23 Lifestyle Issues: Exercise

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Keypoints

- Regular exercise increases insulin sensitivity in both individuals with and without diabetes.
- In individuals without diabetes, plasma insulin levels decrease during low to moderate intensity exercise to compensate for increases in insulin sensitivity. Glucose production and glucose disposal increase in parallel in order to maintain blood glucose homeostasis.
- In individuals with type 1 diabetes (T1DM), low to moderate intensity exercise can result in hypoglycemia, as insulin levels cannot be regulated physiologically.
- During and after high intensity exercise, glucose production can exceed glucose disposal, causing hyperglycemia in individuals both with and without diabetes. In T1DM, hyperglycemia can be more marked and prolonged, as insulin cannot increase in response.
- It is recommended that individuals with T1DM adjust their insulin dose and carbohydrate consumption prior to, during and/or after exercise to accommodate the type, intensity and duration of exercise performed.
- While regular exercise has not conclusively been found to improve glycemic control in T1DM, it is associated with decreased long-term morbidity and mortality in this population.
- Structured supervised diet and exercise interventions can reduce the risk of developing type 2 diabetes mellitus (T2DM) by about 60% in individuals with impaired glucose tolerance.
- Regular exercise improves glycemic control significantly in T2DM.
- Individuals with T1DM and T2DM with moderate or high aerobic fitness have long-term mortality that is 50–60% lower than individuals with diabetes and low cardiorespiratory fitness.
- Resistance training is a safe and effective means of improving glycemic control in individuals with T2DM of all ages. To maximize the impact of lifestyle measures on glycemic control, combined aerobic and resistance exercise is more effective than either type of exercise alone.

Glossary of terms

The definitions in Table 23.1 are adapted from those found in the *Physical Activity Guidelines Advisory Committee Report, 2008* produced by the US Department of Health and Human Services [1].

Types of exercise training and their effects on healthy individuals

Aerobic exercise

Effects of regular aerobic exercise training

Regular aerobic training generally leads to improved lung function and cardiac output, allowing for the provision of more oxygen for working muscles. Higher plasma volume and greater capillary density in the muscles allow increased muscle blood flow during peak exercise. Eventually, a shift in the fuels being used to supply the energy demands of activity is seen as the oxidative metabolic system becomes more efficient. In general, changes become more noticeable when training is of higher volume and intensity.

Fuel metabolism during acute aerobic exercise

During the first 5–10 minutes of exercise, muscle glycogen is the main source of energy. As exercise continues, the bloodborne substrates, glucose and non-esterified fatty acids become increasingly important. If exercise of moderate intensity continues for several hours, the contribution of glucose diminishes and non-esterified fatty acids become the major fuel (Figure 23.1) [2]. During moderate intensity aerobic exercise, blood glucose levels remain virtually unchanged. Insulin secretion is reduced while the release of glucagon is promoted, encouraging a two- to four-fold increase in hepatic glucose production (controlled by the glucagon : insulin molar ratio at the portal vein) [3] to meet the needs of the exercising muscle. Glucose production and utilization fall rapidly and in parallel to baseline during the post-

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Table 23.1 Glossary of terms.

Physical activity The expenditure of energy above that of resting by contraction of skeletal muscle to produce bodily movement

Exercise A type of physical activity that involves planned, structured and repetitive bodily movement performed for the purpose of improving or maintaining physical fitness

Cardiorespiratory fitness/cardiorespiratory endurance/aerobic fitness Refers to the circulatory and respiratory systems' ability to supply oxygen during sustained exercise

Aerobic exercise Exercise that uses primarily aerobic energy-producing systems and involves the repeated and continuous movement of the same large muscle groups for extended periods of time (at least 10 minutes at a time). If performed with sufficient intensity and frequency this type of exercise increases cardiorespiratory fitness. Aerobic activities include walking, cycling, jogging, swimming, etc.

Anaerobic exercise Short, high intensity exercise involving anaerobic energy-producing systems. If performed with sufficient intensity and frequency this type of exercise can increase the body's ability to tolerate acid-base imbalance during high intensity exercise

Intensity of aerobic exercise Generally described in relation to an individual's maximal aerobic capacity ($\dot{V}O_{2max}$), as measured using indirect calorimetry during a graded maximal exercise test. An activity level corresponding to 40–60% of $\dot{V}O_{2max}$ is generally considered to be "moderate" in intensity, while "vigorous" aerobic activities consist of those performed at greater than 60% of $\dot{V}O_{2max}$

Muscular fitness Includes the force a muscle can exert (strength) and the ability of the muscle to perform continuously without fatigue (endurance)

Resistance exercise Also known as strength training or weight training. Resistance exercise involves the use of muscular strength to work against a resistive load or move a weight. Examples include lifting free weights, or using weight machines. Regular resistance exercise at sufficient (moderate to high) intensity increases muscular fitness

Intensity of resistance exercise The intensity of resistance exercise is often considered "moderate" if the resistance provided is 50–74% of the maximum that can be lifted a single time (1 repetition maximum [1 RM]). High intensity resistance exercise involves resistance ≥75% of 1 RM

Repetition The number of times a resistance exercise is repeated during each set

Set A grouping of repetitions of a specific resistance exercise

exercise "recovery" phase, as insulin levels rise and glucagon secretion decreases. If moderate intensity aerobic exercise lasts for several hours without caloric intake, hepatic glucose production can no longer keep pace with increased utilization, and the blood glucose level begins to decline, eventually resulting in hypoglycemia [4].

Effects of regular training on fuel metabolism

Aerobically trained athletes without diabetes have low fasting plasma insulin levels and reduced insulin responses to a glucose challenge in the face of normal glucose tolerance, and increased insulin-mediated glucose uptake under glucose clamp conditions [5]. Physical training is also known to increase muscle and hepatic

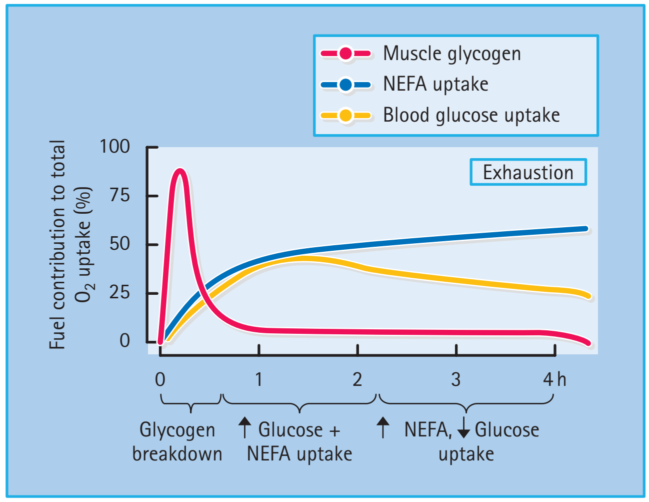

Figure 23.1 The relative contributions of muscle glycogen breakdown and uptake of blood-borne glucose and non-esterified fatty acids (NEFA) to fuel utilization at various stages of prolonged low-intensity exercise in a healthy individual. The exercise intensity corresponds to 30% of maximal. Data from Ahlborg *et al.* [2].

insulin sensitivity in previously untrained individuals [6]. Lipid and lipoprotein profiles become less atherogenic with regular training: serum high density lipoprotein (HDL) cholesterol levels may increase, while total and low density lipoprotein (LDL) cholesterol levels may remain unchanged or decline [7,8]. Some studies have found that serum triglyceride levels decline after training [7,8]. Even when LDL cholesterol concentrations remain unchanged with aerobic exercise training there is an increase in mean LDL particle diameter, reflecting more buoyant and less atherogenic LDL cholesterol particles [9].

Anaerobic exercise

Effects of regular anaerobic exercise training

Regular anaerobic training improves the body's ability to provide the fuels necessary for the production of anaerobic power. Adenosine triphosphate (ATP) and phosphocreatine levels (the main fuels for short powerful bursts) increase within muscle tissue, allowing the individual to sustain higher absolute exercise intensities for longer periods of time.

Fuel metabolism during anaerobic activity

With very intense exercise (more than 80% of $\dot{V}O_{2max}$ – a level sustainable for no more than 15 minutes by most individuals), hepatic glucose production may exceed the rate of glucose utilization, leading to a 5- to 10-fold increase in blood glucose [10–12]. During recovery from very intense exercise, hyperglycemia often occurs in fit individuals without diabetes, as glucose utilization decreases more quickly than glucose production [10–12]. In response to the hyperglycemia, plasma insulin levels increase and glycemia is restored to baseline within about 45 minutes.

Resistance exercise

Effects of regular resistance exercise training

Declines in muscle strength of approximately 12–15% per decade have been reported after the age of 50 years [13,14], with muscle mass decreasing as much as 6% per decade [5,16]. With regular heavy resistance training, increases of greater than 30% in muscle strength [15,17] and gains in muscle mass ranging from 3 to 12% [18,19] have been found within the first couple of months of training, with relative increases typically being higher in elderly subjects [16,18]. Initial strength gains during the first 6 weeks are generally as a result of peripheral nervous system adaptations (improved muscle recruitment) and are not accompanied by muscle hypertrophy. Resistance training can be of additional benefit to older adults as improvements in postural stability and dynamic balance may decrease the risk of fall-related injuries [20].

When muscles are forced to perform for a given period of time at or near their maximal strength and endurance capacity (either by lifting weights or working against some other form of resistance), it will result in an increase in muscle strength, endurance and hypertrophy. Performing more repetitions (up to 2 minutes per set of each exercise) with lower resistance tends to increase endurance, while lifting heavier weights for fewer repetitions will favor strength gains [21].

Fuel metabolism during resistance exercise

High intensity, short duration resistance exercise is fueled by energy generated from the breakdown of stored intramuscular high-energy phosphates, ATP and phosphocreatine. During such exercise, adequate rest periods (2–5 minutes) between sets are necessary to allow regeneration of phosphocreatine stores. Glycolytic anaerobic energy production (with concomitant blood lactate accumulation) becomes more important as intensity decreases, the number of repetitions per set increases, and rest periods between sets become shorter [22]. This can result in local muscle lactate accumulation even after a single set. Where multiple sets are performed, longer sets and shorter rest periods between sets are associated with greater increases in blood lactate (which can reduce muscle contractility) and declines in muscle glycogen [23,24].

Metabolic and hormonal effects of exercise in diabetes

Type 1 diabetes

Higher amounts of habitual physical activity are associated with decreased incidence of diabetes-related complications and reduced mortality in individuals with type 1 diabetes mellitus (T1DM) [25]. In a prospective study, 548 patients with T1DM were followed for 7 years to ascertain the prevalence of complications and mortality [25]. The risk of microvascular complications varied inversely with self-reported activity levels at baseline. Sedentary male patients were three times more likely to die than the active ones after adjusting for age, body mass index, smoking and diabetic complications (Figure 23.2) [25]. A similar, although statistically non-significant, relationship was also seen in females.

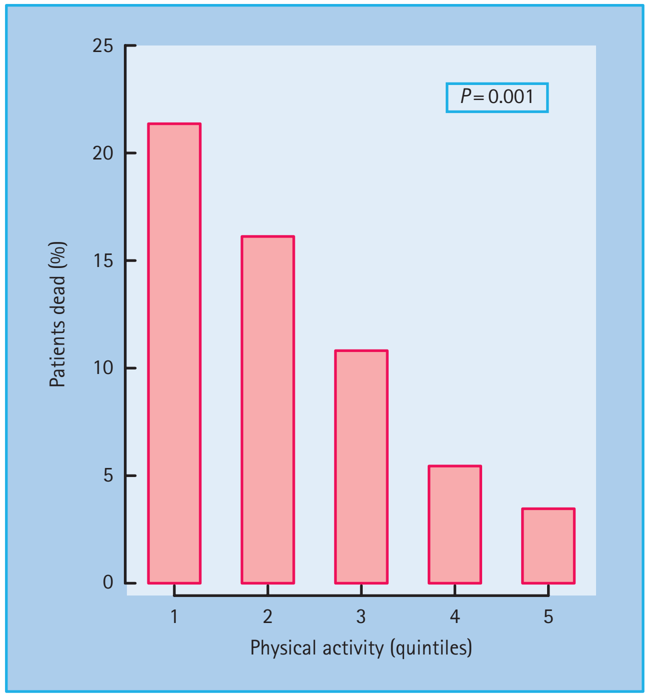

Figure 23.2 Proportion of men who died during a 7-year follow-up period among 548 patients with type 1 diabetes, stratified according to the physical activity quintile. Quintile cut-offs were <398; 398–1000; 1000–2230; 2230–4228 and >4228 kcal/week. The difference among groups is highly significant. Data from Moy *et al.* [25].

Studies have also shown an inverse association between physical activity and the severity of several complications in T1DM [26–29]. A longitudinal study of 1680 individuals with T1DM showed that self-reported leisure time physical activity levels were inversely correlated with measures of glycemic control and insulin sensitivity [29]. Women with diabetes in the study with low levels of leisure time physical activity tended to have poor glycemic control when compared with those with higher activity levels. Estimates of insulin sensitivity were also higher among more active men and women [29]. A follow-up study involving 1945 individuals with T1DM reported that those involved in either little leisure time physical activity or low intensity activity were more likely to have impaired renal function, a higher degree of proteinuria, as well as greater rates of retinopathy and cardiovascular disease when compared with more frequently and more vigorously active counterparts [28]. More recently, a randomized trial showed that the onset of diabetic peripheral neuropathy can be prevented and its progression delayed over a 4-year period by regular exercise [26].

General metabolic considerations

The intensity and duration of exercise, the patient's level of blood glucose control, the type, dose and site of pre-exercise insulin

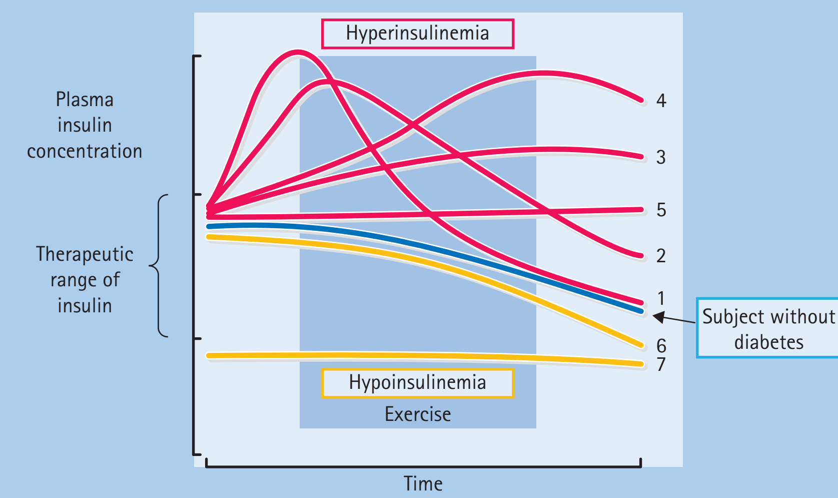

Figure 23.3 Plasma insulin levels may vary widely during exercise in patients with insulin-treated diabetes, whereas healthy subjects (as well as patients with type 2 diabetes) show a steady decline during moderate intensity aerobic exercise. Hyperinsulinemia and hypoglycemia may occur when the peak action of a short-acting insulin analog (1), conventional soluble (regular) insulin (2) or intermediate-acting insulin (3) occurs during exercise, or if exercise itself accelerates the absorption from the injection site (4). Steady-state but elevated plasma insulin concentrations may occur if intermediate or long-acting insulin has been injected a few hours before exercise, or if the patient is using an insulin pump (5). Declining levels (6) or hypoinsulinemia (7) occur when the previous injection depots are exhausted.

injections, and the timing of the previous insulin injection and meal relative to the exercise can all affect the response of an individual with diabetes to physical activity (Figure 23.3). Accordingly, blood glucose concentrations can decline (the most common response in moderate aerobic exercise), increase (particularly in very intense exercise) or remain unchanged (Table 23.2). Whereas insulin secretion declines during moderate intensity aerobic exercise in individuals without diabetes, compensating for exercise-induced increased muscle insulin sensitivity, this physiologic decline in insulinemia cannot occur in T1DM because all insulin is exogenous. Insulin attenuates the appropriate rise in hepatic glucose production and further accelerates the exercise-induced stimulation of glucose uptake into the contracting muscle.

Hyperinsulinemia may occur for several reasons (Figure 23.4). Regular insulin injected a few hours previously may exert its peak action during exercise. This effect is exaggerated if the previously injected limb is exercised, as insulin absorption is accelerated by exercise [30]. Moreover, the use of intermediate or long-acting insulin generally produces higher peripheral insulin levels than would be found in an individual without diabetes of similar body composition. The result is often hypoglycemia, unless the insulin dose prior to exercise is decreased or extra carbohydrate is consumed. Hyperinsulinemia can also prevent the normal increase in lipid mobilization during exercise, leading to reduced availability of non-esterified fatty acids as a fuel.

Conversely, if insulin levels are too low, the inhibitory effect of insulin on hepatic glucose production and its stimulatory effect on glucose uptake are both reduced. In addition, the counter-regulatory response (catecholamines, glucagon, growth hormone, cortisol) to exercise is higher than normal under conditions of insulin deficiency [30]. The overall result is markedly increased hepatic glucose production and diminished glucose utilization by the exercising muscle, thus leading to hyperglycemia.

Table 23.2 Factors determining the glycemic response to acute exercise in people with type 1 diabetes.

Blood glucose tends to decrease if:
- Hyperinsulinemia exists during moderate intensity aerobic exercise
- Exercise is prolonged (>30–60 minutes)
- No extra snacks are taken before or during moderate intensity exercise

Blood glucose generally remains unchanged if:
- Exercise is brief and mild to moderate in intensity
- Appropriate snacks are taken before and during moderate intensity exercise

Blood glucose tends to increase if:
- Hypoinsulinemia exists during exercise
- Exercise is very intense
- Excessive carbohydrate is taken before or during exercise

Aerobic exercise in type 1 diabetes

Effects of regular aerobic exercise training in type 1 diabetes

Insulin sensitivity is reduced to varying degrees in patients who have had T1DM for several years [31]. Participation in a regular exercise training program improves whole-body insulin sensitivity in these patients, as it does in those without diabetes, which may help to induce and prolong remission in newly presenting T1DM [32]. It has been difficult to ascertain whether or not regular aerobic exercise improves glycemic control in T1DM, as outcomes of exercise intervention have been inconsistent. While some studies have demonstrated improvements, albeit not statistically significant, in blood glucose control as measured by decreases in HbA_{1c} [33,34], most studies have either not shown any changes [35] or have produced increases in HbA_{1c} [36]. The main reason for this is probably excessive reductions of insulin dose or disproportionate carbohydrate consumption before exercise in an effort to avoid hypoglycemia. It is important to note

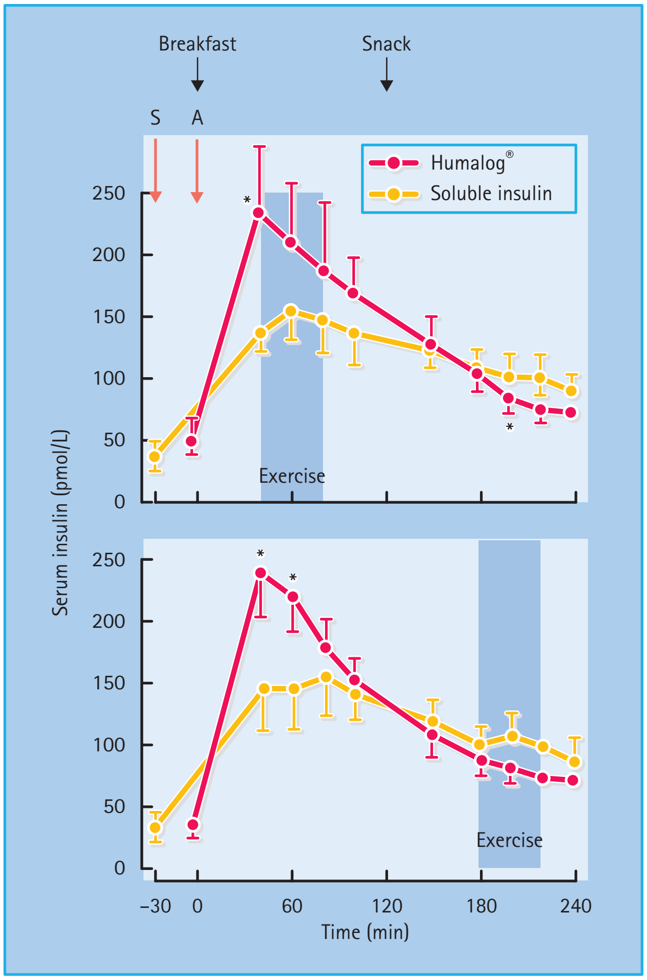

Figure 23.4 Insulin concentrations during exercise depend on the type of insulin and the time interval between the injection and exercise. Serum insulin concentrations during early exercise are higher after injection of the lispro (Humalog) insulin analog (A) than after conventional soluble insulin (S), whereas the opposite situation applies during delayed exercise. Soluble insulin was injected 30-min and lispro insulin 5-min after breakfast, and exercise was started either 40-min (early) or 180-min (late) after breakfast. *$P < 0.05$. Data from Tuominen *et al.* [163].

that participants in several studies still experienced many exercise-related benefits including lower body fat percentage [34], improved muscle mass [37], increased aerobic capacity [34,36,37], improved lipid profiles [34,36,37] and greater insulin sensitivity (with a consequent lower need for exogenous insulin) [36].

Fuel metabolism during aerobic activity

Under ideal conditions of low insulin and euglycemia, fuel selection during mild to moderate exercise can be very similar in people with T1DM as those without diabetes, with a gradual shift towards lipid oxidation with increasing exercise duration [38]. Conversely, if the levels of circulating insulin are too high, muscle, adipose and hepatic cells will continue to take up glucose for storage rather than leaving it available for working muscles. While glucagon can still be produced in individuals with T1DM [39], the glucagon : insulin molar ratio at the portal vein may not reach the level necessary for adequate levels of hepatic glucose production to occur. Compared with individuals without diabetes, those with T1DM may demonstrate a lower reliance on hepatic glycogen stores during low intensity aerobic activity [40]. If the rate of glucose appearance in the system is not high enough to supply the demand, blood glucose levels will drop, thereby increasing the potential for hypoglycemia [39].

Levels of insulinemia and glycemia will also affect the fuels used during aerobic activity. Hyperinsulinemia can lead to a greater reliance on exogenous glucose utilization during moderate aerobic exercise, without sparing glycogen stores [41]. In a study where insulinemia was kept constant, the contribution of carbohydrates to overall energy metabolism during exercise was greater in hyperglycemia than in euglycemia [38]. The shift towards greater carbohydrate metabolism during exercise in hyperglycemia was accompanied by a blunted cortisol and growth hormone response. Insulin, glucagon and catecholamine levels were comparable between conditions [38]. Overall, individuals with T1DM seem to have a greater reliance on muscle glycogenolysis and gluconeogenesis to produce fuel during physical activity than their non-diabetic counterparts [40,42].

Despite the complexities of glucoregulation, well-motivated people with T1DM can successfully undertake several hours of exhaustive aerobic exercise if appropriate insulin and dietary adjustments are made [43–45]. After prolonged exercise, patients may be prone to hypoglycemia for many hours, even extending overnight and to the following day. This can be explained by persistently enhanced glucose uptake by the exercised muscles to replenish the depleted glycogen stores [43]; however, after certain types of prolonged exercise, such as a marathon run, increased lipid oxidation can persist, as occurs in healthy individuals [44]. In this case, the use of glucose as a fuel and insulin sensitivity are reduced after exercise, thereby decreasing the risk of post-exercise hypoglycemia [44]. It should also be noted that individuals who experience frequent bouts of hypoglycemia (whether exercise-related or not), may have further blunting of counter-regulatory responses to exercise, potentially creating a vicious cycle of hypoglycemic events [46–50].

Effects of regular anaerobic exercise training in type 1 diabetes

There is currently a gap in the literature as to how physical and metabolic adaptations to regular anaerobic training in individuals with T1DM differ from those of non-diabetic individuals. People with T1DM who participate in competitive sports may find that their glycemic control worsens, probably secondary to an irregular schedule of very vigorous exercise, insulin dose reduction and high carbohydrate consumption [51]. In spite of the elevation in physical fitness and $\dot{V}O_{2max}$, these individuals may not have increased insulin sensitivity, but instead show enhanced use of non-esterified fatty acids as a fuel [51]. It is likely that many individuals with T1DM will have to compromise some tightness of control to be able to participate effectively in competitive sports and high intensity activities, to avoid the fear of hypoglycemia during exercise. Whether or not this affects their physical and metabolic adaptations to these types of activities requires further research. More details on carbohydrate and insulin adjustments for exercise can be found later in this chapter.

Fuel selection during high intensity exercise

Extremely strenuous acute exercise may cause hyperglycemia even in the presence of normal or high insulin levels. High counter-regulatory hormone action (especially catecholamines) can stimulate glucose production beyond the limits of peripheral utilization [52–56]. In addition, in T1DM the normal physiologic doubling of insulin concentration after cessation of such intense exercise cannot occur, resulting in more prolonged hyperglycemia [52,55,56]. Augmented lipid mobilization and ketogenesis in the liver increase blood ketone-body concentrations; the hypoinsulinemic individuals may thus become hyperketonemic and ketonuric after exercise.

Several recent studies have shown that such high intensity exercise is effective in increasing blood glucose levels and thereby delaying or preventing hypoglycemia related to moderate exercise even when performed in extremely short bouts [57–61]. Bussau *et al.* [57,58] showed that a 10-second sprint performed either prior to [58] or at the completion of [57] 20 minutes of low intensity cycling significantly attenuated post-exercise drops in blood glucose, when compared with exercise sessions where no sprint was performed. Similar results were found by Guelfi *et al.* [59,60] where post-exercise blood glucose levels remained higher after cycling exercise sessions where 4-second sprints were performed every 2 minutes versus those where the participants cycled continuously at constant moderate intensity (Figure 23.5). The post-exercise window in these studies, however, was limited to 120 minutes. One small study using continuous glucose monitoring systems (CGMS) found a trend towards late onset post-exercise hypoglycemia after high intensity activity [62]; however, further studies with larger sample sizes will be necessary to confirm this.

Resistance exercise

Effects of regular resistance exercise training in type 1 diabetes

There is a paucity of information regarding the outcomes of training programs consisting of only resistance exercise in individuals with T1DM. The one study completed to date involved a cross-over design with 10 weeks of heavy resistance exercise three times a week followed by a 6-week period with no resistance training, or vice versa [63]. Mean HbA_{1c} was 6.9 ± 1.4% (52 ± 15 mmol/mol) at the end of the non-resistance exercise period and 5.8 ± 0.9% (40 ± 10 mmol/mol) at the end of the 10-week resistance exercise training period. Serum cholesterol and self-monitored glucose levels were also lower at the end of the resistance training period.

One study has compared the effects of 12 weeks of resistance training with those of a comparable period of aerobic training in individuals with T1DM [64]. While both groups showed decreases in waist circumference, reduced insulin dosage and lower self-monitored blood glucose after the training period, these variables only reached significance in the aerobically trained group. However, HbA_{1c} levels showed a statistically significant increase in the aerobic training group (from 8.7 ± 1.6 to 9.8 ± 1.8%; 72–84 mmol/mol), while a non-significant decrease (from 8.2 ± 2.9 to 7.6 ± 1.6%; 60–66 mmol/mol) was found in the resistance training group.

A handful of pre–post studies have also examined the effects of combined aerobic and resistance training programs in individuals with T1DM [65–67]. Outcomes of these studies were generally positive, with benefits including lower HbA_{1c} [65,67], decreased blood pressure [65,66], improved nerve conduction [65], higher cardiorespiratory fitness [67], greater muscular strength [67], higher lean body mass [65,67] and improvements in lipid profiles [67]. Nevertheless, it should be noted that the interpretation of these studies is limited by their lack of

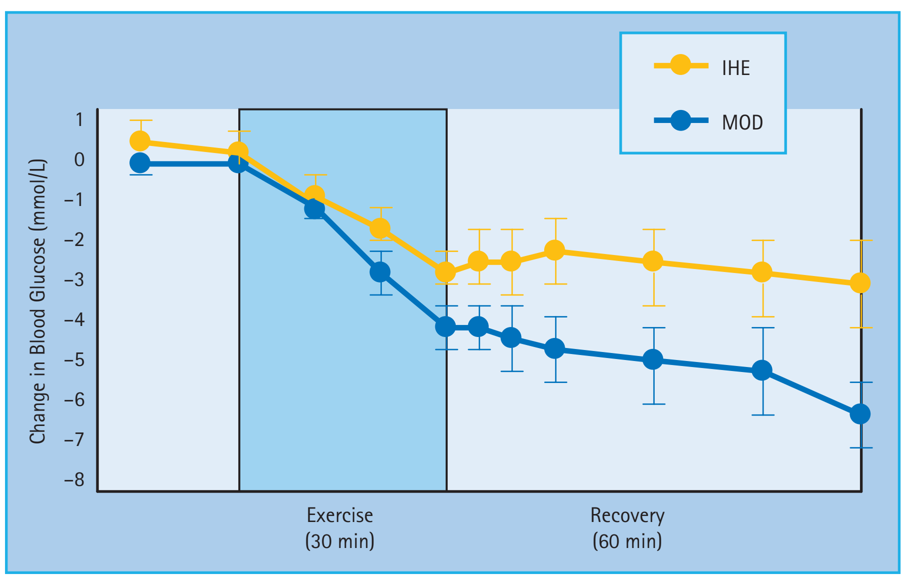

Figure 23.5 Effect of 30 min of intermittent high intensity exercise (IHE) or moderate continuous exercise (MOD) on normalized blood glucose levels. Data from Guelfi *et al.* [59].

Table 23.3 Clinical trials involving resistance exercise with people with type 1 diabetes mellitus.

Source	No. of participants (n)	Sessions/week, no of weeks	No. of exercises	No. of sets, rest interval and intensity of exercise	HbA_{1c} [mean (SD)]
Type 1 diabetes – resistance training only					
Durak *et al.* (1990) [63]	n = 8 (T1DM)	3 sessions/week; 10 weeks Training sessions after 5:00 PM Lunch time injections and food intake completed no later than 12:00 PM	5 lower body and 10 upper body exercises	3–7 sets (varied with exercise; 30 s to 2 min rest interval between sets, pyramid-type training routine used with 12 RM used for set 1, decreased with subsequent sets with addition of weight	6.9 (1.4) after 6 weeks with no resistance training and 5.8 (0.9)* after 10 weeks of resistance exercise training (cross-over design)
Type 1 diabetes – combined aerobic and resistance training					
Mosher *et al.* (1998) [67]	n = 10 (T1DM) n = 11 (control)	3 sessions/week; 12 weeks All training sessions performed between 1100 and 1200. Subjects consumed an evening meal supplemented by 5–10 g complex CHO ≈ 2 h before exercise	Aerobic and weight training circuit; circuit composed of 5 aerobic stations, each followed by 5 strength and callisthenic exercises	4–5 min of aerobic exercise (75–85% HR_{max}) followed by 5 strength and callisthenic exercises (upper and lower body strength exercises performed at 50% and 40% of 1-RM, respectively). Aerobic exercise followed by a 1-min recovery period. 5 successive 30-s strength and callisthenic exercises were then performed	Control group (without diabetes): 4.50 (0.45) to 4.47 (0.60) Intervention group (type 1 DM): 7.72 (1.26) to 6.76 (1.07)
Type 1 diabetes – comparison of aerobic training to resistance training					
Ramalho *et al.* (2006) [64]	n = 7 (aerobic) n = 6 (resistance)	3 sessions/week; 12 weeks All sessions supervised	Aerobic training: Treadmill walking or running Resistance training: 4 upper and 4 lower body exercises using weight machines	40 min walking/running with intensity increasing progressively every 2 weeks from 60–70% HR_{max} at week 0 to 70–90 HR_{max} at 12 weeks 10 min stretching and 30 min resistance exercise training. 3 sets of 8 to 12 reps progressing from 60 to 80% of 1-RM. 60-s rest between sets	Aerobic group: 8.7 (1.6) to 9.8 (1.8)* Resistance group: 8.2 (2.9) to 7.6 (1.6)

CHO, carbohydrate; DM, diabetes mellitus; HR_{max}, maximum heart rate; 1-RM, maximum weight that can be lifted once; T1DM, type 1 diabetes mellitus.
* Indicates significant difference from baseline at $P < 0.05$.
The following equation should be used to convert HbA_{1c} to IFCC Units: DCCT result (%) = (0.0915 × IFCC result in mmol/mol) +2.15.

concurrent diabetic control groups. All studies involving resistance exercise interventions in individuals with T1DM (alone or in combination with aerobic exercise) published by March 1, 2009 are outlined in Table 23.3.

Fuel selection during resistance exercise

Very little is known about the acute hormonal and resulting blood glucose responses to resistance exercise in individuals with T1DM. Resistance exercise in individuals without diabetes produces elevated epinephrine levels, which enhance hepatic glucose production, resulting in an increase in blood glucose levels [68]. As studies involving high intensity exercise demonstrate that catecholamine responses are similar in young fit individuals with and without T1DM [55,57,59], it is likely that resistance-type activities are associated with increases in blood glucose during and after exercise. However, the authors are unaware of any published research examining the glycemic response during and after this type of exercise in people with T1DM.

Type 2 diabetes

Exercise and type 2 diabetes prevention

In large prospective cohort studies, higher levels of physical activity and/or cardiorespiratory fitness have consistently been associated with reduced risk of developing T2DM [69–81]. After adjustment for confounding variables, participants who exercised the most had a 25–60% lower risk of subsequent diabetes compared to those who were most sedentary. This was true regardless of the presence or absence of additional risk factors for diabetes such as hypertension, parental history of diabetes and obesity in most studies. Comparable magnitudes of risk reduction are seen with walking compared to more vigorous activity when total energy expenditures are similar [77].

Several clinical trials have demonstrated that supervised structured physical activity programs, with or without concomitant dietary interventions, reduce the risk of developing T2DM in individuals with impaired glucose tolerance (IGT) [82–85]. In the non-randomized Malmö trial [82,86,87], 260 men aged 47–49 years with IGT were identified through population screening and were offered a 6–12-month intervention including supervised exercise programs and dietary counseling. Among those attending a 5-year follow-up examination, 21% of the control participants (those who had declined the intervention) had developed diabetes, compared to only 11% of those receiving the intervention. Over 12 years, mortality among the controls was 14.0 per 1000 person-years, but only 6.5 per 1000 person-years in the intervention group [87].

In the Da Qing IGT and Diabetes Study [83], 577 people with IGT from 33 clinics were cluster-randomized by clinic to diet only, exercise only, diet and exercise or control, and followed for 6 years. The cumulative incidence of T2DM was 68% in controls, but only 44%, 41% and 46% in the diet, exercise, and diet and exercise groups, respectively. Li *et al.* [88] recently published a follow-up paper to the Da Qing Study [83] assessing the long-term effect of the 6-year intervention on the risk of diabetes. They found that, 14 years after the end of the trial, incidence of diabetes remained significantly lower in those originally randomized to one of the intervention groups versus controls.

In the Finnish Diabetes Prevention Study [89], 523 Finnish adults with IGT were randomized to an exercise and diet intervention or control. Patients in the control group had one meeting per year with a physician and dietitian, at which they received standard advice on diet and exercise. The intervention group received individualized exercise plans, thrice-weekly supervised facility-based aerobic and resistance exercise, and seven 1-hour meetings with a dietitian focusing on weight reduction, reduced fat intake and reduced total caloric intake. At 4 years, 22% of the control group and only 10% of the intervention group had developed diabetes – a 58% risk reduction. Three years after the end of the study, participants originally randomized to the intervention group continued to have much higher levels of physical activity than those originally in the control group [90]. Incidence of diabetes in the individuals who were previously in the intervention group remained 43% lower than in those who were previously in the control group [90].

In the US-based Diabetes Prevention Program [85], 3234 American men and women with IGT were randomly assigned to placebo, metformin or a lifestyle modification program. The goals of the lifestyle modification program included a 7% weight loss and at least 150 minutes of exercise per week. The lifestyle intervention included 16 lessons in the first 24 weeks, covering diet, exercise and behavior modification (delivered one-on-one by a case manager). A minimum of two supervised exercise sessions per week and at least monthly contact with the study personnel were maintained thereafter. The study was ended after a mean of 2.8 years of follow-up, 1 year earlier than originally planned, because of clear-cut superiority of the lifestyle arm. Cumulative incidences of T2DM were 11.0 per 100 person-years in the placebo group, 7.8 per 100 person-years in the metformin group and only 4.8 per 100 person-years in the intensive lifestyle group. The risk of T2DM was 58% lower in the lifestyle group than in the placebo group, and 39% lower than in the metformin group. An epidemiologic analysis of the data by Hamman *et al.* determined that, after adjusting for changes in self-reported diet and physical activity, there was a 16% reduction in diabetes risk for every kilogram of weight loss among the lifestyle intervention participants [169]. Increased physical activity was a significant predictor of weight loss and had an important role in weight maintenance. In addition, participants who met the goal of more than 150 minutes of moderate exercise per week had a 46% reduction in diabetes risk.

Aerobic exercise in type 2 diabetes

Regular exercise is associated with reduced morbidity and mortality in T2DM. A 10-year follow-up of a large prospective cohort study including 347 individuals with diabetes and 1317 individuals without diabetes) found that the lowest aged-adjusted all-cause death rate was among those with diabetes who walked a mile or more daily [91]. Similarly, a prospective study of 1263 men with diabetes followed over 12 years found that, compared with the least fit men (bottom 20% as determined by maximal treadmill testing), those with moderate cardiorespiratory fitness had a 60% lower risk of cardiovascular and overall mortality [79]. The effect of fitness on mortality was considerably greater than the effect of body mass index. Further follow-up of this cohort confirmed these findings [92,93]. Greater habitual exercise was also associated with a lower subsequent risk of cardiovascular disease among women in the Nurses Health Study [94].

Effects of regular aerobic exercise training in type 2 diabetes

Exercise-induced stimulation of glucose uptake may involve many factors (Figure 23.6), as reviewed by Ivy *et al.* [95]. They include increased post-receptor insulin signaling [96], increased glucose transporter protein and mRNA [97], increased activity of glycogen synthase [98] and hexokinase [99], decreased release and increased clearance of free fatty acids [95], increased muscle glucose delivery as a result of increased muscle capillary density [99–101], changes in muscle composition favoring increased glucose disposal [99,102,103] and changes in adipose tissue mass and distribution [104]. Decreases in visceral fat result in decreased concentrations of tumor necrosis factor α [105] and free fatty acids [106], leading to decreased insulin resistance.

Inflammatory markers present in the bloodstream predict the onset of cardiovascular disease and related complications. Regular aerobic exercise training is generally associated with improvements in metabolic profile and results in anti-inflammatory effects in individuals with T2DM [107,108]. Exercise training in individuals with T2DM has been reported to produce anti-atherogenic blood lipid changes and to reduce other risk factors for coronary heart disease (hypertension, obesity, coagulation abnormalities) in some but not in all studies [109–115]. For instance, in elderly patients with relatively advanced atherosclerosis, exercise training may be less effective in retarding atherogenesis [113]. The prophylactic value of exercise against atherosclerosis might be greater in younger healthier individuals who have not yet developed disease.

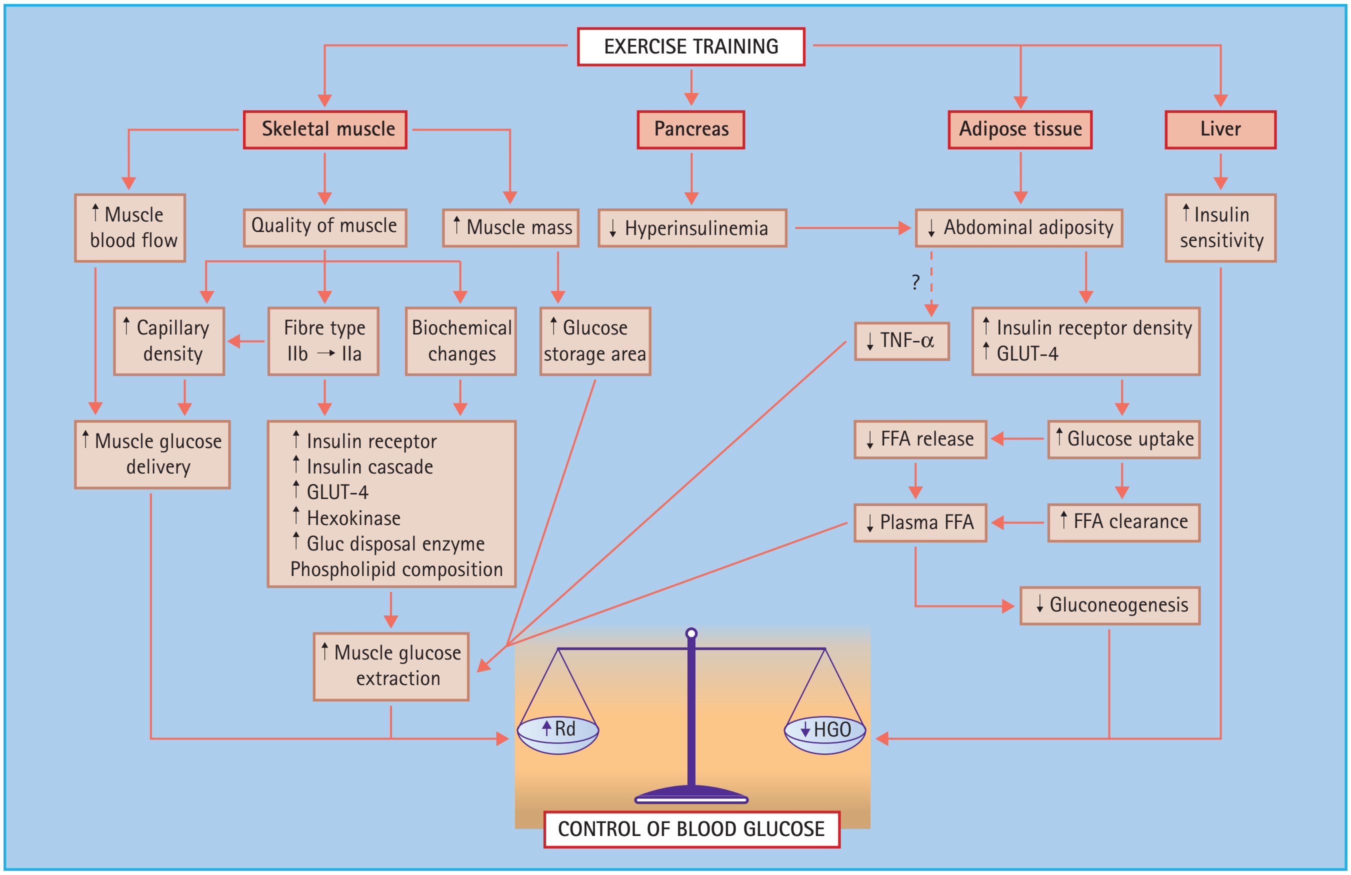

Figure 23.6 Mechanisms by which exercise training may improve insulin action and the control of blood glucose in type 2 diabetes. FFA, free fatty acid; GLUT, glucose transporter; HGO, hepatic glucose output; Rd, glucose uptake; TNF-α, tumour necrosis factor-α. Reproduced from Ivy *et al.* [95], with permission from Lippincott Williams & Wilkins.

Fuel metabolism during aerobic activity

Individuals with T2DM are characterized by both hepatic and peripheral insulin resistance and by hyperinsulinemia in the fasting state. During moderate intensity exercise, peripheral glucose uptake usually rises more than hepatic glucose production, and the blood glucose concentration tends to decline [116]. At the same time, plasma insulin levels fall, and the risk of exercise-induced hypoglycemia in individuals with T2DM not taking exogenous insulin is relatively small, even during prolonged exercise [117]. It has been shown that moderate intensity exercise decreases glycogen content similarly in individuals with and without diabetes [118]; however, glycogen and plasma glucose decreases more in obese individuals with diabetes compared with those without diabetes whether obese or lean [118]. The effects of moderate exercise on glucose tolerance and insulin sensitivity are similar whether the activity is performed in single versus multiple bouts of the same total duration [119]. Moderate aerobic exercise has also been shown to attenuate the increase in circulating triglyceride levels following ingestion of a high fat meal [120].

Anaerobic exercise in type 2 diabetes

Fuel metabolism during high intensity activity

If individuals with T2DM perform strenuous glycogen-depleting exercise, both peripheral and hepatic insulin sensitivity are increased and remain so for 12–16 hours thereafter [121]. Following maximal aerobic exercise (>85% $\dot{V}O_{2max}$), sedentary individuals with T2DM demonstrate higher levels of blood glucose compared with sedentary individuals without diabetes and active individuals with diabetes [122].

Resistance exercise

Effects of regular resistance exercise training in type 2 diabetes

The age-related decline of muscle mass may cause reduced insulin sensitivity. Resistance training can potentially counteract the age-associated decrease in muscle mass, and therefore warrants important consideration as an effective intervention in managing T2DM [95,123]. Resistance training has been shown to improve insulin sensitivity and glucose metabolism in both men and women [124–130] and has also been associated with modest improvements in lipid profiles [63,67,128]. In longitudinal studies involving healthy untrained adults, insulin responses to an oral glucose challenge are lower in both healthy younger [124,131] and older [131,132] individuals after resistance training. Resistance exercise, and its resulting increase in lean body mass, has also been associated with greater resting energy expenditure in older adults [133]. Whether or not this occurs in T2DM is still uncertain [134].

Studies published by Dunstan *et al.* [135] and Castaneda *et al.* [136], involving high intensity resistance training resulted in decreases in HbA_{1c} of 1.2% (13 mmol/mol) with a 26-week program, accompanied by a moderate energy restriction diet [135] and 1.0% (11 mmol/mol) with a 16-week program [136], respectively. Meta-analyses have confirmed that resistance training exercise effectively reduces HbA_{1c} in individuals with T2DM [137,138]. In a meta-analysis of clinical trials examining the effect of aerobic and resistance exercise interventions on glycemic control and body mass in T2DM (Figure 23.7), Boulé *et al.* [138] found no difference in HbA_{1c} between aerobic and resistance exercise. Overall, participants in exercise intervention groups had HbA_{1c} levels that were 0.66% (7 mmol/mol) lower post-intervention than those in control groups. Post-intervention body weight did not differ between exercise and control participants, suggesting that exercise is beneficial in its own right, not merely as an avenue to reduce body weight. Snowling & Hopkins [137] found in a more recent meta-analysis that the two types of exercise had similar effects on glucose control. An overview of clinical trials involving resistance exercise (both on its own and when combined with aerobic exercise training) in T2DM is provided in Table 23.4.

Fuel metabolism during resistance exercise in type 2 diabetes

The authors were unable to find any published research on fuel metabolism during resistance exercise in T2DM.

Combined aerobic and resistance exercise training

Snowling & Hopkins [137] reviewed controlled studies published in May 2006 or earlier that assessed the effects of aerobic training, resistance training or combined training on glucose control in T2DM. All three exercise modalities showed clinically significant reductions in HbA_{1c}, while the combined training showed an additive and large beneficial effect on insulin sensitivity. The HbA_{1c} meta-analyzed mean decreased by 0.8% (9 mmol/mol) in the combined exercise training studies compared to 0.7% (8 mmol/mol) and 0.5% (5 mmol/mol) for the aerobic and resistance training groups, respectively.

Three recent studies have investigated the combination of aerobic training and resistance training exercise on glycemic control [19,139,140] and one other study has examined the combined exercise effect on cardiac function in T2DM [114,115]. Study outcomes have been consistent, showing increases in aerobic fitness and muscular fitness [114,115,134] as well as improvements in body composition [139,140] and cardiovascular disease risk profile [19,114,115,139,140].

Balducci *et al.* [139] assessed the effects of a supervised facility-based combined aerobic and resistance exercise training program on glycemic control, cardiovascular disease (CVD) risk factors and body composition in previously sedentary individuals with T2DM. Participants (aged 60–70 years) were randomized into an exercising intervention group (three times per week) or a non-exercising control group for 1 year. The exercise group showed a significant decrease in body mass index, fasting glucose, HbA_{1c} and improved lipid profile. In addition, those in the exercise group using medication showed a decreasing trend in medication use whereas the control group showed an increasing trend. A study of shorter duration by Cauza *et al.* [140] also found improvements in HbA_{1c} and lipid profiles in a combined aerobic and resistance exercise intervention group in comparison to a sedentary control group.

In the Diabetes Aerobic and Resistance Exercise (DARE) trial [19], 251 previously sedentary individuals with T2DM were randomized into four arms: aerobic exercise training; resistance exercise training; combined aerobic and resistance exercise training; or a non-exercising control group. Intervention groups performed exercise three times per week for 6 months in community facilities, supervised by personal trainers. Improvements in glycemic control were found in all exercise groups, and the improvements in the combined aerobic and resistance exercise group were significantly greater than with either aerobic training or resistance training alone. In contrast to this, a smaller study with participants randomized to combined exercise, aerobic exercise or non-exercise control did not find significant differences between the two exercising groups [141]. In this smaller study, there was no provision to keep dietary intake and/or medication use the same among groups, and statistical power was far more limited than in the DARE trial.

In the Italian Diabetes and Exercise Study [142], 606 individuals with T2DM from 22 clinics in Italy were randomized to a full year of either exercise counseling alone or supervised facility-based combined aerobic and resistance exercise training twice weekly plus exercise counseling. The group receiving the combined aerobic and resistance exercise training had significantly more favorable results for glycemic control, lipids, body composition, blood pressure and estimated cardiovascular risk than the group receiving exercise counseling alone. This study provides compelling evidence for incremental benefits of supervised structured exercise over exercise counseling alone for people with T2DM.

Recommendations for exercise in diabetes

Most types of exercise can be recommended to both individuals with T1DM and T2DM. Exercise does not need to be strenuous, and even regular walking has beneficial effects [79,94]. Specific recommendations and guidelines for exercise in individuals with diabetes have been published by the American Diabetes Association [143,144] and the American College of Sports Medicine [145]. These and other guidelines are summarized in Tables 23.5–23.7. Advice should be tailored to individuals, taking

Source (year)	Period	No. of subjects/HbA_{1c} Mean (SD) (%) Exercise group	Control group	Weight (%)	WDM, % (95% CI)
Exercise vs non-exercise control					
Dunstan *et al.* 1998	Baseline	11/8.2 (1.7)	10/8.1 (1.9)	5.8	0.1 (−1.43 to 1.63)
	Post	11/8.0 (1.7)	10/8.3 (2.2)	3.7	−0.3 (−1.98 to 1.38)
Honkola *et al.* 1997	Baseline	18/7.5 (1.3)	20/7.7 (1.3)	19.9	−0.2 (−1.03 to 0.63)
	Post	18/7.4 (0.9)	20/8.1 (1.3)	20.9	−0.7 (−1.41 to 0.01)
Wing *et al.* 1998	Study 1				
	Baseline	10/9.7 (1.6)	12/9.4 (1.7)	7.1	0.3 (−1.08 to 1.68)
	Post	10/8.0 (1.3)	12/7.9 (1.7)	6.7	0.1 (−1.15 to 1.35)
	Study 2				
	Baseline	13/10.6 (1.8)	15/10.9 (1.9)	7.1	−0.3 (−1.69 to 1.09)
	Post	13/8.2 (1.1)	15/9.0 (1.2)	15.5	−0.8 (−1.63 to 0.03)
Tessier *et al.* 2000	Baseline	19/7.5 (1.2)	20/7.3 (1.7)	16.2	0.2 (−0.72 to 1.12)
	Post	19/7.6 (1.2)	20/7.8 (1.5)	14.4	−0.2 (−1.05 to 0.65)
	Exercise and diet vs. diet alone				
Dunstan *et al.* 1997	Baseline	14/8.3 (1.5)	12/8.0 (1.5)	10.2	0.3 (−0.86 to 1.46)
	Post	14/7.7 (1.5)	12/7.9 (1.5)	7.8	−0.2 (−1.36 to 0.96)
	Exercise alone vs. control				
	Baseline	11/8.8 (2.7)	12/8.1 (1.4)	4.3	0.7 (−1.08 to 2.48)
	Post	11/8.1 (2.7)	12/7.6 (1.4)	3.3	0.5 (−1.28 to 2.28)
Lehmann *et al.* 1995	Baseline	16/7.5 (1.6)	13/7.8 (1.7)	9.3	−0.3 (−1.51 to 0.91)
	Post	16/7.5 (1.6)	13/8.4 (1.7)	7.1	−0.9 (−2.11 to 0.31)
Raz *et al.* 1994	Baseline	19/12.5 (2.9)	19/12.4 (4.0)	2.8	0.1 (−2.12 to 2.32)
	Post	19/11.7 (2.6)	19/12.9 (4.2)	2.1	−1.2 (−3.42 to 1.02)
Ronnemaa *et al.* 1986	Baseline	13/9.6 (1.6)	12/10.0 (1.5)	9.3	−0.4 (−1.62 to 0.82)
	Post	13/8.6 (1.9)	12/9.9 (1.7)	5.2	−1.3 (−2.71 to 0.11)
Mourier *et al.* 1997	Baseline	10/8.5 (1.9)	11/7.4 (1.0)	7.9	1.1 (−0.21 to 2.41)
	Post	10/6.2 (0.6)	11/7.7 (1.3)	13.6	−1.5 (−2.38 to −0.62)
Overall	**Baseline**	**154**	**156**	**100**	**0.08 (−0.29 to 0.45)**
	Post	**154**	**156**	**100**	**−0.66 (−0.98 to −0.34)**
Exercise and diet vs non-exercise, non-diet controls					
Agurs-Collins *et al.* 1997	Baseline	32/11.0 (1.7)	32/10.0 (1.9)	43.4	1.0 (0.12 to 1.88)
	Post	31/9.5 (1.8)	27/10.3 (1.9)	34.0	−0.8 (−1.76 to 0.16)
Vanninen *et al.* 1992	Men				
	Baseline	21/7.1 (1.5)	24/7.3 (1.7)	38.7	−0.2 (−1.13 to 0.73)
	Post	21/7.0 (1.9)	24/7.4 (1.6)	29.0	−0.4 (−1.43 to 0.63)
	Women				
	Baseline	17/7.1 (1.5)	16/8.1 (2.4)	17.9	−1.0 (−2.38 to 0.38)
	Post	17/6.2 (1.0)	16/7.2 (1.6)	37.0	−1.0 (−1.92 to −0.08)
Overall	**Baseline**	**70**	**72**	**100**	**0.18 (−0.40 to 0.76)**
	Post	**69**	**67**	**100**	**−0.76 (−1.32 to −0.20)**

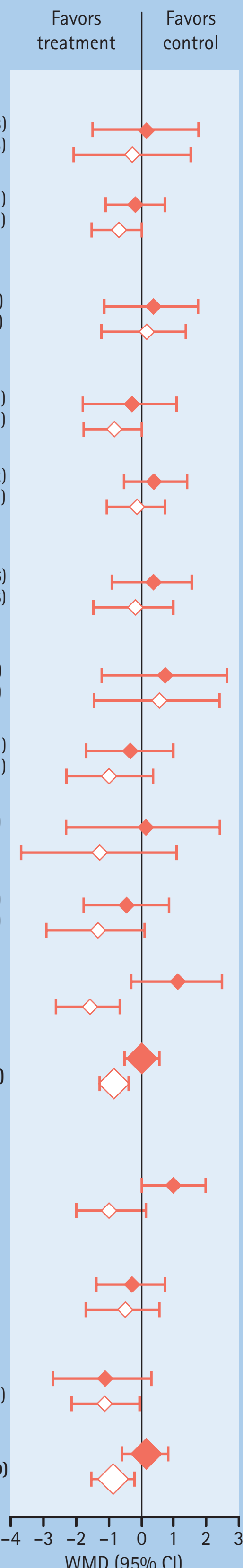

Figure 23.7 Meta-analysis of exercise interventions in type 2 diabetes and the effect of glycemic control, as measured by HbA_{1c}. CI, confidence interval; WMD, weighted mean difference. Studies are placed in ascending order of the intensity of the exercise intervention and represent the mean difference and the 95% CI for baseline and post-intervention measurements. Exercise vs. non-exercise control: baseline values, the chi-squared test for heterogeneity was 4.78 ($P = 0.91$) and the z score for overall effect was 0.45 ($P = 0.65$); post-intervention values, the chi-squared test for heterogeneity was 9.76 ($P = 0.46$) and the z score for overall effect was 4.01 ($P < 0.001$). Exercise and diet vs. control: baseline values, the chi-squared test for heterogeneity was 6.77 ($P = 0.03$) and the z score for overall effect was 0.60 ($P = 0.55$); post-intervention values, the chi-squared test for heterogeneity was 0.74 ($P = 0.69$) and the z score for overall effect was 2.66 (P = 0 008). The following equation should be used to convert HbA_{1c} to IFCC Units: DCCT result (%) = (0.0915 × IFCC result in mmol/mol) +2.15. Data from Boulé *et al.* [138].

Table 23.4 Clinical trials involving resistance exercise with people with type 2 diabetes mellitus.

Source	No. of Participants (n)	Sessions/week, no. of weeks	No. of exercises	No. of sets, rest interval and intensity of exercise	HbA_{1c} [Mean (SD)]
Type 2 diabetes – resistance training only					
Castaneda *et al.* (2002) [136]	n = 31 (resistance) n = 31 (control)	3 sessions/week; 16 weeks	3 lower and 2 upper body exercises	Control group: no exercise Intervention group: 3 sets of 8 reps at 60–80% 1RM	Control group: 8.4 (SE 0.3) to 8.3 (SE 0.5) Intervention group: 8.7 (SE 0.3) to 7.6 (SE 0.2)** (Note: all subjects were Hispanic-American)
Dunstan *et al.* (2002) [135]	n = 19 (resistance) n = 17 (control)	3 sessions/week; 26 weeks	1 core, 2 lower and 6 upper body exercises	Control group: 5 min cycling and 30 min of static stretching ("placebo exercise") Intervention group: 1) initial 3 sessions: 8–10 reps at 50–60% of 1-RM; 2) increased to 3 sets in the subsequent 3 sessions; and 3) 8–10 reps at 75–85% of 1-RM for the duration of the intervention	Control group (placebo exercise): decreased 0.4 (0.8) Intervention group (type 2 DM): decreased 1.2 (1.0)**† (Note: all subjects followed a moderate energy restriction diet)
Type 2 diabetes – combined aerobic and resistance exercise training					
Balducci *et al.* (2004) [139]	n = 62 (aerobic and resistance) n = 58 (control)	3 sessions/week; 52 wks	6 exercises for trunk, upper body and lower body for resistance exercise component	Control group: no exercise Intervention group: 30 minutes of aerobic activity at 40–80% HRR and 30 minutes of resistance exercise: 3 sets of 12 reps at 40–60% 1-RM	Control group: No significant change from baseline Intervention group: 8.31 (1.73) to 7.1 (1.16)‡
Cauza *et al.* (2006) [140]	n = 10 (aerobic and resistance) n = 10 (control)	3 sessions/week; 32 wks	1 core, 1 lower and 4 upper body exercises for resistance exercise component	Control: either aerobic or resistance exercise for the first 16 weeks, no exercise for the last 16 weeks Intervention group: either aerobic or resistance exercise for the first 16 weeks, combined exercise for the last 16 weeks Aerobic component consisted of 20–30 minutes of cycling (60% $\dot{V}O_{2peak}$). Resistance component consisted of 3 sets of 10–15 reps	Control group: Baseline: 8.1 (0.5) 16 wks: 7.5 (0.4) 32 wks: 8.7 (0.6)* Intervention group: Baseline: 8.1 (0.8) 16 weeks: 6.9 (0.4) 32 weeks: 6.2 (0.2)**

Continued on p. 370

Table 23.4 *Continued*

Source	No. of Participants (n)	Sessions/week, no. of weeks	No. of exercises	No. of sets, rest interval and intensity of exercise	HbA_{1c} [Mean (SD)]
Cuff *et al.* (2003) [166]	n = 10 (aerobic and resistance) n = 9 (aerobic only) n = 9 (control)	3 sessions/week; 16 wks	3 lower and 2 upper body exercises for resistance exercise component	Control group: no exercise Combined group: total duration of 75 min. Aerobic component: 60–75% HRR and resistance exercise component: 2 sets of 12 reps Aerobic group: 75 minutes at 60–75% HRR	Control group: decreased 0.03 Combined group: decreased 0.1 (0.22) Aerobic group: 0.1 (0.11)
Lambers *et al.* (2008) [141]	n = 17 (aerobic and resistance) n = 18 (aerobic) n = 11 (control)	3 sessions/week; 12 wks	Unavailable	Control group: no exercise Aerobic group: 60–85% HRR Combined group: aerobic component plus 3 sets of 10–15 reps at 60–85% of 1-RM for the resistance component	Control group: 6.7 (0.97) to 7.0 (0.88) Aerobic group: 7.4 (1.70) to 7.0 (1.61) Combined group: 7.4 (1.45) to 6.9 (1.20)*
Loimalaa *et al.* (2003) [115]	n = 24 (aerobic and resistance) n = 25 (control)	2 sessions/week; 12 months	8 for trunk, upper body and lower body exercises for resistance exercise component	Control group: no exercise Combined group: 3 sets of 10–12 reps at 70–80% of 1-RM for resistance component plus 65–75% $\dot{V}O_{2max}$ for aerobic exercise component	Control group: 8.0 (1.3) to 8.3 (1.4) Combined group: 8.2 (2.1) to 7.6 (1.4)**
Sigal *et al.* (2007) [19]	n = 64 (aerobic and resistance) n = 60 (aerobic) n = 64 (resistance) n = 63 (control)	3 sessions/week; 26 weeks	1 core, 2 lower and 4 upper body exercises for resistance exercise component	Control group: no exercise Aerobic group: 15–45 min at 60–75% HR_{max} Resistance group: 2–3 sets of 7–9 reps Combined group: aerobic component plus resistance training component	Control group: 7.44 (1.38) to 7.51 (1.47), significant difference of change $P < 0.05$ from aerobic group and resistance group Aerobic group: 7.41 (1.50) to 6.98 (1.50)**, significant difference of change $P < 0.05$ from combined group Resistance group: 7.48 (1.47) to 7.18 (1.52)**, significant difference of change $P = 0.001$ from combined group Combined group: 7.46 (1.48) to 6.56 (1.55)†, significant difference of change $P < 0.05$ compared to aerobic training group and $P = 0.001$ compared to resistance training group

HR_{max}, maximum heart rate; HRR, heart rate reserve; $\dot{V}O_{2max}$, maximal oxygen uptake; 1-RM, maximum weight that can be lifted once.

* Indicates significant difference from baseline at $P < 0.05$.

** Indicates significant difference of change compared to control group at $P < 0.05$.

† Indicates significant difference from baseline at $P < 0.01$.

‡ Indicates significant difference from baseline at $P < 0.0001$.

The following equation should be used to convert HbA_{1c} to IFCC Units: DCCT result (%) = (0.0915 × IFCC result in mmol/mol) +2.15.

Table 23.5 Exercise recommendations.

Aerobic training				Resistance training		
Reference	**Frequency**	**Intensity**	**Duration**	**Frequency**	**No. of exercises**	**Sets/Repetitions**
Healthy/sedentary adults						
2008 CDC Guidelines [1]	At least 3 days/ week	Moderate/vigorous	Accumulate 150 min/week of continuous moderate activity or 75 min/week of intense activity	At least 2 days/week	Involve all major muscle groups	At least 1 set of 8–12 reps, 2–3 sets preferable
2007 ACSM/AHA [146]	3–5 days/wk	Moderate/vigorous Start at lower intensity if initially unfit or sedentary	30–60 min of moderate aerobic activities or 20–30 min vigorous aerobic activity. Can be accumulated in bouts lasting >10 min	2 days/week (non-consecutive)	8–10 exercises involving major muscle groups	1 set, 8–12 reps
Elderly persons (65 or older)						
2007 ACSM/AHA Physical Activity Guidelines [147]	3–5 days/week	Moderate/vigorous	30–60 min of moderate aerobic activities or 20–30 minutes of vigorous aerobic activity Can be accumulated in bouts lasting >10 min	2 days/week (non-consecutive	8–10 exercises involving major muscle groups	1 set, 10–15 reps
Cardiac patients						
1995 AHA Exercise Standards [167]	Minimum 3–5 days/week	50–60% $\dot{V}O_{2max}$ or HRR	Minimum of 30 min of continuous physical activity	2–3 days/week	8–10 exercises involving major muscle groups	1 set, 10–15 reps
2006 AACVPR [168]	3–5 days/week	50–60% $\dot{V}O_{2max}$ or HRR	30–45 min of continuous or intermittent aerobic activity	2–3 days/week	Incorporate all major muscle groups	1 set, 10–15 reps
Individuals with type 2 diabetes						
2006 ADA Consensus Statement on Physical Activity/ Exercise and Type 2 Diabetes [144]	3–5 days/week No more than 2 consecutive days without exercise	50–70% HR_{max} (moderate) or >70% HR_{max} (vigorous)	at least 150 min/week of moderate aerobic exercise and/ or at least 90 min/week of vigorous aerobic exercise	3 days/week	Targeting all major muscle groups	Progressing to 3 sets of 8–10 reps

AACVPR, American Association of Cardiovascular and Pulmonary Rehabilitation; ACSM, American College of Sports Medicine, ADA, American Diabetes Association; AHA, American Heart Association; CDC, Centers for Disease Control.

Table 23.6 Precautions and advice regarding exercise in diabetes.

Relative contraindications

- If receiving insulin treatment: sports in which hypoglycemia would be dangerous (e.g. diving, climbing, single-handed sailing, motor racing). Individuals participating in this type of sport must test the capillary blood glucose concentration very frequently and take strict measures to avoid hypoglycemia. Whenever possible, another person should be close by and able to assist when needed. Note that the Amateur International Boxing Association prohibits people with insulin-requiring diabetes from participating in boxing
- With untreated proliferative retinopathy: very strenuous exercise, because of the risk of hemorrhage. However, a patient whose retinopathy has been adequately treated with laser therapy and is regularly followed by a retinal specialist can probably undertake strenuous exercise without undue risk

Cautions

Cardiovascular disease: there is a high prevalence of this in middle-aged and older people with diabetes. Middle aged and older individuals with diabetes wishing to undertake exercise more vigorous than brisk walking should probably first have a maximal exercise stress test with continuous electrocardiography monitoring. Patients with abnormal stress test results should be referred for additional cardiac investigations

Table 23.7 Guidelines for exercise diabetes mellitus.

General guidelines
- Exercise used to reduce weight should be combined with dietary measures
- Moderate intensity aerobic exercise should be part of the daily schedule if possible, accumulating 150 minutes each week. More vigorous exercise ($\geq$70% of $\dot{V}O_{2max}$) undertaken 3–5 times per week will provide additional health benefits. Previously sedentary patients may have to build up exercise volume gradually, starting with as little as 5–10 min/day
- Multiple shorter exercise sessions lasting at least 10 min each in the course of a day are probably as useful as a single longer session of equivalent length and intensity
- Include low intensity warm-up and cool-down periods especially if vigorous exercise is undertaken
- Exercise should be appropriate to the person's general physical condition and lifestyle
- Resistance exercise performed 2–3 times per week will provide benefits over and above those of aerobic training. The studies reporting greatest impact of resistance exercise on HbA_{1c} have had subjects progress to 3 sets of approximately 8 resistance type exercises at relatively high intensity (8 repetitions performed at the maximum weight that can be lifted 8 times)
- Use proper footwear and, if appropriate, other protective equipment
- Avoid exercise in extreme heat or cold
- Inspect feet before and after exercise

Specific considerations for exercise in type 1 diabetes
Avoid hypoglycemia during exercise by:
- Avoiding heavy exercise during peak insulin action
- Using non-exercising sites for insulin injection
- If using multiple daily injections reducing pre-exercise insulin dosages by 20–50% or more if necessary. If using an insulin pump, decrease basal rate and/or amount of last bolus before exercise. These reductions should be individualized and based on blood glucose monitoring; not all individuals will require an insulin dose reduction
- Monitor glycemia before, during and after exercise as necessary
- Taking extra carbohydrate before and hourly during exercise. This amount should be individualized and based on blood glucose monitoring
- After prolonged exercise, monitor glycemia and take extra carbohydrate to avoid delayed hypoglycemia. The quantity required can be estimated using the semi-quantitative technique (1 g CHO/kg body weight/hour of activity) or by consulting tables of energy requirements for particular activities
- Use extra caution in monitoring glycemia if exercise is being performed within 24 hours of a hypoglycemic episode

Specific considerations for exercise in type 2 diabetes
- Hypoglycemia is less common during exercise than in type 1 diabetes, and extra carbohydrate is therefore usually unnecessary
- Patients taking insulin or sulfonylureas may need to reduce the doses of these medications during days when they exercise. Such adjustments should be guided by glucose monitoring

into account their interests, personal goals, levels of fitness, possible contraindications and available resources. If the patient is interested in sports or is even a professional athlete, diabetes should not interfere with his or her athletic career, and treatment should be adjusted according to the demands of the activity. For activities and competitions considered to be higher risk for individuals with insulin-treated diabetes (e.g. car racing, flying, boxing), individual governing bodies should be consulted regarding restrictions in competition. It is also important to note that insulin is considered a banned substance by the World Anti-Doping Agency, and that elite level athletes with diabetes will be required to apply for a Therapeutic Use Exemption certificate prior to competition.

Aerobic training

It is generally recommended that all individuals accumulate at least 150 minutes of moderate aerobic activity, and/or at least 90 minutes of vigorous aerobic exercise every week, and that this activity be spread over at least 3–5 days [143,146,147]. A day's activity need not occur in a single session, but may be accumulated in bouts of 10 or more minutes at a time, performed throughout the day. Performing progressively greater amounts of moderate activity (in excess of the minimum 150 minutes) is associated with progressively greater benefits. Studies have also shown that group exercise environments can provide motivation, social support and enjoyment for individuals starting and maintaining exercise training programs [148].

Resistance training

A recent meta-analysis showed that resistance exercise can be safe and effective even for vulnerable cardiac patients [149]. High intensity weightlifting in healthy older men (mean age 64 years) caused less circulatory stress than walking up 192 stairs [150]. Weightlifting was not associated with increased proliferative retinopathy risk in the Wisconsin Epidemiologic Study of Diabetic Retinopathy, although the statistical power of the study was limited [151]. When properly performed, resistance training can be safe and enjoyable while at the same time producing significant health benefits.

Resistance training programs should be progressive in nature. Previously sedentary individuals should always start with a low intensity workload. It is important that individuals receive proper instruction on lifting and breathing techniques used during resistance training in order to maximize the benefits of the exercise, while at the same time minimizing the risk of injury. The authors recommend that beginners use weight machines in the initial stages of a training program, before moving on to free-weight exercise once sufficient strength has been gained and appropriate lifting techniques have been mastered [21]. Warming up before each training session with low intensity aerobic activity or light sets of selected exercises is also thought to help minimize the risk of injury [21]. When multiple exercises are performed in a workout, exercises involving the use of large muscle groups (e.g. lunges or pull-downs) should be performed before exercises requiring the use of smaller muscle groups (e.g. calf raises or bicep curls). Multiple joint exercises such as squats, chest press or seated row should precede single joint exercises such as leg extensions or tricep extensions [21]. Although one set of each exercise may be sufficient to increase muscle strength [152], the resistance exercise studies with the greatest HbA_{1c} reductions [63,153,154] have used three or more sets of each exercise. The authors therefore suggest that three sets of each exercise be performed on three non-consecutive days per week (assuming the same muscle groups are being targeted) to ensure the best possible metabolic benefits [1,143,146,147].

Special considerations in people with long-term complications of diabetes

Some advanced long-term complications of diabetes may limit individuals' ability to perform certain types of exercise safely, but should not prevent them from becoming active at all. Where proliferative or severe non-proliferative retinopathy is present, it has been suggested that individuals may want to avoid vigorous activity (both aerobic and resistance) because of the possible increased risk of triggering vitreous hemorrhage or retinal detachment [155]. Mild to moderate activity can still be encouraged for these individuals. In individuals with peripheral neuropathy, weight-bearing activity could, in theory, increase the risk of skin breakdown and infection as well as Charcot joint destruction [156,157]; however, a recent study showed that the incidence of foot ulcers was no greater in individuals with diabetic neuropathy than in individuals without neuropathy after a 6-month walking intervention [158]. As exercise training is important in delaying the progression of peripheral neuropathy [26], it can be recommended that these individuals stay active by walking, swimming or bicycling. Before changing or adding activities for individuals with autonomic neuropathy, it is generally recommended that these individuals undergo cardiac investigation [159,160], as the risk of CVD in such individuals is high. Decreased cardiac responsiveness to exercise, postural hypotension, unpredictable carbohydrate delivery increasing the risk of hypoglycemia where gastroparesis is present and impaired thermoregulation have all been associated with autonomic neuropathy, warranting caution in the practice of certain activities in this population [157]. The authors know of no evidence justifying any specific exercise restrictions in nephropathy.

Insulin and oral hypoglycemic agent adjustments for exercise

In individuals with T1DM or T2DM treated with multiple insulin injections, the dosage of short-acting insulin taken before exercise can be reduced instead of using dietary adjustment. The amount of such reduction, if required, should be tailored to each individual, based on blood glucose monitoring results before, during and after exercise, at least until the pattern of glucose response to exercise for that individual is known. Depending on the intensity and duration of exercise, the reduction required can be as much as 75% of the usual dose [30], although dose reductions of 20–50% are more typical. The insulin formulation (short- or intermediate-acting) to be reduced is that which has its maximal action at the time of exercise. For brief, very intense exercise such as competitive hockey, weightlifting or sprinting, there may be no need to reduce insulin dose. If the blood glucose concentration increases during exercise, the insulin dosage may need to be slightly increased or the injection schedule changed in order to achieve higher plasma insulin concentrations during exercise. Use of an insulin pump may be advantageous for many physically active individuals, as circulating insulin levels can be more easily adjusted to accommodate meals, snacks and exercise [161]. The variability of glucose absorption is also generally decreased, lowering the risk of hypoglycemia [161]. Decreases in insulin for pump users may or may not need to be accompanied by carbohydrate supplementation [161].

In individuals with T2DM, exercise does not usually cause hypoglycemia, and in obese individuals it can be a valuable tool to improve glycemic control and assist with weight maintenance. For these reasons, carbohydrate supplementation is usually unnecessary with exercise (Table 23.7). If blood glucose declines rapidly during exercise, as may occur in individuals taking oral hypoglycemic agents or insulin, the dosage of the drug should be reduced or the drug withheld on exercising days.

Carbohydrate supplementation

There are few controlled studies regarding the appropriate type and amount of carbohydrates to be taken with exercise in people with T1DM. A reasonable starting point is to take approximately 15 g carbohydrate before and 15–40 g at 30–60-minute intervals during longer exercise sessions. Supplementation should be advised if pre-exercise blood glucose levels are <5.6 mmol/L. The amount of carbohydrate consumed should be adjusted according to blood glucose monitoring results; some individuals will not require any carbohydrate supplementation whereas some will require large amounts. During strenuous exercise, at least part of this can be taken as a sucrose-containing beverage. If exercise is performed post-prandially, there is less need for carbohydrate supplementation, whereas larger snacks should be taken if some hours have elapsed since the last meal. Also, the risk of hypoglycemia and subsequent need for exogenous carbohydrate supplementation decreases as the amount of time since the last insulin injection increases [162,163].

A recent review by Perkins & Riddell [161] describes several methods of carbohydrate supplementation. The goal is for the patient to consume a quantity of oral carbohydrate that matches the amount of glucose being used by the working muscles during activity. This can involve either a basic approach (where 15–30 g of carbohydrate is consumed for every 30–60 minutes of exercise), a semi-quantitative approach (consuming approximately 1 g glucose/kg body weight/hour of activity) or a quantitative method, based on standardized tables of energy requirements for specific activities, intensities and individual body weights [161]. The latter is referred to as "excarbs" (extra carbohydrates for exercise), developed originally by Walsh & Roberts [164]. However, it should be noted that only a finite amount of carbohydrate (40–60 g/hour) can be absorbed while the body is moderately or vigorously active [165], requiring that a certain amount of the carbohydrate be consumed prior to exercise or during recovery. Regular glucose monitoring is still recommended, especially where the participant is experimenting with new types, intensities or durations of exercise training.

Acknowledgments

The authors are grateful for the contributions of Veiko Koivisto to this chapter in previous editions of this textbook. Jane Yardley was supported by a Doctoral Student Award from the Canadian Diabetes Association and funds from the Ottawa Hospital Research Institute Research Chair in Lifestyle Research. Glen Kenny holds a University Research Chair from the University of Ottawa. Ronald Sigal is a Senior Health Scholar of the Alberta Heritage Foundation for Medical Research.

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