Exercise and the Development of the Artificial Pancreas: One of the More Difficult Series of Hurdles

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Abstract

Regular physical activity (PA) promotes numerous health benefits for people living with type 1 diabetes (T1D). However, PA also complicates blood glucose control. Factors affecting blood glucose fluctuations during PA include activity type, intensity and duration as well as the amount of insulin and food in the body at the time of the activity. To maintain equilibrium with blood glucose concentrations during PA, the rate of glucose appearance (Ra) to disappearance (Rd) in the bloodstream must be balanced. In nondiabetics, there is a rise in glucagon and a reduction in insulin release at the onset of mild to moderate aerobic PA. During intense aerobic -anaerobic work, insulin release first decreases and then rises rapidly in early recovery to offset a more dramatic increase in counterregulatory hormones and metabolites. An “exercise smart” artificial pancreas (AP) must be capable of sensing glucose and perhaps other physiological responses to various types and intensities of PA. The emergence of this new technology may benefit active persons with T1D who are prone to hypo and hyperglycemia.

Keywords

exercise, artificial pancreas, metabolism, insulin

The primary deficiency in type 1 diabetes (T1D) is the autoimmune destruction of the insulin producing β -cells within the pancreas. Other more subtle endocrine disturbances also exist in T1D making glucose control challenging, either at the time of diagnosis or as the disease duration increases, including dysregulated glucose counterregulatory hormone secretion during hyper and hypoglycemia.¹ The prevalence of T1D has been increasing worldwide by 2-5% and its prevalence is approximately 1 in 300 in the United States by 18 years of age.² Between 80% and 90% of all new cases of T1D are in children and adolescents and the management can be quite challenging from both a behavioral and physiological perspective.³ Life expectancy in T1D is increasing in the developed world with the implementation of intensive insulin therapy,⁴ but most patients develop micro- and macrovascular complications. T1D patients have a 4-8 times higher risk of developing cardiovascular disease (CVD) compared to those without diabetes^{5,6} and most patients will develop some form of chronic kidney disease that appears to predict early all-cause mortality.⁷

Insulin therapy for T1D is currently an imperfect solution, since exogenous insulin delivery, either by subcutaneous multiple daily injections or continuous subcutaneous insulin infusion (CSII) does not completely restore physiological insulin replacement into the portal circulation. Moreover,

numerous factors including food intake, physical activity (PA) levels, stress, and illness can cause fluctuations in blood glucose concentrations in T1D and thus insulin needs can change rapidly and sometimes unpredictably.

Because of the numerous health and fitness benefits associated with increased PA, including reduced CVD risk, patients with T1D of all ages are encouraged to be physically active. PA is a blanket term that includes structured exercise and nonexercise activities associated with daily living that are above the resting state. The term “exercise” is assigned to activity that is planned, structured, and engaged in to improve 1 or more aspects of one’s physiological fitness and/or health status.⁸⁻¹⁰ Regular PA increases insulin sensitivity, improves

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the blood lipid profile, lowers body adiposity, and increases muscular strength and endurance.¹¹ However, glucose turnover is dramatically influenced by PA acutely and glucose control often deteriorates both during the activity and in recovery.

Over the past 10 years, research developments have focused on creating a “closed-loop” automated insulin delivery system to better mimic islet physiology (ie, the artificial pancreas [AP]). The AP system is comprised of a few essential components including insulin pump therapy, continuous glucose monitoring, rapid-acting insulin analogs and a computer-based control algorithm.¹² The AP design uses 1 or more algorithms that generate insulin dose recommendations based on blood glucose levels that are detected by a continuous glucose monitor.¹³ The ultimate goal of the AP system is to improve overall diabetes management through a more intelligent delivery of insulin needs based largely on a feedback system (ie, sensing glucose levels and directional changes). However, a complex physiology (which normally includes the feed forward control of insulin secretion from the pancreatic islet), the limitations in the manner in which insulin is delivered, and the lag time of current glucose sensing makes the development of an “exercise smart” AP a major hurdle. Many clinical studies with various control algorithms have been tested; however, disturbances in glycemia, especially the risk of low blood sugars (hypoglycemia) remain an issue.^{12,14} The purpose of this review is to provide an overview of the cardiorespiratory responses to different forms of PA that can be monitored in real-time and highlight the typical metabolic characteristics of aerobic, anaerobic, and mixed forms of PA to help better inform the development of the exercise smart AP.

Current Strategies for Managing Glycemia During Exercise

At present, there is no perfect strategy for maintaining glucose control during or after exercise in individuals with T1D. This is likely because different forms of exercise exist, the timing of exercise relative to food and insulin administration is varied and patients appear to have their own unique glycemic responses to PA. However, recommendations for normalizing glycemia around mild to moderate aerobic-type exercise usually involve insulin dose reductions (basal and/or bolus insulin) as well as increased carbohydrate ingestion^{15,16} while more intense anaerobic exercise may necessitate an insulin correction for hyperglycemia.¹⁷ High glycemic index snacks can limit reductions in glucose concentrations if consumed during aerobic exercise,¹¹ while the consumption of low glycemic index foods combined with a reduction in insulin dosage before the onset of exercise can protect against hypoglycemia and may minimize the likelihood of postprandial hyperglycemia.^{18,19} None of these strategies are guaranteed to work for all patients, in all situations and different types of PA require modifications to these general strategies.

Overview of PA Classifications, Types, and Intensities

PA includes any movement produced by the skeletal muscle that results in increased energy expenditure, often expressed as kilocalories (kcal), from the resting state (sitting or lying down).⁴ The relative energy expenditure and effort of PA is typically described using the following global descriptors: sedentary or inactive, light, moderate, vigorous, and vigorous to maximum (Table 1).

The body's ability to effectively respond to the variable intensities of PA is dependent on the continuous interplay between the aerobic and anaerobic systems. Although both energy systems contribute to total metabolism in most kinds of PA, a greater or lesser reliance of each system is dictated primarily by the intensity of the activity. At low intensity continuous rates of energy expenditure, the aerobic metabolic system is dominant. As the rate of energy demand increases, there is a concomitant greater reliance on both the aerobic and anaerobic metabolic systems. At the initiation of muscle contractions, and at very intense contraction rates, the main fuel used is muscle phosphocreatine and muscle glycogen, metabolized via non-oxidative phosphorylation (ie, anaerobic metabolism). As the exercise duration increases, there is a greater reliance on aerobic metabolism of both carbohydrate and lipids. During all forms of aerobic PA, plasma glucose is a key source of energy provision. During intense aerobic work and during anaerobic work, plasma glucose uptake/utilization is minimal.

The hormonal and metabolic responses to the different forms of PA are distinct. Aerobic PA is typically characterized from light-to-vigorous intensity, and can be performed for an extended period of time, depending on the individual's aerobic abilities. An example of light-to-moderate intensity PA includes purposeful walking at a pace of 15 to 20 minutes per mile (3.0-4.0 mph) or jogging (5.0-6.0 mph), which is associated with an intensity ranging from 3-6 metabolic equivalents (METs), or ~50-75% of an individual's age-predicted maximum heart rate (HR).²⁰ During these activities, circulating insulin levels drop and glucose counterregulatory hormones rise gradually.¹

Mixed aerobic-anaerobic PA classically consists of intermittent moderate-to-vigorous and vigorous-to-maximum intensity bouts, generally interspersed with light-to-moderate intensity PA. Some examples of this type of PA include individual and team sports (eg, tennis, soccer, baseball) or interval training. Frequently, anaerobic energy supply (muscle phosphagens, anaerobic glycolysis of muscle glycogen) is called on during an endurance event, such as in an all-out effort in the final stages of a distance run, swim, or cross-country skiing race. These types of mixed activities are associated with workloads upward of 6-10+ METs, corresponding to about 75-100% of an individual's maximum HR (Table 1). Given the high rate of energy demand required for intense muscle contractions, there is a greater reliance on muscle phosphagens and anaerobic glycolysis. Even maximal sprints, jumping events, or maximal lifts lasting for less than 30

Table 1a. Common Endurance Physical Activity Intensity Descriptors (Nonresistance).

	Intensity	%HR _{max}	Borg RPE (6-20 scale)	Modified RPE (0-10 scale)	METs	Breathing rate	Body temperature	Example activity	Typical exercise duration
Predominantly aerobic physical activity	Inactive (sedentary)	<50	<10	0-1.5	<2	Normal	Normal	Sitting watching TV, working on the computer	Several hours
	Light	50-63	10-11	1.5-2	2 to <5	Slight increase	Start to feel warm	Dusting, light gardening	Several hours
	Moderate	64-76	12-13	3-4	5 to <7	Greater increase can still carry on a conversation	Warmer	Brisk walking, walking on an incline, light jog	Hours
Predominantly anaerobic metabolism	Vigorous	77-93	14-16	5-7	7 to <10	More out of breath, difficult to carry on a conversation	Quite warm	Running	Minutes/hours
	Vigorous- maximum	>93	17-19	8-9	≥ 10	Out of breath, unable to carry on a conversation	Hot	Running fast	Minutes
	Maximal- supermax	100	20	10		Completely out of Breath	Very hot/ perspiring heavily	Sprinting all-out	Seconds

Source: Table modified with permission from Warburton et al.²⁰

Note: MET = metabolic equivalents (units), relative to resting metabolism; %HRmax = percentage maximum heart rate; %RM = percentage repetition maximum; RPE= rating of perceived exertion.

Table 1b. Common Resistance Exercise Intensity Descriptors.

	Resistance activities % of 1RM (# of RM)	Example activities	Typical exercise duration
Light	30-49 (>100RM)	Watering the lawn, general house cleaning, ironing	Several hours
Moderate	50-69 (>10, ≤100RM)	Raking leaves, vacuuming, carrying a light load of laundry or groceries (~5 lbs)	Hours
Hard	70-84 (6 to 10RM)	Wood splitting, shoveling snow	Minutes
Very hard	>84, <100 (2 to 6RM)	Carrying groceries upstairs	Seconds-minutes
Maximal	100 (1RM)	Lifting a heavy load that you can only lift once	Milliseconds-seconds

Source: Table modified with permission from Warburton et al.²⁰

Note: 1RM= 1 repetition maximum: refers to the maximum amount of weight lifted *one time* using proper form during a standard weight-lifting activity.

seconds have a small aerobic component during the exercise and then a prolonged period of increased oxygen consumption in the recovery period.²¹ In fact, these short intermittent bouts of “supramaximal” exercise increase oxygen consumption for 4 hours or more.^{22,23} These types of activities can have less predictable effects on the endocrine system but typically promote less of a reduction in insulin secretion with a more dramatic rise in glucose counterregulatory hormones (catecholamines, glucagon, cortisol, and growth hormone).¹ Pure sprint based activities cause a dramatic rise in counterregulatory hormones and a rise in insulin secretion early in recovery.¹¹

Exercise smart AP hurdle 1: PA comes in a variety of different forms and intensities, each with their own unique mix and pattern of energy utilization. Blood glucose turnover

rates increase during exercise anywhere from 2- to 10-fold, depending on the form of exercise. To address this hurdle, the exercise smart pump may need to assess the type of PA performed and adjustments in the insulin delivery algorithm need to occur in real-time.

The Impact of Quality and Quantity of Physical Activity on 24-Hour Energy Expenditure

Total daily energy expenditure (TEE) is a function of basal (resting) metabolic rate (BMR), dietary thermogenesis, non-exercise PA (standing, the basic body movements of daily living), and structured exercise. Although the BMR composes a greater proportion of the TEE, it is a fairly stable component

Figure 1. Representative activity report from a physically active individual (A) and the daily caloric expenditure, and its various subcomponents, in a less active (B) and more active (B') individual. As shown in panel A, PA levels are often spontaneous, intermittent in nature, at varying intensities and for varying lengths. During light activity, glucose turnover may be elevated 2-fold compared to rest. During more intense activity, glucose turnover may be elevated 10-fold above rest.

that cannot be easily manipulated in the short term.²¹ In contrast, the effect of PA on TEE is quite variable, both between and within individuals (Figure 1A). In comparison to a sedentary person (Figure 1B), the active individual who exercises regularly expends close to 50% of their TEE as PA (Figure 1B'). Since PA is often interspersed throughout the day (and differs from day to day), the development of an exercise smart AP may require both discrete PA “triggers” and PA intensity threshold monitors.

Energy expenditure during PA, and thus blood glucose turnover rate, are influenced by a number of factors including; intensity, duration, mode, weight-bearing/non weight-bearing activity, and fitness level. Intensity and duration are important factors affecting energy expenditure. The duration of exposure to PA will dictate the intensity or work rate and, therefore the overall energy expenditure and substrate selection (ie, the types and ratios of carbohydrates and lipids utilized). For example, if 2 individuals of similar body composition and body mass participate in a marathon; the speed they select to work at will dictate both the relative intensity and the total PA time. If 1 individual runs at 7.0 mph

while the other walks at 3.5 mph, the individual that runs expends more energy and utilizes more glucose as a fuel, even though he or she is exposed to the stimulus for half of the time. Thus, these 2 individuals may not require the same percentage reduction in circulating insulin levels for this task and likely not for the same time duration. In theory, the person exercising at a higher intensity (7.0 mph) would be expected to have lower insulin requirements since the glucose utilization rate would be considerably higher (higher glucose utilization by contracting muscle means less need for insulin). On the other hand, the increase in glucose counterregulatory hormones (glucagon, cortisol, growth hormone, and catecholamines) associated with the higher relative exercise intensity may offset the higher rate of glucose disappearance (R_d) by increasing the glucose rate of appearance (R_a) from the liver. As the exercise duration increases, however, a greater reliance on fuels from outside of the muscle necessitates a greater reduction in circulating insulin levels with time. As such, the person who is walking will likely require a more gradual reduction in circulating insulin levels during their longer activity. This will be a

Figure 2. Typical hormonal and blood glucose responses to different types and intensities of exercise in individuals with and without T1D. In the resistance/strength training modality, 3 repetitions of 4 different muscle groups are shown (ie, muscle group A-D). Note: the glucose trends for individuals with T1D are variable and sometimes unpredictable.

challenge for the development of the exercise smart AP for a number of reasons since it is difficult to drop insulin levels in the circulation rapidly with CSII and because PA sensors that can categorize relative exercise intensity have yet to be integrated into the AP algorithm.

Exercise smart AP hurdle 2: TEEs and the various subcomponents of PA differ markedly from person to person and from day to day. Sensing when the activity occurs and the intensity of the activity might be a challenge for the exercise smart AP. To overcome this hurdle, accurate PA sensors that categorize effort may need to be developed and integrated.

Types of Physical Activity, Glucose Turnover, and Insulin Requirements

PA of different types and intensities cause distinct patterns of fuel utilization and hormonal responses (Figure 2). The hormonal and blood glucose responses to PA are often abnormal in T1D.

Individuals Without T1D

Aerobic exercise can increase glucose Ra and Rd by up to ~10-fold.^{24,25} This precise match in Ra and Rd maintains

blood glucose concentrations during prolonged moderate intensity exercise in most individuals who do not have T1D by a rise in glucagon secretion and a reduction in insulin secretion, along with less critical changes in other glucose counterregulatory hormones.²⁵ During prolonged aerobic exercise, blood glucose contributes up to about 40% of the total energy provision, equivalent to ~1 gram of plasma glucose being oxidized per minute in 80kg (~176lbs) adult males.²⁶ In contrast, during vigorous intensity aerobic exercise^{25,27,28} and during brief high intensity anaerobic work,²⁹⁻³¹ glucose Ra exceeds glucose Rd, resulting in a transient rise in blood glucose concentration even in “control” individuals, which is soon corrected by a rise in insulin secretion (Figure 2). Obviously, without endogenous insulin replacement into the portal vein, even with accurate glucose sensing and with some sort of feedforward mechanism to regulate insulin secretion from a CSII device, mimicking the normal insulin response to exercise in T1D will be a challenge.

Exercise smart AP hurdle 3: The relationship between exercise intensity and insulin requirement to maintain euglycemia is not linear. Mild and moderate intensity exercise requires a drop in insulin while more intense activities necessitate a rise in insulin, at least in early recovery. To overcome this hurdle, the exact relationship

between insulin needs and relative PA intensity level needs to be determined. Moreover, ways to deliver insulin into the circulation more rapidly need to be developed.

Individuals With T1D

For exercise smart AP development, it is imperative to understand the generalized glycemic responses to different forms of PA in T1D (Figure 2). It is well known that sustained very light-to-moderate intensity aerobic PA typically results in a rapid drop in glucose in T1D, which often results in hypoglycemia.^{32,33} The rise in glucose R_a during sustained light-to-moderate intensity aerobic exercise is attenuated compared with the rise in R_d , because portal insulin levels do not decrease at the onset of exercise.²⁵ The failure to drop insulin levels in the portal circulation at the onset of light-to-moderate intensity aerobic exercise impairs glucagon effectiveness in increasing liver glucose R_a .²⁵ The exercise-mediated increase in skeletal muscle blood flow, glucose, and insulin delivery, as well as the mobilization of additional contraction-mediated (non-insulin-mediated) glucose transporters within muscle,³⁴ also contributes to the drop in blood glucose level in individuals with T1D. Hypoglycemia occurs within 1 hour of light-to-moderate intensity aerobic exercise in approximately one-third of persons with T1D.^{35,36} The rapid reduction in glucose levels at the start of aerobic exercise, even when basal insulin stops at the onset,³⁷ is problematic for AP development since the circulating insulin levels may not drop rapidly enough to prevent hypoglycemia in some individuals. Importantly, exercise may increase insulin absorption rates from the subcutaneous depot,³⁸ thereby causing circulating levels to rise even if pump infusion rates are unchanged or suspended, which might also be problematic for single hormone exercise smart AP development. In these situations of initial relative hyperinsulinemia, even if the insulin pump is suspended at the onset of exercise, fast acting carbohydrates or exogenous glucagon administration may be needed. In a recent experiment, a bihormonal closed-loop AP was shown to be successful in stabilizing glucose levels during moderate aerobic exercise, although a significant drop in glycemia was still observed at the start of exercise.³⁹

Exercise smart AP hurdle 4: The normal physiological reduction in insulin secretion into the portal circulation at the onset of moderate-to-vigorous/maximum-intensity exercise cannot easily be emulated in T1D. Exercise may cause increased subcutaneous absorption rates from already infused insulin. To overcome this hurdle, glucagon delivery or carbohydrate intake may be required even if insulin infusion stops at the onset of aerobic exercise.

Mixed aerobic-anaerobic PA and resistance training typically result in either a more stable glucose trend⁴⁰ or a small rise in glucose levels.^{29-31,41} Brief intense aerobic-anaerobic

PA will frequently result in hyperglycemia, which can be prolonged unless insulin is administered.^{17,27,28} The increase in glycemia during or after aerobic-anaerobic PA primarily stems from physiological by-products of anaerobic energy metabolism (ie, lactate) and the release of catecholamines, cortisol, and growth hormone.⁴²⁻⁴⁵ This stark difference in glucose homeostasis and insulin needs when intense PA is performed will make the development of an exercise smart AP a challenge.

Exercise smart AP hurdle 5: The normal physiological rise in insulin secretion into the portal circulation at the end of vigorous-to-maximal PA cannot easily be emulated in T1D. This hurdle may require alternate ways to deliver insulin into the circulation quickly post exercise (eg, inhaled insulin).

Theoretical Insulin Needs for PA Based on Intensity Thresholds

Since insulin needs generally drop with continuous light-to-moderate intensity aerobic exercise, remain relatively neutral for intermittent moderate-to-vigorous intensity work, and rise soon after maximal work is performed (Figure 2), it may be important to consider 1 or more PA intensity thresholds for the AP development, perhaps as categorized by MET equivalents (see Figure 1A for changes in MET equivalents throughout the day in a study subject). Advancements in the wearable technology show promise in testing the efficacy of different AP PA intensity threshold algorithms. If PA intensity thresholds are needed for exercise smart AP development, then 1 or more physiological variables that reflect the relative PA intensity would need to be measured in a wearable device.

Exercise smart AP hurdle 6: Several cardiorespiratory variables change with exercise that can be measured to help better inform the exercise smart AP. What one(s) can be measured accurately and simply enough to be useful? To overcome this hurdle, clinicians, scientists, engineers and human factors experts will need to collaborate. Prospective users (physically active patients and athletes with diabetes) will need to be identified and consulted.

Cardiorespiratory Responses to PA and Their Measurement Tools

The development of the exercise smart AP requires consideration of the cardiorespiratory responses to the various types and intensities of PA. A primary function of the cardiorespiratory system is to maintain the consistency of the body's chemical and thermal environment—oxygen and nutrients are carried to the working muscles, carbon dioxide and heat are carried away from the muscles, the acid-base disturbances associated with an imbalance in lactate production

and clearance are managed, and other metabolic by-products are removed.

HR, stroke volume, arterial-venous O_2 difference, blood pressure (BP), and total peripheral resistance (TPR) all change rapidly with exercise to influence cardiac output, blood flow and nutrient delivery to the working muscles. The magnitude of the responses in these parameters is related to the intensity and engaged muscle mass. BP can be measured during PA remotely, but likely has limited utility as a physiological variable to inform the exercise smart AP. This is because the relationship between BP and exercise intensity is not entirely predictable and both posture and involved muscle mass influence the BP response. At the same PA intensity, for example, there is less increase in systolic BP involving the legs than with the arms, in spite of the fact that the legs have more muscle mass than the arms. This is because the larger leg muscles produce a large vasodilatory response that attenuates the rise in BP compared to the arms.⁴⁶ Moreover, BP increases and decreases transiently as the muscle contracts and relaxes, making BP a weak indicator of relative exercise intensity. Finally, an intense sustained muscle contraction will lead to an exaggerated increase in BP, thereby making it difficult to estimate exercise intensity reliably for exercise smart AP development.

Indirect calorimetry is considered the best indicator of aerobic exercise intensity and it is technically possible, to measure oxygen consumption (VO_2), carbon dioxide production (VCO_2), and ventilation rates (V_E) during PA with a portable device (eg, Cosmed KB5 or FitMate). During PA, the O_2 demand can increase 20-fold from rest (from an VO_2 consumption of 3-5 $mL \cdot kg^{-1} \cdot min^{-1}$ at rest to 25-60 $mL \cdot kg^{-1} \cdot min^{-1}$ or higher during PA). If the increase in oxygen uptake and blood flow match the demands of work, then the activity remains aerobic, but if the delivery is inadequate to match the rate of ATP turnover and creatine phosphate in the muscles, the limited reserves of these substances are reconstituted by anaerobic mechanisms. Although direct measurements of VO_2 would be the most accurate way of determining aerobic exercise intensity, the requirement of breathing through a mouthpiece and carrying around a portable O_2 sensor along with an exercise smart AP is simply not practical for everyday use.

Blood flow to the muscles during PA is regulated by the sympathetic nervous system, catecholamines, and the build-up of metabolic by-products in the active tissues, which cause an increase in the dimensions of the arteries supplying the muscles thereby reducing resistance to the working muscle. The heart responds to this need mainly by an increase in its cardiac output through increased HR and contractility. As such, HR, typically expressed as a percentage of maximum HR, is a good index of aerobic exercise intensity. HR monitors gauge PA intensity and these devices can now be streamed in real-time to various android devices and smart phones. The use of a HR threshold to trigger an exercise algorithm in an exercise smart AP system has shown good

efficacy in attenuating the drop in glycemia associated with steady state aerobic exercise⁴⁷—a threshold of 150 bpm was used to switch the AP system over to a modified AP algorithm for PA. It is important to note; however, that during progressive exercise, HR increases linearly to a maximum (~ 220 minus a person's age in years) even when the anaerobic threshold is surpassed (when insulin needs tend to rise, see Figure 2). Thus, a single HR threshold would likely not be appropriate for individuals who exercise regularly above the anaerobic threshold. Moreover, HR and BP are influenced by other factors than PA, such as caffeine intake, age, fitness status, level of arousal, core temperature, medications, hydration levels and diabetes-related complications. Thus, AP systems relying exclusively on HR may be prone to confounding effects. Combining HR with an accelerometer might help with confirming that the increase in HR was exercise related.⁴⁸

Determining an increased reliance on anaerobic metabolism during PA would be advantageous for the AP development since insulin requirements are higher than during aerobic activity. During aerobic-anaerobic work, the acid-base disturbance associated with lactate production typically limits PA duration (<10 -20 minutes), except in the small percentage of people (ie, endurance athletes) who can tolerate it. Ventilation rates provide clues for the transition to higher rates of anaerobic metabolism. In the blood, the increased acid production during anaerobic PA causes the person to ventilate at a high rate to buffer the lactic acid by “blowing off” CO_2 from the bicarbonate pool. Individuals become breathless rapidly at this threshold, usually to the point where it is difficult to talk.⁴⁹ The ventilatory threshold “talk test” may be the simplest way to determine if there is a significant rise in anaerobic metabolism during PA,⁵⁰ although integration of the “talk test” to the AP system might be a challenge. In contrast, discrete measurements of ventilation rate might help inform the exercise smart AP of the threshold for increased anaerobic work during intermittent activities. Another consideration might be to manually input a numeric intensity descriptor (eg, Borg rating of perceived exertion scale) into the exercise smart AP and have the intensity algorithm built into the device (Table 1).

Monitoring Physical Activity: Established and Emerging Self-Wear Technology

Advances in PA “sensing” self-wear technology have emerged that quantify movement (ie, accelerometry, global position satellite) and gauge the relative PA intensity. There is an abundance of products on the market which all vary in their measurement techniques, costs and accuracies (eg, Polar and Garmin HR monitors, Fitbit, Nike FuelBand, Sense-Wear, Jawbone, etc). Typically the devices will operate on proprietary formulas and assumptions that are based on the individual's HR, accelerometry, pedometer, or a combination of these.

Other technologies capture variables such as skin electrical conductance, skin temperature, near body ambient temperature, breathing rates/frequencies, heat flux and sweat rate. Although wearable devices are typically not as accurate as traditional laboratory practices (ie, indirect calorimetry using expired gas collection) and may never be, there is certainly no doubt in the accessibility and practicality of these devices. For the purposes of the general population, the information that is provided with the respective degree of error is likely accurate enough to draw some conclusions about general activity levels, but questions should be raised when implementing these devices in clinical populations, especially for AP development. For example, attenuations in accuracy are frequently observed with wearable technologies when individuals participate in higher intensity PA.⁵¹

To date, HR monitoring provides one of the most efficient means of estimating energy expenditure.⁵² Other technologies that may turn out to be useful for AP development capture variables such as skin electrical conductance, skin temperature, near body ambient temperature, breathing rates/frequencies, heat flux, sweat rate, and accelerations in triaxial planes. However, the accuracy and reliability of these devices is less well established.

Caution should be exercised when implementing these devices with clinical populations, especially for AP development. As noted in a recent review by Colberg et al, new methodology is required to better integrate wearable PA monitors and glucose sensing technology to enhance glycemic control during and following exercise.⁵³ An integrative multivariable adaptive AP approach, using wearable technology, augmented with a hypoglycemia early alarm system was used to improve glucose control and prevent hypoglycemia during prolonged light-to-moderate aerobic exercise in individuals with T1D.¹⁴

Summary and Conclusions

PA has wide ranging effects on insulin requirements and glucose turnover making the development of an exercise smart AP challenging. Therefore, for effective glycemic control, it is imperative that the AP device has the capacity to respond to varying modalities, intensities, and durations of PA. Having an exercise smart AP system may encourage persons with T1D to increase their PA which would lead to several positive contributions in the management of diabetes such as improving insulin sensitivity, controlling body mass and lipid profiles, improving cardiovascular function, enhancing self-esteem, and improving overall quality of life.

Abbreviations

AP, artificial pancreas; ATP, adenosine triphosphate; BMR, basal (resting) metabolic rate; BP, blood pressure; CSII, continuous subcutaneous insulin infusion; CVD, cardiovascular disease; kcal, kilocalories; METs, metabolic equivalents; mph, miles per hour; 1RM, 1 repetition maximum; PA, physical activity; %HRmax,

percentage heart rate maximum; Ra, rate of appearance; Rd, rate of disappearance; RPE, rating of perceived exertion; TEE, total daily energy expenditure; T1D, type 1 diabetes; TPR, total peripheral resistance; TV, television; VCO₂, volume of carbon dioxide production; V_E, ventilation; VO₂, volume of oxygen consumption.

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