose appearance,[30] which would be expected to occur during both the exercise and recovery periods. Furthermore, the method of calculation that we employed has been shown to be relatively insensitive to changes in model parameters and minimizes the degree of smoothing in the fitting procedure.[27]

## RESULTS

The mean $\dot{V}O_2$ max of the subjects was 54.7 ± 4.2 ml/kg/min (range 40–80). During the exercise, the mean work load employed was 199 ± 9 W, which corresponded to 85 ± 2% of the $\dot{V}O_2$ max. The mean duration of the exercise was 11.7 ± 1.4 min (range 6–22 min).

The basal glucose concentration was 85 ± 2 mg/dl and was maintained at the same level during the first 5 min of the exercise (Figure 1). Subsequently, there was a trend toward an increase that reached statistical significance only at the point of exhaustion ($P < 0.05$). During the recovery phase there was a further rise in plasma glucose concentration, reaching a peak concentration of 120 ± 5 mg/dl at 5 min of recovery ($P < 0.001$ versus basal and $P < 0.001$ versus exhaustion value). Beyond 5 min there was a gradual decline in plasma glucose concentration, but the values remained 15–20 mg/dl above basal even after 30 min of recovery ($P < 0.001$). This pattern, with individual variations in the absolute glucose concentrations, was observed in all subjects studied. The rise in plasma glucose concentration did not correlate with the workload ($r = 0.03$, P = NS), the $\dot{V}O_2$ max ($r = 0.03$, P = NS), or the duration of the exercise ($r = 0.23$, P = NS).

Blood lactate (0.83 ± 0.08 mM in the basal state) rose ninefold, to peak values of 7.42 ± 0.32 mM at exhaustion. By 30 min of recovery blood lactate fell to 3.88 ± 0.36 mM.

The basal plasma insulin concentration was 16 ± 3 μU/ml. As expected, there was a decrease in mean plasma insulin levels during the exercise, but the decline (to 14 ± 2 μU/ml at exhaustion) failed to reach statistical significance ($0.05 < P < 0.1$) (Figure 1). During the recovery phase there was an immediate rise in plasma insulin concentration, reaching a peak value of 29 ± 3 μU/ml at 5 min ($P < 0.001$ versus exhaustion, $P < 0.001$ versus basal). Thereafter, there was a gradual decline in plasma insulin, the mean values remaining 25–50% above basal at 10–30 min. The plasma glucagon concentration was 111 ± 7 pg/ml in the basal state and did not show any significant change either during the exercise (107 ± 14 at exhaustion) or during recovery (122 ± 21 at 5 min; 118 ± 19 at 20 min).

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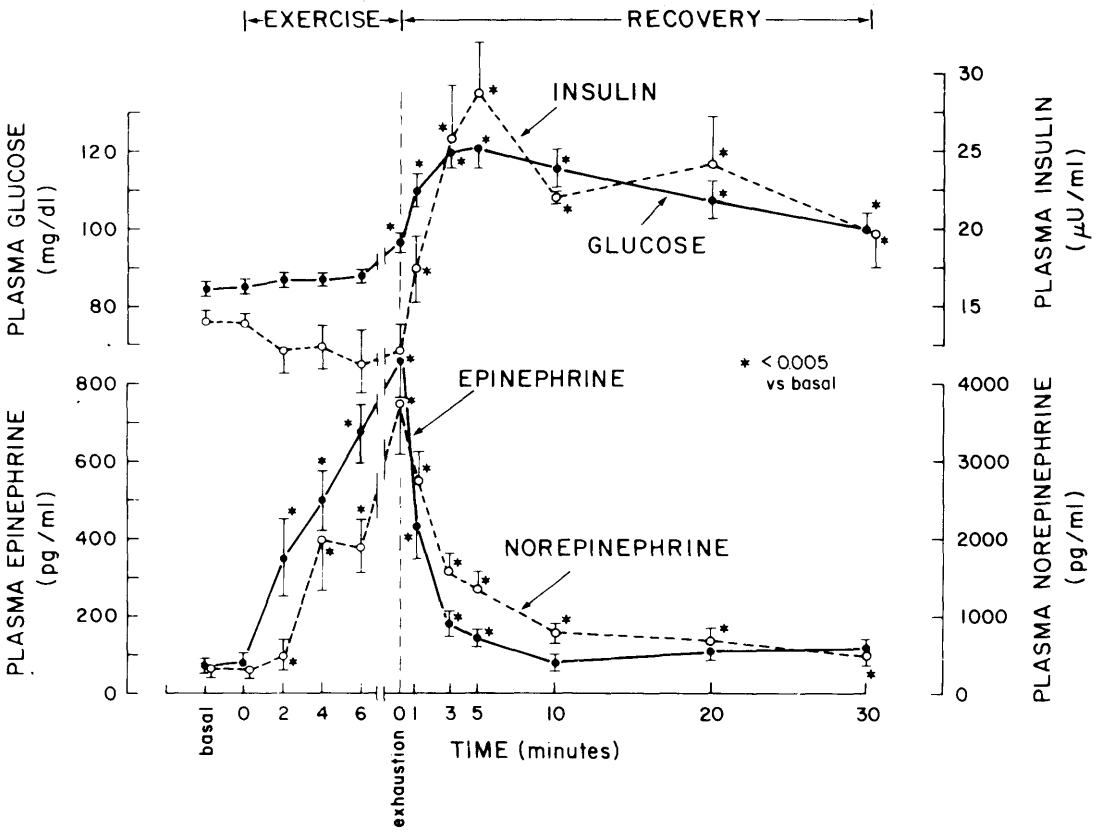


**FIGURE 1. Plasma concentrations of glucose, insulin, and catecholamines in response to acute exercise (85% $\dot{V}O_2$ max) and during the postexercise recovery period. Values shown are the mean ± SEM. The duration of exercise varied from 6 to 22 min (mean 11.7 ± 1.4 min). The mean value shown for 6 min of exercise includes the value observed at exhaustion in 4 of the 15 studies.**

The plasma epinephrine and norepinephrine concentrations are shown in Figure 1. As expected, there was a rapid and sustained increase of both catecholamines during the exercise. Epinephrine rose 10-fold above its basal value and reached a concentration of 864 ± 168 pg/ml at the point of exhaustion. The rise in norepinephrine was 10-fold and reached a peak concentration of 3748 ± 567 pg/ml. During the recovery phase there was a rapid and marked decrease in circulating catecholamines. Values for epinephrine were not significantly different from basal by 10 min of recovery, while plasma norepinephrine remained above basal ($P < 0.005$) during the entire 30 min of recovery.

The data on glucose kinetics are shown in Figure 2. In the basal state, glucose turnover was 1.93 ± 0.12 mg/kg/min. During the exercise period, both Ra and Rd rose but the rise in Ra exceeded that of Rd ($P < 0.005$). This imbalance between Ra and Rd was particularly true in the last minute of exercise, with values of 9.66 ± 1.57 mg/kg/min for Ra versus 5.10 ± 0.23 mg/kg/min for Rd ($P < 0.001$).

During the recovery period Ra and Rd differed in the direction of change. Ra initially tended to rise and at 5 min of recovery remained at values comparable to those observed at exhaustion and fivefold greater than those observed in the basal state ($P < 0.001$). In contrast, Rd fell by 33% ($P = 0.06$) over the first 5 min of recovery. As a result, Ra markedly exceeded Rd. The largest discrepancy between Ra and Rd occurred at 3 and 5 min of recovery [(Ra − Rd = 6.66 ± 1.9 mg/kg/min at 3 min ($P < 0.005$), and 5.70 ± 1.4 at 5 min ($P < 0.005$)]. Beyond 5 min of recovery, Ra and Rd again showed different responses. Ra fell rapidly to baseline resting values by 10 min and remained stable at 20 and 30 min. In contrast, Rd remained 77% above baseline values at 10, 20, and 30 min (Figure 2). As a result Rd exceeded Ra by 1.39 ± 0.45 mg/kg/min at 20 min ($P < 0.05$) and 1.31 ± 0.40 mg/kg/min at 30 min ($P < 0.05$).

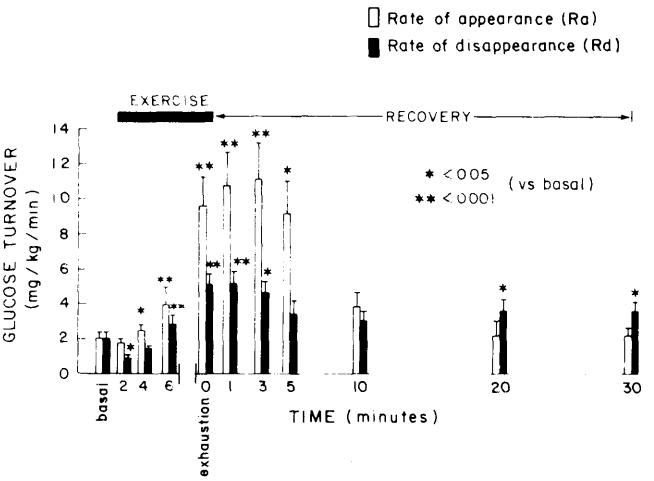


**FIGURE 2. Glucose turnover in six subjects during and after intensive exercise (85% $\dot{V}O_2$ max). Values represent the mean ± SEM. Exercise duration varied from 6 to 15 min (mean 10.1 min). The mean value shown for 6 min of exercise includes the value observed at exhaustion in two subjects.**

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## DISCUSSION

Previous studies examining the effects of exercise on plasma glucose homeostasis have documented increased,[1,5,6] decreased,[3,4] or unchanged[1,2,8] plasma glucose concentrations depending on the intensity and duration of the exercise. The effect of acute intermittent exercise on plasma glucose is an increase of 15–45 mg/dl above basal values.[5,6] This last observation is consistent with the hypothesis that plasma glucose changes in this situation may depend to a large extent on alterations in glucose turnover during the recovery phase from exercise. The present data clearly demonstrate that an acute bout of intensive exercise is followed by an increase in plasma glucose concentration of 30–40 mg/dl above basal values in normal well-trained subjects during the initial 5 min of recovery. The mechanisms for this phenomenon are indicated by the changes in glucose turnover in this phase. In the first 5 min of recovery the rate of appearance of glucose remains markedly increased above basal values. In contrast, glucose disappearance fell during the first 5 min of recovery to a value 33% below that observed at exhaustion. Sustained overproduction of glucose in a setting of declining glucose utilization was thus responsible for the rise in plasma glucose during early recovery from intensive exercise. This imbalance clearly differs from the closely matched changes in glucose production and utilization that are observed during[1] and after[15] less intensive exercise.

Concerning the factors responsible for the imbalance in glucose production and utilization during early recovery, it is noteworthy that while plasma insulin concentration tended to decline slightly during exercise, it rose to values 100% above basal during the first 5 min of recovery. Furthermore, plasma catecholamines, which reached peak values at exhaustion, fell by 60–80% over the first 5 min of recovery. Thus, the ongoing overproduction of glucose and rapid fall in glucose utilization during early recovery cannot be ascribed to the maintenance of the hormonal secretory pattern observed during exercise. On the other hand, it may reflect a persistence of the action of the hormone profile observed during exercise, particularly the elevation in catecholamines.

In contrast to the early recovery phase, beyond 10 min a fall in plasma glucose occurred and an imbalance in glucose kinetics was observed in which the rate of glucose disappearance exceeded the rate of glucose appearance. Furthermore, while Ra had returned to basal values beyond 10 min, Rd remained 77% above basal at 10–30 min. The latter observation is compatible with earlier studies demonstrating an ongoing increase in glucose uptake by previously exercising muscle during recovery from mild to moderate exercise.[4,15,31] In contrast, observations on arteriofemoral venous differences for glucose during recovery after intermittent intensive leg exercise have been interpreted as showing "almost no uptake of glucose by muscle."[16] In fact, however, those authors demonstrated that as compared with the basal state there was a twofold increase in leg blood flow and that A-FV differences for glucose were either unchanged or increased by 50%,[16] indicating at least a twofold increase in glucose uptake during recovery.

Although plasma insulin remained at modestly elevated levels of 20–25 μU/ml (25–50% above baseline) during recovery, it is noteworthy that previous studies in resting subjects have shown that comparable increments in plasma insulin (to levels of 28 μU/ml) fail to increase peripheral glucose utilization.[32] Recent studies have shown, however, that after prolonged low-intensity exercise associated with severe glycogen depletion there is an increase in muscle sensitivity to insulin.[4,18] The current findings suggest that an increase in peripheral insulin sensitivity may also occur after short bouts of maximal exercise in which muscle glycogen depletion is less severe. In this regard it should be noted that the modest elevation in plasma glucose may also be contributing to the increase in glucose utilization.

While the glucose disappearance rate remained elevated above basal values in the late recovery phase, glucose appearance returned to basal values beyond 10 min. It is noteworthy in this regard that the maintenance of basal rates of glucose production during late recovery occurred in a setting in which plasma insulin levels were increased by 25–50% and plasma glucose concentrations were 20–35 mg/dl above basal resting levels (Figure 1). Previous studies in resting subjects have shown that an infusion of glucose resulting in plasma glucose increments of 15 mg/dl and 40–60% increments in plasma insulin result in an 85% inhibition of hepatic glucose production.[33] Furthermore, even in the absence of increments in plasma glucose, half-maximal suppression of glucose production occurs in resting subjects with peripheral plasma insulin concentrations of 29 μU/ml.[32] The current findings of ongoing basal rates of glucose production in the face of modest increases in plasma glucose and insulin thus raise the possibility that the recovery period after intensive exercise may be characterized by hepatic resistance to insulin. On the other hand, since data are not available on portal vein insulin and/or glucagon levels, the precise status of hepatic sensitivity to insulin during recovery remains to be established.

It should be noted that in determining glucose kinetics during and immediately after exercise, some of the sampling intervals were quite brief (1–3 min), yet the equations employed have only been validated during non-steady-state conditions for intervals greater than 5 min.[28,30] To reduce this potential problem we used a data-fitting procedure[27] that minimized smoothing of the data and a model that is responsive to rapid changes in glucose flux and is relatively insensitive to alterations in model parameters.[27,30] Furthermore, when we recalculated the data assuming a larger or smaller pool size or using longer sampling intervals (by deleting some of the data points), the results were quantitatively similar and qualitatively identical. Finally, the rising plasma glucose concentration observed at 1 and 3 min of recovery (Figure 1) also suggests that the marked imbalances between Ra and Rd calculated at those time points (Figure 2) are, in fact, valid observations.

In conclusion, the current findings have shown that during recovery from intensive exercise in well-trained subjects there is an initial rise in plasma glucose that reaches peak values of 35 mg/dl above basal resting concentrations at 5 min. This hyperglycemic response is due to an imbalance between glucose production and utilization, in which the latter begins to decline toward baseline more rapidly than the former. In contrast, beyond 10 min of recovery glucose utilization remains significantly elevated above basal levels for at least 30 min while glucose production is maintained at basal values. This discrepancy in glucose utilization and

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production results in a secondary decline in plasma glucose. The hormone-substrate milieu (modest increments in plasma insulin and glucose) in which these later events occur suggests an increase in peripheral sensitivity to insulin, which may facilitate muscle glycogen repletion during exercise recovery.

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