Prolonged Exercise and Its Effects on Type 1 Diabetes Mellitus

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Prolonged Exercise and Its Effects on Type 1 Diabetes Mellitus

Honors Thesis, Spring 2016

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Introduction to Type 1 Diabetes Mellitus

Type 1 diabetes mellitus (DM) is presumably caused by an immunological or viral cumulative destruction of the β cells of the pancreas. The β cell eradication leads to a complete or near complete inability to produce endogenous insulin 1, 2. Without insulin, significant amounts of glucose cannot be absorbed by cells and used in metabolic processes.

Insulin is a hormone that regulates glucose uptake in skeletal and cardiac muscle cells and adipose tissue by causing insertion of glucose transporter 4 (GLUT4) on cellular membranes. GLUT4 is not stimulated in type 1 diabetes unless synthetic (recombinant) insulin is present. GLUT1 and 3 are not insulin responsive and uptake glucose at a basal rate in red blood cells and neural tissue, respectively. GLUT2 is responsive after meals and uptakes glucose in the liver and pancreas for glycogen storage 55.

Type one DM presents with polyuria (frequent urination), ketonuria (ketone bodies in the urine), polydipsia (increased thirst), weight loss, hunger, and mood swings. In 77.1% of new adolescent diagnoses, the patient also presents with diabetic ketoacidosis (DKA) 28. In the past, type 1 DM was known as “juvenile diabetes” because it was primarily diagnosed in children, with diagnoses peaking between 8-12 years of age. Increasing numbers of diagnoses in teens and adults has lessened use of the term (in fact, the only organization to still use the term is the Juvenile Diabetes Research Foundation [JDRF]. JDRF was founded in 1970, and has become a cornerstone of the type 1 research community 29). Initial diagnosis is made by a fasting fingerstick blood glucose test that reads greater than 126 mg/dL, a diminished glucose tolerance, or a hemoglobin A1c blood test (HbA1c) of greater than 6.5% 23. HbA1c is a measurement of
the percentage of circulating glycated hemoglobin, which can be equated to an estimation of blood glucose levels over the past three months\textsuperscript{34}.

In untreated type 1 DM, cells cannot maintain homeostatic glucose uptake,\textsuperscript{35} due to lack of GLUT4 stimulation to insert on cellular membranes. The body then releases glucagon as a counter regulatory measure in response to decreased insulin reactions on adipocyte and myocyte membranes\textsuperscript{37}, a reaction also triggered nonpathologically by hypoglycemia. Glucagon releases hepatic-origin glucose through glycolysis and gluconeogenesis. Due to the lack of insulin, the cells still cannot uptake the glucose\textsuperscript{30}. The body then turns to other sources of energy. Adipocytic free fatty acids are broken down by $\beta$ oxidation into acetoacetate and $\beta$-hydroxybutarate. The body uses $\beta$-hydroxybutarate as energy when it cannot access glucose, but the presence of ketone bodies acidifies the blood. The bicarbonate buffering system soon becomes overwhelmed, blood pressure drops, heart rate increases, and a type of respiratory alkalosis, known as Kussmaul breathing (rapid deep breathing that reduces blood CO$_2$ and acidosis\textsuperscript{30}), begins. If not corrected through careful administration of intravenous (IV) insulin- and, in severe cases of acidosis, bicarbonate- DKA may result in coma or death. Late or incorrect diagnosis of type 1 DM can be life threatening. In fact, the Center for Disease Control (CDC) reported 2,417 deaths annually from DKA, approximately 17.3 deaths per every 100,000 diabetics\textsuperscript{32}. Up to a third of DKA deaths occur in individuals with no history of ketoacidosis\textsuperscript{33}.

Polyuria, a symptom of untreated type 1 DM, is caused by lack of glucose reuptake by the kidneys. Under non-pathological circumstances, glucose is completely reabsorbed in the renal tubules, but in hyperglycemia or untreated diabetes, glucose
transporters are saturated, and glucose is passed out of the body in urine. The high glucose concentration in the renal filtrate keeps water from being reabsorbed by aquaporins in the kidney and going against its concentration gradient. Because of the high osmolarity of the filtrate, there is a greater urine volume, higher frequency of urination, and polydipsia.

Fig. 1: Diagram of amino acid sequence of endogenous human insulin (top) and insulin Lispro (Humalog). (Top- Eli Lilly and Company. Amino Acid Sequence of U-100 Insulin Lispro (Humalog). Digital image. Prescribing Information. Eli Lilly and Company, Nov. 2015. Web. 11 Feb. 2016. Lower-McCance, Kathryn L., and Sue E. Huether. Pathophysiology: The Biologic Basis for Disease in Adults and Children. 5th ed. Maryland Heights: Mosby, MO. Print.) Both human and Lispro insulin have a molecular formula of C_{257}H_{389}N_{65}O_{77}S_{6} and a molecular weight of 5,808 grams/mol. The cysteine bonds are anchored on the same amino acids (AA), as well. The difference lies in B-28 and B-29 (highlighted on Lispro). They switch places from human to Lispro sequences, allowing Lispro to break into monomers for more rapid, human insulin-like absorption. Endogenous proinsulin (insulin precursor) has a C-peptide that is cleaved to form active insulin. Synthetic insulins do not possess a C-peptide in any state.

**Treatment of Type 1 DM**

Type 1 diabetes is a chronic, insulin-dependent disease, currently without a cure. Following diagnosis, patients begin subcutaneous injections of synthetic insulin analog, made from recombinant DNA of *E. coli* and yeast cells.
11. Typically, short-acting insulin lispro (Humalog, Eli Lilly) or aspart (Novolog, Novo Nordisk) are used in conjunction with basal insulin such as glargine (Lantus, Sanofi Diabetes) or detemir (Levemir, Novo Nordisk). The U.S. Food and Drug Administration (FDA) approved a novel basal insulin degludec (Tresiba, Novo Nordisk) in September 2015.

Fig. 2: Insulin action profiles of short-acting insulin Lispro (Humalog, Eli Lilly), Aspart (Novolog, Novo Nordisk), and basal insulin Glargine (Lantus, Sanofi Diabetes), and Detemir (Levemir, Novo Nordisk). Lispro and Aspart both begin working within 15 minutes of injection and are completely metabolized after 3-4 hours. Glargine works at a basal level for 24 hours, whereas Detemir is metabolized after 22 hours in the bloodstream. Adapted from Chase, H. Peter., MD. "Chapter 8- Insulin: Types And Activity. " Understanding Diabetes. 11th ed. Denver, CO: Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, 2002. 65-76. Print.

The biggest difference between Tresiba and Lantus or Levemir is that Tresiba has been found to be effective for at least 42 hours. Alan Moses, Novo Nordisk’s Chief Medical Officer, claims that participants in Tresiba’s clinical studies asked for the study to be ended after this point, as they were bed-bound for the purposes of isolating Trisiba’s
effects on blood glucose\textsuperscript{13}. He believes Tresiba could be injected for use as basal insulin once every other day, as opposed to traditional once-a-day Lantus or Levemir injections\textsuperscript{11}, but Novo Nordisk chose not to seek FDA approval for an unorthodox treatment schedule and is currently prescribed for once-daily use\textsuperscript{13}. Tresiba’s relative activity remains even for about 30 hours after injection, and then decreases linearly as the time after injection approaches 42 hours\textsuperscript{60}.

Since it is only approved for a 24-hour gap between doses, Tresiba’s single clear clinical advantage over glargine and detemir is a 25% reduction in incidence of overnight hypoglycemia\textsuperscript{10}, because Lantus has been found to cause regular occurrence of nocturnal hypoglycemia in individual clinical cases and larger studies\textsuperscript{15}. Some people use a lesser does of Tresiba than they would of Lantus, but the mechanism of hypoglycemia reduction is currently unclear\textsuperscript{10}. (It is worth noting that most major health insurance companies do not currently cover the costs of Tresiba. Novo Nordisk, the parent company, does offer patients a card that reduces the cost of prescriptions to $15 for 24 months. The card does not seem to be accepted by all pharmacies, however\textsuperscript{60}.)

Nocturnal hypoglycemia in type 1 DM is frequently caused by an increase in insulin sensitivity beginning around midnight and lasting about three hours\textsuperscript{37}. Lantus is a flat-rate insulin that does not decrease during those hours\textsuperscript{11}, thus potentially causing the hypoglycemia. A study using continuous glucose monitoring technology found that up to 75\% of severe hypoglycemia episodes occur overnight\textsuperscript{57}. Nocturnal “hypos” cause poor daytime control of blood glucose, as the body naturally rebounds in the morning to a high level of circulating glucose\textsuperscript{17}. This ricochet is known as the Somogyi effect, and occurs
in part because of a release of epinephrine and some glucagon that allows the liver to release glucose into the bloodstream\textsuperscript{14} by means of gluconeogenesis.

Conversely, an overnight circadian release of growth hormone (GH) frequently causes “fasting hyperglycemia,” also known as dawn phenomenon. GH also promotes hepatic gluconeogenesis. In non-diabetics, the release of GH and glucose is countered by endogenous insulin release\textsuperscript{27}, but diabetic patients have a significantly harder time countering this phenomenon, due to their ever-changing insulin requirements. Current treatments for dawn phenomenon range from sharply increasing basal insulin about one hour before waking to early morning workouts to low/no carbohydrate breakfasts and “pre-bolusing.” Humalog insulin takes fifteen minutes to begin working, and

\textbf{Fig. 3: Glucose Uptake in Normal Cells and in Diabetes.} Chase, H. Peter, MD. “What is Diabetes?” \textit{Understanding Diabetes.} 11th ed. Denver. CO: Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, 2002. 11. Print.
Novolog takes five to ten. Patients are often encouraged to “pre-bolus” by injecting their insulin up to thirty minutes before eating.

It is important to understand that not all patients with type 1 DM experience nocturnal hypoglycemia, the Somogyi effect, or dawn phenomenon. Those who do will experience it to varying degrees, and the effects will change from day to day, depending on variation in daily exercise, diet, sleep, emotions, and stress, among other variables and events.

These variables lead many diabetic patients to use insulin pumps. An insulin pump is essentially a small computer attached to a reservoir of fast-acting insulin-Humalog or Novolog- attached via a hollow plastic cord to a six or nine millimeter subcutaneous plastic or steel catheter, usually inserted in the hips, abdomen, or thigh. The pump delivers insulin in boluses (for carbohydrate intake and hyperglycemia correction) and at constant basal (user-programmed hourly rates of insulin delivery, accurate to 0.0001 mL in most pumps). The physician or patient programs the pump with varying insulin to carbohydrate ratios, basal insulin rates, target blood glucose levels, and insulin sensitivities. For a bolus, the user inputs blood glucose and carbohydrates ingested, and the pump calculates the needed insulin and delivers it after user confirmation of the amount (a program known colloquially as a wizard). The pump automatically administers basal insulin.

Patients using syringe injections or pre-filled insulin pens generally administer a bolus of long-lasting basal insulin- typically Lantus or Levemir- once every 24 hours. Short acting insulin (Humalog or Novolog) doses are manually calculated and injected several times a day. Injections are often associated with a higher risk of incorrect
bolusing or insulin usage, eg: taking 30 units of short acting Humalog rather than 30 units of long-lasting Lantus. Although this can be corrected if the patient quickly realizes their mistake, severe hypo- or hyperglycemia could result from incorrect insulin usage.

One recent advance in preventing nocturnal hypoglycemia is the Medtronic Minimed 530G System, which is comprised of an insulin pump that communicates wirelessly with its paired continuous glucose monitor (CGM) (a subcutaneous catheter that measures blood glucose levels of interstitial fluid). The 530G comes with “Threshold Suspend- SmartGuard” programming that prompts the pump to cease all insulin delivery when the CGM registers a blood glucose level below a user-set number. This closed loop system is especially useful for small children or people who routinely suffer from nocturnal hypoglycemia.

Tandem Diabetes, an up-and-coming insulin pump company, has a similar system, incorporating a Tandem tslim insulin pump and a Dexcom G5 CGM into a single device. The CGM, rather than transmitting information to a separate receiver, sends blood glucose readings directly to the tslim pump.

In what seems to be an effort to push Tandem out of the market, Medtronic and United Healthcare, a major insurance provider, signed a deal to make Minimed United’s preferred insulin pump. Beginning July 1, 2016, adult diabetics covered by United will be required to switch to Minimed pumps when their current pump reaches the end of its warranty. Patients will not be provided insurance for Tandem, Animas, or Roche insulin pumps, although it is unclear how coverage for the Omnipod pump may change.

It is worth noting an independent third party called openAPS has created an approximately 200-line code that functions as a closed loop system for overnight blood
glucose control. The code is only promoted for overnight control, as the programming and variables are simpler when the patient isn’t eating or exercising. openAPS is free for use and open source, but requires the user to build their own artificial pancreas from a Minimed pump, CGM, Raspberry Pi computer, and various other small pieces of hardware. The organization’s hope is that manufacturers and type 1 DM patients alike will use and better the code for the better of all 61.

The insulin receptor pathway is the same, regardless of insulin analog type or injection method. Cells have two-part insulin receptor that is part of the receptor tyrosine kinase (RTK) family. Insulin, insulin-like growth factor 1 (IGF-1), and IGF-2 activate the receptor and cause dimerization 47. The receptor then autophosphorylates itself with

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**Fig. 4:** Insulin receptor pathway in cells. Navratil, Amy. "MHA- Receptor Tyrosine Kinases." Mechanisms of Hormone Action. Laramie. Mar. 2016. Lecture.
tyrosine residues from its own β subunit, which allows a Grb protein to bind on to it. The Grb has a special region called an SH2 domain that binds primarily to phosphorylated RTKs. Son of Sevenless (SOS) protein binds to the other end of Grb at the SH3 domain. SOS can then activate Ras-MAP phosphorylation cascades to initiate insulin-related gene transcription. PI-3 kinase (PI-3K) is another protein that binds to the insulin receptor with a SH2 domain. PI-3K phosphorylates phosphatidylinositol 4,5-bisphosphate (PIP2) to PIP3 (PI 3,4,5-triphosphate), which begins a phosphorylation cascade and ultimately activates glycogen synthase kinase 3 (GSK-3) by phosphorylation. When phosphorylated, GSK-3 cannot deactivate glycogen synthase, thus allowing cells to uptake glucose for conversion to glycogen and reducing circulating blood glucose levels. After this process, insulin receptors and molecules are typically endocytosed by the cell and degraded.

**Part II: Exercise and Diabetes**

Alpha (α) cells produce glucagon, a polypeptide that stimulates liver-mediated glycolysis in response to low blood sugar. Although α cells are not destroyed with the onset of type 1 DM, their function is compromised by decreased α/β cell communication. As a result of this, there is not an innate physiological counter to hypoglycemia (<70 mg/dL or 3.89 mmol/L) in patients with type 1 DM. β cell loss also increases with time from the onset of type 1 DM, so any remaining α cell communication or response to hypoglycemia drastically decreases.

Exercise can cause different reactions in relation to blood glucose concentration, depending on duration and intensity. High intensity aerobic workouts, such as cardio or
high intensity interval training (HIIT), cause blood glucose to drop, with or without the presence of active or “on board” exogenous insulin.

Lower intensity exercise, weight lifting or sprints, for example, can cause blood glucose to rise\(^7\). This can cause problems for the patient in terms of diabetic management during exercise, as patients often over-compensate for an expected glucose drop by eating carbohydrates and taking a reduced bolus amount of insulin (or no insulin at all) in anticipation of a sharp blood glucose drop. Patients, especially those who are young or newly diagnosed, often do not understand the mechanisms of glycolysis in anaerobic exercise\(^3\).4\).

Anaerobic exercise is usually an explosive, short-distance activity, such as sprinting, jumping, and “maxing out” while weight lifting. It is characterized by fast, strong muscle contractions. The phosphagen system produces much of the needed energy. Creatine phosphate is catalyzed by creatine kinase to donate a phosphate to adenosine diphosphate (ADP) to make adenosine triphosphate (ATP), the primary energy source for the body (Fig. 5). Creatine phosphate is stored in skeletal muscle, and does not

require carbohydrates, fats, or oxygen, making it the first source of energy during exercise\(^1\). After about ten seconds, energy production moves to anaerobic glycolysis, although glycolysis only generates energy for about 180 seconds. In glycolysis,

![Glycolysis Diagram]

\(\text{Glucose} \rightarrow \text{ATP generated} \rightarrow \text{Hexokinase} \rightarrow \text{Glucose 6-Phosphate} \rightarrow \text{Phosphoglucone Isomerase} \rightarrow \text{Fructose 6-Phosphate} \rightarrow \text{Phosphofructokinase} \rightarrow \text{Fructose 1,6-bisphosphate} \rightarrow \text{Dihydroxyacetone Phosphate} \rightarrow \text{Glyceraldehyde 3-phosphate} \rightarrow \text{Phosphoglycerate Kinase} \rightarrow \text{Enolase} \rightarrow \text{Pyruvate Kinase} \rightarrow \text{Pyruvate} \)

*Fig. 6:* Direct ATP generation from glycolysis. One molecule of glucose travels down the pathway, ultimately generating 1 molecule of nicotinamide adenine dinucleotide (NADH), 4 molecules of ATP, and 2 molecules of pyruvate. The pyruvate enters lactic acid fermentation or the citric acid cycle and continues to create energy. Adapted from McCance, Kathryn L., and Sue E. Huether. *Pathophysiology: The Biologic Basis for Disease in Adults and Children.* 5th ed. Maryland Heights: Mosby, MO. Print.
circulating blood glucose and glycogen stored in myocytes are catabolized to pyruvate (Fig. 6) \(^{19}\). One molecule of glucose can generate two molecules of pyruvate, which then enters the aerobic citric acid cycle or undergoes anaerobic conversion to lactic acid through fermentation.

Anaerobic exercise also increases levels of catecholamines, growth hormone, and cortisol in the bloodstream all of which inhibit insulin \(^{42}\) through disruption of cellular signaling pathways. In a rat model, catecholamines actually decreased the number of insulin receptors on the cellular surface \(^{44}\). Growth hormone breaks up PI-3 kinases, which- when dimerized with themselves- are used as part of the insulin signaling pathway for glucose uptake \(^{43}\).

When basal insulin is reduced or bolus is reduced in anticipation of blood glucose drop during exercise, blood glucose can end up rising at rates of more than 2-3 mg/dL/minute if insulin rates are reduced too greatly, blood or urine ketones are present, or exercise is primarily anaerobic \(^{16,47}\). Given that blood glucose levels optimally remain below 126 mg/dL, a thirty-minute weight workout could potentially raise blood glucose by 90 mg/dL and catapult athletes out of their recommended range.

Exercising with hyperglycemia is strongly discouraged, because glucose begins to spill over into urine in the form of ketones when blood glucose levels reach about 175 mg/dL. It is recommended that ketone levels be tested by fingerstick blood test or urine test anytime fasting blood glucose is > 240 mg/dL, daytime blood glucose is > 300 mg/dL, the patient vomits, or is otherwise ill \(^{47}\). Extra Humalog or Novolog insulin is generally administered for mild to moderate ketones (0.6-3.0 mmol/L). Although insulin brings blood glucose down much faster when combined with exercise, exercise also
encourages acidosis. Significant water is lost through sweat, so the resultant dehydration increases the concentration of acidic compounds in the body\textsuperscript{45}, namely β-hydroxybuteric acid in the blood and acetoacetic acid in the urine\textsuperscript{47}. Patients in DKA can often be identified by their fruity, acetone breath, which is comparable to the smell of Juicy Fruit chewing gum.

<table>
<thead>
<tr>
<th>Blood/Urine Ketone Level (mmol/L)</th>
<th>Suggested Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-0.6</td>
<td>Within normal range.</td>
</tr>
<tr>
<td>0.6-1.0</td>
<td>Mild elevation, drink fluid.</td>
</tr>
<tr>
<td>1.0-3.0</td>
<td>Moderate elevation, take fast-acting insulin such as Humalog or Novolog, drink fluids, call physician.</td>
</tr>
<tr>
<td>≥3.0</td>
<td>Severe elevation, go to emergency room.</td>
</tr>
</tbody>
</table>

*Table 1:* Diagram of blood/urine ketone levels and suggested treatment, adapted from Chase, H. Peter. "Chapter 5: Ketone Testing." Understanding Diabetes. Denver, CO: Barbara Davis Center for Childhood Diabetes, U of Colorado Health Sciences Center, 2002. 29-34. Print.

While anaerobic lactic acid fermentation indirectly generates a small amount of energy, as does the citric acid cycle, most ATP (36 molecules) is generated through the aerobic electron transport chain\textsuperscript{19}. A series of four intramembranous mitochondrial complexes (NADH dehydrogenase, succinate dehydrogenase, cytochrome c reductase, and cytochrome c oxidase) pump hydrogen ions against their concentration gradients to create an electrochemical gradient\textsuperscript{25}. NADH is oxidized to form this proton gradient, and oxygen is used as the oxidizing electron receptor in the cytochrome c oxidase reaction\textsuperscript{53}. Oxygen is reduced with two hydrogen ions to form water and drive the
gradient allowing the ATP synthase F₁ subunit to rotate about the F₀ subunit and synthesize ATP from ADP and phosphate ³⁸.

As glycolysis begins to produce ATP, aerobic mitochondrial respiration also begins producing energy from pyruvate. Mitochondrial respiration is the dominant form of energy genesis, responsible for about 60% of energy production within five minutes of initiating constant exercise ²⁴. It can produce far more energy than any of the anaerobic energy generation pathways, usually estimated around 38 ATP in total, 2 ATP from glycolysis, 2 ATP from the citric acid cycle, and 34 from the electron transport chain ³⁸.

An endurance event, such as long-term backpacking, primarily utilizes aerobic respiration. Aerobic exercise is categorized as “moderate-long lengths of motion at 50-80% of an individual’s maximum heart rate” ⁵⁴. There is a low rate of aerobic ATP generation, but it can be sustained for far longer than glycolysis or the phosphagen system. However, the mitochondria still draw on blood glucose reserves, as well as myocytic and hepatic glycogen stores, adipocytes, and intramuscular fat reserves ¹⁹.

This makes endurance events still harder for a diabetic to manage. During moderate-intensity exercise, the amount of actively circulating blood glucose increases from about 4 grams (for a 68 kg person) to 20-40 grams ⁷, while usage is about 1-1.5 grams of glucose per kg of body mass per minute ¹⁶. The circulating glucose level must be maintained to prevent hypoglycemia. In an physically fit person without type 1 DM, the body can produce up to 10 mg of glucose per kg of body mass per minute ⁷. Since type 1 diabetics lack the α/β cell communication that produces glucagon as well as the insulin-mediated regulation of other reactions, aerobic exercise can quickly cause hypoglycemia, as gluconeogenesis and glycogenolysis are slower energy generation
processes than circulating blood glucose uptake. The hypoglycemia caused by exercise may have a lingering metabolic effect and depress blood glucose for several hours after the end of the workout - or even overnight which can be especially problematic when interacting with Lantus-mediated nocturnal hypoglycemia or poorly adjusted basal rates. In fact, the American Diabetes Association (ADA) recommends exercising after eating a meal or snack and following the activity up with at least 15 grams of carbohydrate within 30-120 minutes of ending the exercise. The ADA also proposes changing medications and insulin rates and ratios if “hypoglycemia regularly interferes with [the] exercise routine”.41

A Finnish study found that a 30-minute workout equivalent to “moderate walking or low-intensity running” did not significantly decrease blood glucose when trial participants injected only 70% of their normal daily basal insulin. It is also worth noting the trial used novel insulin degludec (Tresiba, Novo Nordisk) rather than the well-established basal insulins glargine (Lantus, Sanofi Diabetes) or detemir (Levemir, Novo Nordisk). However, basal insulin reduction varies between patients, anywhere from 80% to 30% of rates. Complete suspension of insulin administration is also used, but generally not for more than 60-90 minutes, at most, as blood glucose levels will quickly rise after cessation of exercise. Without any active insulin, it takes longer to bring blood glucose back into a recommended range 34.

**Bringing Diabetes into the Backcountry**

As Henry David Thoreau said, “I took a walk in the woods and came out taller than the trees.” People have backpacked since they first had something to carry, but the
sport has recently gathered attention in the light of movies and novels such as Cheryl Strayed’s *Wild*, Bill Bryson’s *A Walk In The Woods*, and Frank Delaney’s *Shannon*.

Especially now, with increasing urbanization and technological advances, backpacking is becoming a way to escape the modern world and reconnect with one’s sense of being or identity. Forays into the woods and mountains range in length from a one-night, ten-mile loop to the six-month long Appalachian Trail, spanning 14 states and 2,200 miles.  

Despite possible medical and logistical concerns, diabetics still feel the pull of the wilderness. Children’s summer camps funded by the American Diabetes Association host night and week-long backpacking trips, complete with physicians, dieticians, and medical supplies. The Appalachian Trail Conservancy keeps registers of long-distance hikers and certain other subsets, including diabetic hikers. Although registration is not required, the rosters are made available at request to interested hikers.

Equipment requirements are fairly standard. Beyond clothing and a sleeping bag, most backpackers bring a tent with a waterproof fly, camp stove, fuel (such as propane), matches, a first aid kit, a hatchet or saw-blade knife, map, headlamp, dish and utensils, pot, bear canister, rope, lantern, and toiletries. Diabetics need to bring along all supplies-infusion sets, lancets, syringes, glucometers, batteries, insulin (typically kept in a cooling wallet or coat pocket, depending on weather), glucagon, sharps container, alcohol swabs, and glucose tabs- that would normally be used during an equivalent time period, as well as spare and back-up parts in case of equipment failure or emergency.

Nonetheless, the true variant in backpacking supplies is food. The quantity needed depends on the length and intensity of the hike, with an average expenditure of 3000-
5000 calories per day \(^{62}\), usually about 1.5-2.5 pounds of food per day \(^{63}\). Hikers typically pack calorie-dense foods, such as nuts, cheese, dried fruit, M&Ms, dehydrated rice or pasta, and dried meat. Vegetables and fresh food are typically reserved for short trips or used within the first few days of a long-distance hike. During trips lasting more than a week or two, hikers often mail care packages to general delivery or go grocery shopping in towns along their route.

Despite such nutrient-dense diets, most backpackers do not manage to intake a sufficient number of calories, averaging a daily 2,722 calorie deficit. \(^{62}\). Similar energy deficiency trends are noted in other long-distance sports, such as ultra-endurance cycling \(^{64}\) and sled dog racing \(^{65}\). Studies of both cyclists and dogsled racers also found moderate dehydration was common \(^{64, 65}\).

Caloric deficit should not affect blood glucose levels, as long as insulin ratios are adjusted accordingly \(^{8}\). The only major stimulus of blood glucose change during chronic hiking is the activity itself. Pre-event physical fitness plays into the effect of exercise on blood glucose. Typically, patients with a higher level of fitness require less basal and bolus insulin and do not suffer large blood glucose decreases when compared to less fit peers, although this is not universal \(^{65}\). Carla Cox (PhD, RD, CDE) recommends cutting boluses in half if they are within two hours of strenuous exercise, decreasing basal to 75-30% of normal about ninety minutes before activity, and keeping basal reduced overnight if blood glucose is less than 130 mg/dL before going to bed. Although this greatly reduces hypoglycemic episodes, or “lows”, it does not eliminate them. Dr. Cox recommends treating mid-hike lows with a combination of carbohydrate and protein-such as Lärabars or fruit snacks with string cheese- to quickly raise blood glucose and
then sustain the increase. (An object of note: up to 55% of severe hypoglycemic episodes and 43% of all hypoglycemic episodes occur overnight, and nocturnal hypoglycemic episodes last an average of 86 minutes.) It is also recommended to eat carbohydrate-heavy meals for dinner, using whole grains, if possible, to slow digestion. In fact, 50-60% of daily calories while backpacking are recommended to be carbohydrates.

As one’s body adjusts to the physical demands of backpacking, blood glucose, insulin requirements, and energy requirements normalize. With stabilization and practice, management of diabetes on the trail becomes easier. Generally, by the end of the first week on the trail, diabetics can usually keep a majority of blood glucose values in-range (80-180 mg/dL) with decreased total daily insulin, sometimes using only 70% or less of their usual insulin.

After a backpacking trip ends, insulin and dietary requirements return to near pre-hike levels, unless a similar amount of physical activity is sustained or the patient has significant weight loss.

**Conclusion**

Type 1 diabetes mellitus is a chronic disease of indeterminate origin—likely parts genetic, epigenetic, and viral, resulting in destruction of pancreatic β cells. Currently, treatment consists of lifelong blood glucose monitoring and subcutaneous injection of synthetic insulin, with care options ranging from using fast-acting insulins lispro and aspart in insulin pumps to combined lispro or aspart with basal rate insulins glargine, detemir, or degludec.
Management of the disease is difficult, especially when exercising. Anaerobic exercise has a tendency to raise blood glucose through glycolysis and cortisol hormone mechanisms. Aerobic exercise is primarily dependant on the electron transport chain and draws on blood glucose reserves, causing a drop in blood glucose levels.

The best treatment for type 1 DM and prolonged aerobic exercise seems to be continuous glucose monitoring alongside great daily insulin reduction, whether injections or an insulin pump are used. Lantus (insulin glargine) seems to be counter indicated in backpacking usage, due to its effect on overnight hypoglycemia combined with exercise. Tresiba (insulin degludec) may be a more appropriate choice, although this has not been studied. With an insulin pump, basal and bolus insulin ratios can easily be reduced and changed from day to day.

Advanced meal planning, with consideration for carb-heavy dinners and snacks, is necessary. Snacks for mid-hike and overnight hypoglycemia should be accounted for.
during planning. Extra snacks should be allotted for the first several days of a backpacking trip, as the patient learns how their body reacts to long-duration, aerobic exercise.

Insulin rates reduce with acclimatization to physical activity, and blood glucose stabilizes concurrently. Nonetheless, proper nutrition and hydration are key to the maintenance of health while in the backcountry, especially as long-distance athletes tend to suffer from caloric deficits and dehydration.

However, there is no reason for type 1 diabetics to avoid the great outdoors. After a steep initial learning curve with appropriate precautions and monitoring, a diabetic may freely backpack any desired distance (Fig. 7).
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