

Chapter 2

The Impact of Type 1 Diabetes on the Physiological Responses to Exercise

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2.1 Brief Overview of the Normal Endocrine Response to Exercise

To provide energy in the form of carbohydrates, lipids, and protein in the face of increased energy demands during exercise, the healthy body must orchestrate a complex neuroendocrine response that starts at the onset of the activity. This response is continuously modulated as the duration of the exercise increases and as the intensity of the activity changes. Since one of the main fuels for exercise is carbohydrate, glucose utilization by the working muscle must be matched equally by glucose provision, predominantly by the liver, or hypoglycemia will ensue. If the liver cannot keep up with glucose utilization, then carbohydrate intake is critical to maintain performance. Glucose homeostasis during prolonged moderate-intensity exercise (~40–60% maximal oxygen uptake [$\text{VO}_{2\text{max}}$]) is primarily regulated by a reduction in insulin secretion and an increase in glucagon release from the pancreatic islets, which together helps to increase liver glucose production [1]. The increase in the glucagon-to-insulin ratio raises the rate of glucose appearance (Ra) to match almost perfectly the increased rate of peripheral glucose disposal (Rd) into working muscle (Fig. 2.1).

Increased hepatic glucose production during exercise occurs primarily through enhanced glycogenolysis and gluconeogenesis, with a greater reliance on the latter pathway as the duration of exercise increases [2]. Hypoglycemia can occur, even in nondiabetic individuals, when hepatic glucose production fails to match the elevated glucose uptake by working muscle, which is particularly pronounced during prolonged exercise (usually >3 h of activity), if not enough carbohydrate is consumed [3]. If hepatic glycogen stores are depleted during prolonged exercise,

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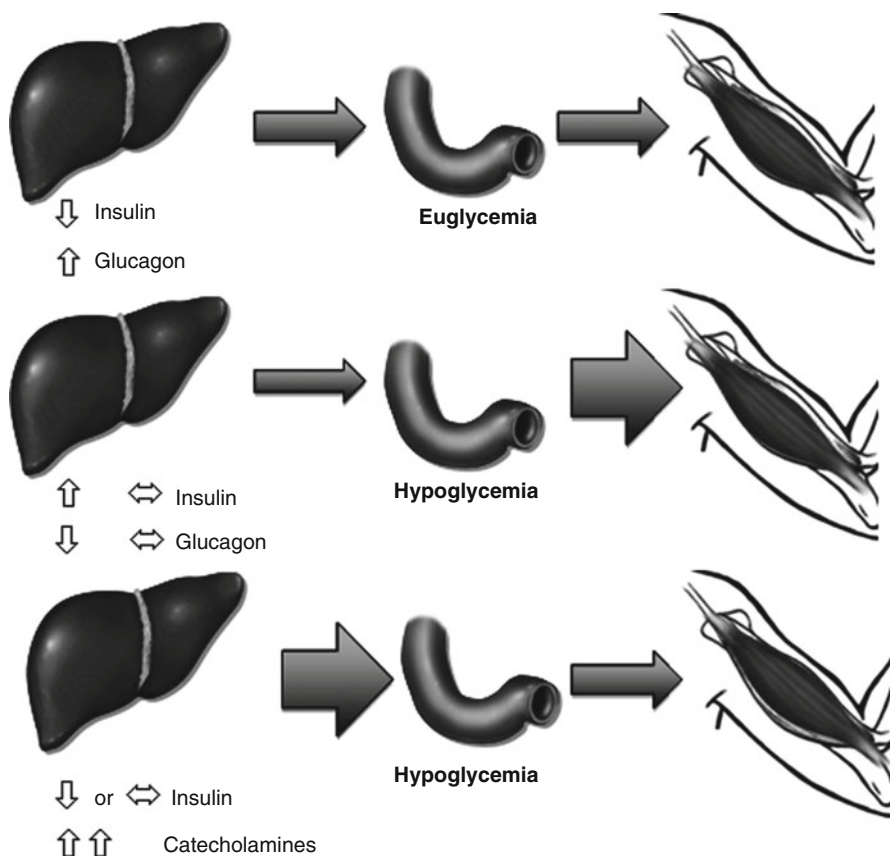


Fig. 2.1 Blood glucose responses to exercise in nondiabetic or ideally controlled patient with type 1 diabetes (*upper panel*), overinsulinized patient (*middle panel*), and underinsulinized patient or patient performing high-intensity exercise under competition stress (*lower panel*). The thicknesses of the *arrows* represent glucose flux. In the *upper panel*, hepatic glucose production is balanced with muscle glucose uptake and normal blood glucose levels are maintained. In the *middle panel*, high circulating insulin levels reduce hepatic glucose production and increase muscle glucose uptake, thereby resulting in hypoglycemia. In the *lower panel*, low circulating insulin levels and/or elevated counterregulatory hormones increase hepatic glucose production and decrease muscle glucose uptake, resulting in hyperglycemia (Reprinted by permission of the publisher from Chu et al. [94], JTE Multimedia)

gluconeogenesis alone is unable to provide adequate glucose to supply the working muscles. To help reduce the reliance on endogenous carbohydrate as a fuel source, reductions in insulin levels and increases in growth hormone along with increases in sympathoadrenal activity and other factors help promote increased lipid provision for oxidation by muscle [4]. Even with very prolonged exercise, when reliance on lipid as a primary fuel source is maximal, carbohydrate provision, either by the liver through gluconeogenesis or by oral ingestion, is essential to prevent hypoglycemia even in nondiabetics [5].

In healthy individuals, several glucose counterregulatory mechanisms (i.e., anti-hypoglycemic actions) exist to help limit hypoglycemia, both when fasting occurs at rest and when prolonged exercise is performed. For example, [6] a slight decrease in glycemia from normal (normal being ~90 mg/dL or 5 mmol/L) lowers insulin secretion and activates the release of various counterregulatory hormones including glucagon, catecholamines, growth hormone, and cortisol in a stepwise and hierarchical fashion [7]. During exercise, other humoral and muscle factors also likely help augment glucose production [100]. All of these hormones act to increase hepatic glucose production and lower peripheral glucose disposal, thereby defending against ensuing hypoglycemia. As such, several safeguards need to be breached before hypoglycemia occurs in nondiabetic individuals.

Interestingly, heavy aerobic exercise ($>80\% \text{ VO}_{2\text{max}}$) also generates a complex neuroendocrine response, similar to that of acute stress, perhaps as a means of elevating glucose provision for “fight or flight”. In intense exercise, glucose is the exclusive muscle fuel, and it must be mobilized from muscle and liver glycogen in the fed and fasted state. This process is largely governed by increases in catecholamines, which facilitate glucose production but limit glucose uptake. As such, in healthy individuals, insulin secretion actually increases post-exercise to help normalize this transient hyperglycemia caused by intense exercise [8]. This complex neurohormonal regulation during exercise, performed at a wide range of differing intensities and durations and at different environmental conditions, makes it nearly impossible to mimic in the patient with type 1 diabetes.

2.2 Abnormalities in the Endocrine Responses to Acute Exercise in Type 1 Diabetes

The blood glucose response to exercise in patients with type 1 diabetes varies considerably both between and within individuals, likely depending on several factors including the type and intensity of exercise performed, the duration of the activity, and the level of circulating “on board” insulin during and after the exercise. Even if all of these variables are taken into consideration, the blood glucose response differs markedly between individuals but has some reproducibility within an individual [9]. One of the key determinates of the glycemic response to exercise is the general classification of the exercise (i.e., aerobic vs. anaerobic).

2.2.1 Aerobic Exercise

Aerobic exercise may be defined as any activity that uses large muscle groups at relatively low rates of muscular contraction. This type of activity can be maintained continuously (or rhythmically) for prolonged periods (minutes to hours) through oxidative metabolism of various fuel sources including carbohydrates, fats, and some protein. Moderate-intensity aerobic exercise generally involves continuous,

aerobic activity between 40% and 59% of $\text{VO}_{2\text{max}}$ or 55–69% of maximal heart rate (HR_{max}) [10]. Examples of moderate-intensity exercise include continuous aerobic activities such as jogging, cycling, and swimming. Typically, this type of exercise promotes a lowering of blood glucose concentration, both during and after the end of the activity, and thus requires nutritional intervention and/or adjustments in insulin dosages to limit hypoglycemia. The physiological mechanisms by which aerobic exercise causes undesirable alterations in glycemia in individuals with type 1 diabetes are detailed below and highlighted in Fig. 2.1.

2.2.1.1 Hypoglycemia

For individuals with type 1 diabetes, the inability to reduce exogenous insulin levels during aerobic exercise is a key factor that contributes to an increased risk of exercise-induced hypoglycemia [11]. As discussed above, insulin levels in the portal circulation normally drop after the onset of aerobic exercise, and this drop helps to sensitize the liver to increasing glucagon concentrations [2, 12]. Since, in the insulin-dependent type 1 patient, exercise is often performed in a 0–4-h time frame post-insulin injection, concentrations of insulin typically do not decrease during exercise and may actually increase just because of the kinetics of peak insulin action [13, 14]. A second related factor that increases the risk of hyperinsulinemia and hypoglycemia is the accelerated absorption of insulin from subcutaneous tissues, once it has been injected or infused [15]. Even if no bolus insulin has been injected or infused in the hours preceding exercise, it is still possible, but less likely to have hypoglycemia because of elevated basal insulin concentrations, compared to nondiabetics who are exercising [13]. Relative hyperinsulinemia during exercise in the patient with type 1 diabetes limits the effect of glucagon on hepatic glucose production and promotes insulin-induced peripheral glucose uptake, further decreasing blood glucose levels. A third factor that may contribute to an increased risk for exercise-associated hypoglycemia in patients with type 1 diabetes may be the loss in glucagon response to developing hypoglycemia [16] or an impaired stimulation of hepatic glucose output in response to glucagon secretion [17]. Although it has been established that the glucagon response to exercise may be intact in people with type 1 diabetes, if they are not hypoglycemic [18], there may be deficiencies in the glucagon response during exercise if the patients were previously exposed to hypoglycemia [19] or perhaps if they are, in fact, exercising while hypoglycemic. Moreover, there may also be impaired adrenergic responses to exercise in patients with type 1 diabetes under hypoglycemic conditions [18]. Finally, other factors such as a low level of hepatic glycogen content in poorly controlled diabetes [20] and/or reduced gluconeogenesis and/or increased peripheral glucose disposal in the face of hyperinsulinemia [21] may contribute to exercise-induced hypoglycemia in patients with type 1 diabetes. A summary of the factors that may predispose the patient to hypoglycemia during aerobic exercise is shown in Table 2.1.

Table 2.1 Factors that can affect changes in blood glucose levels during exercise

Drop in blood glucose	Blood glucose unchanged	Increase in blood glucose
Hyperinsulinemia due to usual insulin injection (or infusion) prior to exercise and increased insulin absorption kinetics and action	Pre-exercise insulin adjusted appropriately	Hypoinsulinemia and ketoacidosis prior to exercise
Prolonged aerobic type activity with no carbohydrate intake or without a reduction in insulin administration	Appropriate consumption of carbohydrate before and during exercise	Prolonged pump disconnect
Unfamiliarity with the activity		Very vigorous aerobic exercise (>80% of maximal oxygen consumption)
Defective glucose counterregulation to hypoglycemia and/or exercise		Repeated or intermittent anaerobic exercise
		Excessive carbohydrate consumption
		Post-exercise when glucose production or carbohydrate feeding exceeds disposal

2.2.1.2 Hyperglycemia

Although aerobic exercise is typically associated with an increased risk for hypoglycemia, certain types of activity may promote hyperglycemia. Specifically, high-intensity aerobic exercise (i.e., above the lactate threshold) tends to increase blood glucose levels because insulin levels do not rise in the portal circulation of the patient with diabetes to compensate for the normal increase in circulating catecholamine levels. It is well established that heavy aerobic exercise (short- and middle-distance running, short track cycling, some other individual and team sports, etc.) induce increases in catecholamines that increase hepatic glucose production and limit peripheral disposal (Fig. 2.1). In individuals who do not have diabetes, the increase in catecholamines and hyperglycemia is compensated for by increases in insulin secretion, usually at the end of the activity. If hyperglycemia occurs post-exercise, this phenomenon is usually transient in the individual with diabetes, lasting for 1–2 h in recovery. No current guidelines are available on the amount of insulin to administer in the presence of hyperglycemia after high-intensity exercise for patients with type 1 diabetes. Although some limited experimental data suggests that a doubling in insulin levels relative to when the vigorous exercise was performed may be needed to counter this transient hyperglycemia [22].

Patients and caregivers should be aware of the potential for a rise in blood glucose before “stressful” competition. Even if blood glucose levels are normal in the hours before exercise, anticipatory stress increases counterregulatory hormones and hyperglycemia can occur. Typically, this “stress-related” increase in glycemia at the

onset of exercise does not need to be corrected for since the increased glucose utilization rate during the activity, as long as it is aerobic in nature, will often lower blood glucose levels. However, frequent self-monitoring of blood glucose is needed to make sure that any pre-exercise hyperglycemia is not worsened during the exercise, to which continuous glucose monitoring (CGM) may be an asset.

In situations of prolonged and severe hypoinsulinemia (missed insulin injections, blocked insulin pump, illness, etc.), patients may have elevations in circulating and urinary ketone bodies. In these situations, vigorous exercise may cause further increases in hyperglycemia and ketoacidosis, particularly if elevated blood ketones are present at the time of exercise. In these situations, hepatic glucose production continues to rise, while glucose utilization remains impaired and glycemic control deteriorates even further. For these reasons, it is recommended to delay exercise if blood glucose is higher than 14 mmol/L and if blood or urinary ketones are also elevated [23, 24]. A summary of the possible reasons for exercise-associated hyperglycemia during sport is shown in Table 2.1.

For patients on insulin pump devices with hyperglycemia and elevated ketone levels, infusion sets should be changed, and individuals may need to temporarily change to needles, with rapid-acting insulin injected until glucose is restored. Hyperglycemia and ketoacidosis may cause dehydration and decrease blood pH, resulting in impaired performance and severe illness. Rapid ketone production can precipitate ketoacidotic abdominal pain and vomiting. In these situations, patients are advised to seek emergency care for intravenous insulin and rehydration protocols.

2.2.2 Anaerobic Exercise

Anaerobic activities are characterized by high rates of intense muscular contraction. With purely anaerobic exercise, muscle contractions are sustained by the phosphagen and anaerobic glycolytic systems to produce lactic acid and energy in the form of adenosine triphosphate (ATP). Anaerobic activities include sprinting, power lifting, hockey, and some motions during basketball and racquet sports. In reality, however, most of the sports and physical activities that athletes perform are a mix of both anaerobic and aerobic actions (soccer, basketball, mountain biking, squash, football, etc.). Anaerobic fitness refers to the ability to work at a very high level during these activities for relatively short periods (5–30 s).

With anaerobic exercise, lactate production within the muscle rises dramatically. This lactate, which is a glycolytic end product, can either be used within the cells of formation or transported through the interstitium and vasculature to adjacent and anatomically distributed cells for utilization by other tissues [25]. Elevations in lactate and catecholamines during anaerobic exercise are known to lower the uptake of plasma glucose and free fatty acids into skeletal muscle [26] and increase hepatic glucose production [27], thereby increasing the likelihood of hyperglycemia in patients with type 1 diabetes. Moreover, anaerobic flux of muscle glycogen also lowers

skeletal muscle glucose uptake [26], which could contribute to hyperglycemia in persons with diabetes if hepatic glucose production is elevated.

Interestingly, just a 10-s high-intensity anaerobic sprint has been shown to help prevent early post-exercise hypoglycemia in persons with type 1 diabetes [28, 29]. In addition, performing weight training before the onset of aerobic exercise may also attenuate the drop in blood glucose levels in patients with type 1 diabetes [30]. Similarly, performing intermittent high-intensity exercise (with repeated anaerobic work) may be superior over continuous moderate-intensity aerobic exercise for glycemic stability, particularly in early and late recovery [31, 32].

2.2.3 Early Post-exercise Hyperglycemia

Just after the end of either vigorous aerobic or anaerobic work, individuals with type 1 diabetes may experience increases in blood glucose levels through a number of mechanisms. First, any reduction in insulin dosage prior to exercise might promote hyperglycemia once the activity is finished, since glucose disposal will eventually return toward pre-exercise levels but glucose production will remain elevated because of the reduction in circulating insulin concentration. If the individual wears an insulin infusion device (insulin pump) and has removed the pump altogether, then circulating insulin levels may be very low by the end of prolonged exercise and hyperglycemia is likely [33]. In addition, some individuals may be motivated to consume carbohydrates early in recovery, which may drive up blood glucose levels. In addition, as mentioned above, very vigorous aerobic exercise with a heavy anaerobic (producing catecholamines and lactate) component will increase glycemia for 1–2 h in recovery [8]. In these situations, it may be necessary (or desirable) to lower glycemia by injecting rapid-acting insulin analogs or by increasing the basal infusion rates to normal (or slightly above normal) early in recovery.

2.2.4 Late Post-exercise Hypoglycemia

Post-exercise late-onset hypoglycemia has long been a complaint of patients with type 1 diabetes [34]. If patients develop hypoglycemia during sleep, it may go unnoticed. If patients perform just 45 min of moderate-intensity exercise during the day, then the risk of nocturnal hypoglycemia may be as high as 30–40% in the evening following exercise [35–39]. An investigation in children with type 1 diabetes indicates that increased insulin sensitivity occurs immediately after exercise and again 7–11 h later [40], which may further elevate their risk for late-onset post-exercise (nocturnal) hypoglycemia.

This is particularly problematic as patients may not perceive hypoglycemia during sleep, and the hypoglycemic duration may last for just a few minutes or for several hours. In these situations, a reduction in bedtime basal insulin by ~20% is

recommended, with a reduction in basal infusion rate from bedtime to ~4 AM if on a pump [35]. Otherwise, a complex carbohydrate snack with some protein is advised, either without an insulin bolus at all or with a drastically reduced bolus dose.

2.3 Abnormalities in Fuel Utilization During Exercise in Type 1 Diabetes

A number of subtle alterations in fuel metabolism during exercise have been noted in persons with type 1 diabetes [41–45]. In patients deprived of insulin for 12–24 h, prolonged moderate-intensity exercise is associated with a lower respiratory exchange ratio, and thus a reduced rate of carbohydrate oxidation, than that shown in control subjects at the same exercise intensity [42, 46]. As such, it would appear that a patient with type 1 diabetes who is underinsulinized would have a greater reliance on lipid oxidation during exercise compared to when they have elevated insulin levels. When insulin is administered to the patient, to levels somewhat representative of nondiabetics, the overall ratio of carbohydrate to lipid utilization during exercise performed in the postprandial state looks remarkably normal [43, 44, 47, 48]. Indeed, in a study conducted by Francescato et al. [44], which was conducted at various time intervals after insulin injection and with different amounts of glucose ingested, fat oxidation and CHO oxidation were not significantly different from those observed in control subjects.

The ingestion of fast-acting carbohydrate during exercise clearly helps to limit the hypoglycemic effect of endurance type exercise in individuals with type 1 diabetes [49, 50]. Largely, the oxidation of orally ingested carbohydrate is normal in those with diabetes, if the circulating insulin levels are elevated, although the rate of oxidation may be initially slightly impaired [41, 43, 45]. Moreover, rates of plasma glucose disappearance during exercise in patients with diabetes are comparable to control subjects [11, 51–53] or just slightly impaired [48].

Although total fat and carbohydrate oxidation rates may be normal during exercise in persons with type 1 diabetes who are well insulinized, some evidence does exist to suggest that muscle glycogen utilization rates may be higher and plasma glucose oxidation rates lower during prolonged exercise than in nondiabetic individuals [21]. Unfortunately, a greater reliance on limited endogenous muscle fuels (i.e., muscle glycogen) may put the individual at risk of early fatigue.

A recent study has shown that a low-glycemic-index carbohydrate and reduced insulin dose administered 30 min before running maintains control of both pre- and post-exercise blood glucose responses in type 1 diabetes [54]. The amount of carbohydrate needed to limit hypoglycemia is at least partly related to the proximity of the last insulin injection [44]. As such, anywhere from 1.0 to 1.5 g of carbohydrate per kilogram body mass per hour of exercise is required when the exercise is within 1–2 h of insulin administration [24], but this amount drops to about 0.2 g/kg by about 5.5 h postinjection [44]. Estimating glucose utilization rates during exercise, either via respiratory exchange ratio or via heart rate, appears to be an

effective means for determining the appropriate carbohydrate feeding regimen to help prevent hypoglycemia [50, 55].

2.4 Effects of Type 1 Diabetes on Performance

Normally, insulin therapy is rapidly initiated at the time of diagnosis in patients with type 1 diabetes, and dramatic metabolic improvements are achievable within a fairly short time frame (days to weeks after the initiation of treatment) [56]. However, clinical diagnosis may be delayed and the overall management in youth with the disease is usually suboptimal for a variety of physiological and psychosocial reasons [57]. It should also be noted that normal restoration in glucose homeostasis is nearly impossible in type 1 diabetes since the sophisticated control system is no longer in place that maintains a small, but critical, amount of blood glucose constant [2]. As such, a number of physiological challenges in substrate metabolism exist that places the individual with type 1 diabetes at risk for suboptimal exercise performance.

Overall, aerobic capacity can be impaired significantly in young patients with type 1, particularly if they are in suboptimal glycemic control. For example, in one large study of healthy and diabetic adolescents/young adults, matched similarly in age, weight, height, and body composition, aerobic capacity was shown to be about 20% lower in those with type 1 diabetes [58]. Several cardiovascular, muscular, and metabolic impairments in type 1 diabetes might help to explain their potential decrement in aerobic and anaerobic performance. A number of studies report reduced physical work capacity or maximal aerobic capacity ($\text{VO}_{2\text{max}}$) in young patients with type 1 diabetes, despite insulin therapy, when compared to their nondiabetic peers [58–64]. Both end diastolic volume and left ventricular ejection fraction fail to increase normally during exercise in young adults with type 1 diabetes compared with controls [65]. In contrast, Nugent and colleagues [66] report no difference in VO_2 peak during a progressive incremental exercise test in adults with long-standing diabetes, while Veves et al. [67] found that only inactive adults with demonstrated neuropathic complications had reduced $\text{VO}_{2\text{max}}$. Taken together, these studies suggest that if one is physically active with type 1 diabetes, then aerobic capacity can be normal, at least if neuropathy has not yet developed.

Impairments in physical work capacity in those with type 1 diabetes, if observed, appear to be related to the level of glycemic control in the patient. For example, Poortmans et al. [64] and Huttunen et al. [61] both reported that physical capacities were inversely related to the level of metabolic control, as measured by HbA1c. It is unclear, however, if a reduced work capacity in youth with type 1 diabetes is a result of poorer oxygenation of muscle [68], a lower amount of muscle capillarization [69], or if poorer metabolic control is a function of lower amounts of habitual physical activity [70]. In an experimentally induced murine model of diabetes, there is altered expression of several genes involved in angiogenesis and reduced muscle capillarization which could not be normalized even by high-volume endurance exercise training [69].

Studies investigating muscular strength and endurance in individuals with type 1 diabetes have shown mixed results, although a recent review by Krause and colleagues has indicated that a myopathy may exist in type 1 diabetes [71]. A number of investigators report decrements in strength [72–77], while others have shown no strength deficit, but slower rates of muscular recruitment during isometric contraction [78]. Although fatigue is a common complaint of patients with diabetes [79, 80], the effect of type 1 diabetes on endurance capacity during exercise is not well documented. Compared to controls, patients with type 1 diabetes have been reported to have both impaired [78] and enhanced [74] capacity during relatively brief bouts of intense exercise. Ratings of perceived exertion during prolonged exercise have been reported to be higher in boys with type 1 diabetes compared to age, weight, and aerobic fitness matched controls [81]. Also during prolonged exercise, those with type 1 diabetes who are under good glycemic control have a higher glycolytic flux [82] and tend to rely considerably more on muscle glycogen utilization as an energy source [45], which might reduce endurance capacity, although this hypothesis has yet to be tested. Moreover, exercising while hyperglycemic has been shown to increase reliance on muscle glycogen compared to exercising while euglycemic [83], and the individual who is exercising while hypoinsulinemic/hyperglycemic would be expected to be prone to early dehydration and acidosis [84], all factors that might promote early fatigue. Moreover, increasing blood glucose levels to 16 mmol/L has been shown to reduce isometric muscle strength, but not maximal isokinetic muscle strength, compared with strength measured at glycemia clamped at 5 mmol/L in patients with type 1 diabetes [85]. This reduction in isometric strength might play a role in the development of early fatigue during certain types of resistance exercise.

If individuals with type 1 diabetes are actively engaged in regular exercise, they can clearly achieve a normal, or even an elite, level of sport performance. In one German study of ten middle-aged long-distance triathletes with type 1 diabetes studied over 3 years, overall endurance performance was said to be “normal” despite documented hyperglycemia during the early part of a race, then hypoglycemia during the marathon leg [86]. The degree to which acute changes in blood glucose levels influence sports performance remains somewhat unclear, however. Unfortunately, very few studies have been conducted in which exercise performance is examined during differing levels of blood glucose concentrations in those with type 1 diabetes. Circumstantial evidence suggests that an increase in plasma glucose availability might improve the exercise capacity perhaps because more fuel is readily available for muscle contraction. However, this hypothesis has not been supported by one study that “clamped” nondiabetic cyclists at hyperglycemia and euglycemia and found no difference in endurance performance [87]. Similarly, in one study of prepubertal boys with type 1 diabetes ($n=16$), lowering the insulin dose prior to exercise to reduce the likelihood of hypoglycemia did not influence aerobic capacity during cycling compared to the usual insulin dose [88]. In eight endurance-trained adults with type 1 diabetes, elevating blood glucose levels from 5.3 ± 0.6 mmol/L to 12.4 ± 2.1 mmol/L, via hyperinsulinemic glucose clamp technique, also failed to change peak power output or other physiological endpoints such as lactate, heart rate, or respiratory exchange ratio [89].

In contrast to mild hyperglycemia, mild hypoglycemia probably lowers exercise capacity and sport performance in individuals with type 1 diabetes. For example, capacity was reduced and ratings of perceived exertion increased with hypoglycemia in a group of youth with type 1 diabetes [50, 81], although the exercise was always stopped by the research investigators rather than the subjects for safety reasons. In a recent sports camp field study of 28 youth with type 1 diabetes, Kelly et al. [90] found that the ability to carry out fundamental sports skills was markedly reduced by mild hypoglycemia compared with either euglycemia or hyperglycemia. Importantly, this finding of significantly impaired sports performance with hypoglycemia appeared universally across nearly all subjects and is similar to the well-documented detrimental effects of hypoglycemia on cognitive processing [91].

Profound or sustained hyperglycemia also likely impairs endurance performance in those with type 1 diabetes, although the evidence for this statement is somewhat limited. Prolonged hypoinsulinemia/hyperglycemia would be expected to lower muscle glycogen levels, reduce muscle strength, and predispose the individual to dehydration and electrolyte imbalance [92]. As mentioned above, exercising while hyperglycemic has been shown to increase the reliance on muscle glycogen as a fuel source and limit the capacity to switch from carbohydrate to lipid energy sources [83]. Importantly, substrate oxidation during prolonged endurance exercise can be similar to what is observed in nondiabetics if diabetic subjects are clamped euglycemic [83]. Taken together, it is likely that there is an inverted-U shape relationship between glycemia and exercise/sport performance, with the best performance in the euglycemic range.

2.5 Adaptations to Exercise Training in Type 1 Diabetes

Individuals with type 1 diabetes appear to respond normally to both endurance- and resistance type training, from an adaptive point of view, particularly if they are in good glycemic control.

Endurance training in humans normally results in numerous beneficial adaptations in skeletal muscles, including an increase in GLUT4 expression and glucose transport capacity, resulting in increased insulin sensitivity [93]. Paradoxically; however, despite these adaptations, improvements in glycemic control are not always observed with regular exercise in this patient population [94]. The physiological adaptations to regular exercise are clearly beneficial for patients, even if glycemic control is not improved. For example, in response to endurance training, children with type 1 diabetes have improved vascular function [95] and an improved cardiovascular risk profile [96], which will likely enhance long-term health. Interval sprint training has been shown to reduce metabolic acidosis and enhance oxidative capacity and fitness [97]. Some have even speculated that regular exercise may attenuate the autoimmune event that causes beta cell death [98]. Overall, life expectancy appears to increase with regular activity in this patient population [99].

2.6 Summary

In summary, a number of neuroendocrine disturbances can influence glucose regulation during exercise, making the management of glycemia challenging for the patient and caregiver. In general, aerobic exercise promotes a reduction in blood glucose concentration, while anaerobic exercise can promote transient hyperglycemia. Although individuals with type 1 diabetes can achieve excellence in sport, rigorous glycemic control and the appropriate insulin modifications on exercise days and appropriate nutritional intake is likely critical for maximizing individual performance. Overall, improvements in various health metrics clearly indicate that regular exercise should remain at the cornerstone of clinical care for patients with type 1 diabetes.

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Type 1 Diabetes
Clinical Management of the Athlete
Gallen, I.
2012, XIV, 226 p., Hardcover
ISBN: 978-0-85729-753-2