Adventure Travel and Type 1 Diabetes

The complicating effects of high altitude

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Regular exercise is encouraged in patients with type 1 diabetes (1) and, indeed, the American Diabetes Association states that people with type 1 diabetes should be able to partake "in all forms of physical activity consistent with an individual's desires and goals" (2). In keeping with this philosophy, increasing numbers of people with type 1 diabetes now participate in extreme forms of physical activity, including high-altitude trekking and mountain climbing, as evidenced by several recent publications (3–10). However, exercise at altitude imposes a number of unique challenges for people with type 1 diabetes, including impairment in glycemic control, and it may have negative consequences in patients with complications. This review will consider what is known about the impact of altitude on individuals with type 1 diabetes, and it will propose strategies for dealing with these challenges.

For the purposes of this review, high altitude is defined as 3,000–5,000 m (10,000–16,000 ft) and extreme altitude as >5,000 m. As barometric pressure decreases linearly with increasing altitude, inspired P_{O_2} at the summit of Mount Everest (8,848 m) is <30% of that at sea level (11). Acclimatization refers to the physiological changes that occur consequent to prolonged exposure to the hypoxia and low barometric pressure of altitude, and it includes hyperventilation, with the resultant respiratory alkalosis being reduced over time by compensatory renal bicarbonate excretion. Although erythrocyte levels also increase, this occurs much more slowly, over the course of several weeks (11). It is also important to note that acclimatization does not imply normalization because, despite continued hyperventilation, alveolar P_{O_2} levels remain well below that at sea level even in fully acclimatized individuals.

SUCCESS RATES — Two controlled studies and one uncontrolled study involving only people with diabetes have examined summit success rates in individuals with type 1 diabetes (4–8,10). In the first controlled study, subjects with little or no previous altitude experience rapidly ascended Mt. Kilimanjaro, Tanzania (5,895 m), over the course of 5 days. In the second study, experienced climbers took 37 days to ascend Cho Oyu, Tibet (8,201 m), reaching a higher altitude but also having more time to acclimatize. In the final study, climbers with type 1 diabetes and previous experience at altitude took 14 days to summit Aconcagua, Argentina (6,950 m). In the Cho Oyu study, 100% of individuals with type 1 diabetes ($n = 6$) reached base camp (5,800 m), 50% achieved 7,200 m, and one individual (17% success) summitted Cho Oyu (8,10). There was no significant difference in success rates between the individuals with type 1 diabetes and the control subjects. Similarly, 88% of climbers (seven of eight) with type 1 diabetes reached the summit of Aconcagua, with the one failure to summit not being caused by a diabetes-associated problem (6,7). Only in the Kilimanjaro study did all individuals with type 1 diabetes ($n = 15$) fail to achieve their goal, reaching a lower final altitude than the normal subjects (5,187 vs. 5,654 m) and with a much lower summit success rate (0 vs. 27%) (4,5). The reason for the low success of these individuals is not clear, but it may relate in part to the relative lack of time for acclimatization on this climb, compared with the ascents of longer duration, and/or the lack of experience of these climbers.

One other difference between these studies may involve the selection of subjects because the individuals who climbed Cho Oyu were free of diabetes complications, with an average HbA_{1c} (A1C) of 7.0%, whereas the Kilimanjaro climb included some subjects with background retinopathy and/or microalbuminuria (A1C levels were not given) (4,10). However, it seems unlikely that the very dramatic differences in success rates are consequent to differences in metabolic control because the success rate of the Kilimanjaro expedition for the control subjects was also very low compared with other treks on this route; the author of this review, who also has type 1 diabetes, recently summitted Kilimanjaro along with all seven of her nondiabetic colleagues, and success rates on Kilimanjaro of >60% are routinely claimed on various websites. Finally, consistent with a normal ability to climb to altitude, analysis of aerobic capacity at sea level in subjects with complication-free type 1 diabetes has demonstrated no differences from paired fit or sedentary control subjects, although the fit individuals had a higher $V_{O_{2max}}$ than the sedentary subjects (12). However, A1C levels were inversely correlated with $V_{O_{2max}}$ when both fit and sedentary individuals with type 1 diabetes were examined, suggesting that the fit subjects had better glycemic control. Furthermore, as might be predicted, the presence of cardiac autonomic neuropathy in fit subjects with type 1 diabetes was associated with a reduced $V_{O_{2max}}$ that was similar to that found in the sedentary subjects (12). Nonetheless, cardiovascular performance in healthy subjects with type 1 diabetes is similar to that of normal control subjects at altitudes of up to 5,800 m (8,10). Thus, the available data suggests that people with type 1 diabetes can successfully undertake the physical challenges of high and extreme altitude expeditions with reasonable rates of success compared with normal individuals.

ACUTE ALTITUDE SICKNESS — Acute mountain sickness (AMS) occurs unpredictably, consequent to a recent in-

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Abbreviations: AMS, acute mountain sickness; FDA, Food and Drug Administration; HACE, high-altitude cerebral edema; HAPE, high-altitude pulmonary edema; HARH, high-altitude retinal hemorrhage.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

crease in elevation, and is associated with headache, often severe, plus at least one of the following symptoms: gastrointestinal (anorexia, nausea, vomiting), fatigue/weakness, dizziness/lightheadedness, and difficulty sleeping/sleep disturbances (13–17). Acute altitude sickness includes not only AMS, but also its more severe forms, high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE), both of which can be fatal if not treated (16,17). One additional complication of altitude sickness of relevance to the current discussion is high-altitude retinal hemorrhage (HARH) (16,18,19).

Although the underlying etiology of AMS is not well understood, this condition is highly prevalent in the general population, with 9% of climbers in the Swiss Alps reporting symptoms at 2,850 m, increasing to 53% at 4,559 m (20). In contrast to the relatively common occurrence of AMS, the incidence of HACE and HAPE is much lower (<4%) (16). A slow rate of ascent that allows time for acclimatization can prevent the development of AMS in many individuals, whereas descent to lower altitudes should be undertaken for all individuals with severe symptoms of AMS or its complications (11,16,21). However, pharmacological approaches are also commonly used to both prevent and treat AMS. Prophylactic administration of acetazolamide is most commonly used to prevent the onset of AMS, decreasing its prevalence by up to 51%, and is also used to decrease the severity of symptoms in existing AMS (11,16,21–23). The normal dose is 250 mg twice daily, although 125 mg twice daily has also been used. Furthermore, one meta-analysis has suggested that a total dose of 750 mg/day is required for effectiveness, although this remains controversial. It must also be recognized that acetazolamide is a carbonic acid inhibitor that increases renal excretion of bicarbonate, and its use may therefore be contraindicated in patients who are at risk for ketoacidosis (24). Although somewhat less commonly used, glucocorticoids such as dexamethasone are also effective in both the prevention and treatment of AMS, with the normal dose of dexamethasone being 8 mg divided over the day, although 12 and 16 mg doses are also efficacious (16,23,25). Nonetheless, the negative effects of such very high doses of dexamethasone on glycemic control (26,27) make this a less attractive option for those with type 1 diabetes except in emergency situations. Finally, direct administration of oxygen or placement of the individual into a portable hyperbaric "Gamow" chamber can also used to treat severe AMS or its complications, although these are not always available, while other agents, such as clonidine, nifedipine, spironolactone, ginko biloba, and aspirin, have only been tested in a limited number of studies (15,23).

Relatively few studies have examined AMS in patients with type 1 diabetes. However, those that have do not show any difference in occurrence rates between normal subjects and those with type 1 diabetes at altitudes ranging from 1,700 to 5,800 m. The daily dose of acetazolamide used was reported to be similar in both populations in one of these studies (4,5), but there was little or no use of acetazolamide in the other studies (6–8,10). Furthermore, it was noted that several of the symptoms of AMS (e.g., headaches, nausea, dizziness) made it difficult to recognize hypoglycemia in some subjects with type 1 diabetes (4), although others reported no such difficulties (7). Importantly, neither HACE nor HAPE have been observed in patients with type 1 diabetes in any of the reported studies. However, there were two cases of ketonuria and two of ketoacidosis among the 15 individuals with type 1 diabetes who climbed Mt. Kilimanjaro (4,5). Because both of the climbers who developed ketoacidosis had been taking acetazolamide prophylactically for AMS, this may have served as a contributing factor (4,5). Consistent with this possibility, no such loss of metabolic control was observed in the other expeditions in which acetazolamide was used sparingly, if at all (6–8,10).

Although HARH is uncommon in normal individuals at high altitude (e.g., 4% at 4,243 m) (18), the prevalence is markedly increased at extreme altitudes (e.g., 74% at 4,900–7,700 m and 91% at 7,700–8,900 m) (28). However, no increase in the incidence of retinal hemorrhages has been observed in patients with type 1 diabetes at altitudes up to 8,200 m (4,10). Nonetheless, it should be noted that although the retinal changes with HARH appear to be transient in normal individuals, no clinical studies have been conducted to rigorously determine the prevalence and consequences of HARH in patients with type 1 diabetes. Thus, it has been proposed that those with preexisting diabetic retinopathy may be at higher risk for HARH and/or disease progression, and it is recommended that such individuals have a dilated pupil ophthalmologic examination and/or fluorescein angiogram before considering any trip involving exposure to high altitude (19).

The potential impact of climbing to high altitude on the individual with other diabetes complications has not been rigorously explored. However, a single report demonstrated that patients on hemodialysis exhibit a 12% reduction in workload capacity after acute exposure to an altitude of 3,000 m (29). Individuals requiring hemodialysis would seem unlikely candidates for prolonged high- or extreme-altitude treks. However, because renal bicarbonate excretion is an essential function for the prevention of AMS, and because acetazolamide is contraindicated in patients with severe renal impairment, it would seem prudent that individuals with impaired renal function consequent to nephropathy be particularly cautious about traveling to altitude. Other case reports/discussions have similarly advised caution but have not recommended against high-altitude travel in patients with impaired renal function or in those taking ACE inhibitors for hypertension (30,31). Finally, patients with type 1 diabetes are at increased risk for cardiovascular disease, particularly those who have one or more additional risk factors, including hypertension, dyslipidemia, male sex, and/or cigarette smoking (32). Subjects with coronary artery disease have been found to have reduced exercise-induced reserve at relatively low altitudes (2,500 m) compared with normal control subjects who maintain normal reserve during exercise at altitudes of up to 4,500 m (33). Furthermore, use of β-blockers can reduce exercise tolerance at even moderate altitudes (2,311 m) (34). Because high-altitude travel is contraindicated in patients with cardiovascular disease due to its effects to increase both heart rate and blood pressure (35), all individuals with type 1 diabetes should be screened before travel at altitude for adverse cardiovascular indicators, including silent ischemia.

EFFECTS OF ALTITUDE ON GLYCEMIC CONTROL— Glycemic control is decreased in normal individuals at altitude (36–41). However, it is essential to consider the specifics of the challenge being undertaken because both the duration of the ascent and the final altitude achieved can affect glucoregulation. Thus, normal women who are acutely exposed to "high altitude" (e.g., a

hypobaric chamber simulation of 4,300 m for 16 h) demonstrate increased glycemic responses to a high-carbohydrate meal in association with decreased insulin sensitivity, as determined by the HOMA-IR (homeostasis model assessment of insulin resistance) method (41). In contrast, increased glycemic responses to exercise occurred in association with increases in the rates of both hepatic glucose production (R_a) and glucose uptake (R_d) in men after 2 days of acute exposure to this altitude (36,37). Although plasma epinephrine and norepinephrine levels are elevated in response to acute altitude exposure (36,37,40,41), no correlations with epinephrine levels have been found. In contrast, norepinephrine concentrations change in parallel with hepatic glucose production. Furthermore, neither α- nor β-blockade prevents these acute changes in glucose homeostasis (37,40,41), and the changes are not related to the phase of the menstrual cycle in women (39). In another study, plasma glucose and insulin resistance, as determined using a hyperinsulinemic-euglycemic clamp, were also increased in normal men 2 days after being airlifted to 4,559 m (high altitude); however, in this case, cortisol and norepinephrine were elevated, but glucagon, growth hormone, and epinephrine were not increased (38). Cortisol levels were not determined in the studies discussed earlier. Importantly, in the same men, a restoration to basal levels of both glycemia and insulin sensitivity was found by the 7th day of exposure, indicating adaptation. Similar findings have been made in women after 9 days at 4,300 m, such that the glycemic response to an oral glucose load was actually reduced compared with sea level (39).

Finally, studies have been conducted on adrenergic drive in normal men who walked up to 6,542 m over the course of 18 days and then remained at this extreme elevation for an additional 21 days (42). Compared with sea level, resting heart rate was increased from ~65 to ~110 bpm after both 7 and 21 days at extreme altitude, whereas exercise-induced heart rate (at 70% $V_{O_{2max}}$) actually decreased from ~160 bpm at sea level to ~145 bpm after 7 and 21 days. Furthermore, norepinephrine levels were markedly elevated by ~2-fold at rest and by ~10-fold during exercise after 7 days at extreme altitude, with a small decrease to ~7-fold after 21 days. The findings at 4,800 m were intermediate. When taken together, these findings are consistent with adrenergic overdrive during short-term (≤7 days) exposure to high and extreme altitudes, followed by a small degree of adaptation over time. In summary, therefore, changes in sympathetic tone appear to occur in direct response to decreased arterial oxygen saturation (43) and may play a role in the increased hepatic glucose production observed during acute exposure to altitude. In contrast, because elevated levels of glucocorticoids are associated with insulin resistance (44,45), hypoxia-induced changes in cortisol may contribute to the insulin resistance observed during acute altitude exposure, although this remains to be confirmed.

Whereas normal individuals respond to elevated levels of catecholamines with increased insulin secretion, those with type 1 diabetes may be particularly susceptible to stress-induced hyperglycemia unless insulin doses are adjusted appropriately (44). Thus, although insulin requirements in climbers with type 1 diabetes ascending Kilimanjaro fell by 49% (4), likely in association with the physical exertion required by this rapid 5-day climb, requirements increased by up to 52% in both groups of subjects on longer-duration expeditions (to Cho Oyu and Aconcagua), even when the data were normalized for carbohydrate intake (6–8,10). It may be of some note that the greatest changes were seen between days 4 and 10, during which time the altitude increased from 3,700 to 4,200 m, with some leveling off at later dates and higher elevations (8,10). Therefore, consistent with the data from normal subjects, ascent to extreme altitude in subjects with type 1 diabetes is associated with insulin resistance, with some adaptation appearing to occur over the long term. Optimal management of glycemia at altitude thus requires frequent blood glucose monitoring combined with the ability to acutely change insulin-dosing regimens. A discussion of the reliability of glucose monitors at altitude is included below.

Consistent with the changes observed in normal individuals, two of the major expeditions involving individuals with type 1 diabetes also report decreased glycemic control, despite careful monitoring and appropriate changes in insulin dosing, as described above (4,5,8,10). Only 50% of the recorded blood glucose measurements fell within the target range of 6–14 mmol/l in the diabetic climbers ascending Kilimanjaro, and 4 of the 15 individuals developed ketonuria, with 2 of these progressing to mild ketoacidosis (4,5). Similarly, A1C levels increased from 7 to 7.9% in the diabetic subjects climbing Cho Oyu over 37 days, compared with the statistically smaller increment found in the normal individuals (from 5.1 to 5.4%). Furthermore, blood glucose levels were decreased in normal individuals after a 4-h trek at sea level, 3,700 m, and 5,800 m, but not in those with type 1 diabetes; hematocrit, lactate, and blood gases were not different between the two groups (8,10). Thus, despite careful attention to blood glucose monitoring and insulin dose adjustments in both expeditions, glycemic control deteriorated in the climbers with type 1 diabetes, likely consequent to changes in the hormonal milieu, as discussed above.

Finally, in addition to hyperglycemia, sporadic hypoglycemia has been reported in a number of individuals with type 1 diabetes at altitude (4,6,7). This does not appear to be a consistent finding, and it was likely related to an inappropriate balance between insulin dose, high-intensity exercise, and food intake rather than to any inherent problems caused by the diabetes (as also discussed below). However, the possibility of severe hypoglycemia is present in all individuals with type 1 diabetes undertaking extreme forms of physical activity and is obviously even greater in individuals with hypoglycemia unawareness (46). The dangers of hypoglycemia while trekking or climbing at high altitude cannot be underestimated because cognitive impairment and loss of consciousness can result in physical danger, while the associated sweating may soak through clothing or sleeping bags necessary for protection from the cold. Thus, people with type 1 diabetes are well advised to travel with a glucagon kit for the treatment of severe hypoglycemia (Table 1) and to ensure that at least one of their traveling companions is not only familiar with its use, but is also able to locate the kit in the case of an emergency.

EFFECTS OF ALTITUDE ON GLUCOSE METER PERFORMANCE

— A significant number of studies have examined the accuracy and reliability of various glucose meters at altitudes ranging up to 5,800 m (4–6,10,47–52), with all but a single report (6) indicating problems with glucose meter reliability at altitude. Both over- and underestimation of glycemia and of standard glucose control solutions have been demonstrated for a wide variety of

Table 1—*Diabetes-specific supplies*

Supplies	Numbers/amount
Insulin supplies	
Insulin	Three times the amount anticipated for each type of insulin, stored at nonextreme temperatures
Insulin pens and needles (if applicable)	One extra pen and three times the anticipated number of needles
Pump supplies (if applicable)	Three to five times the amount anticipated
Syringes	Enough to cover the entire trip if on the pen or pump; two to three times the anticipated requirement if using syringes alone
Glucose meter	Two different meters with extra batteries for each
Glucose strips and lance/lancets	Three times anticipated number of strips for each meter, two lances, and three times the anticipated number of lancets; a supply of visually read strips should also be taken as a backup in the event of meter failure
Ketone strips	Two packages
Carbohydrates	
Dextrose tablets ("rapid-acting carbohydrate")	One package (50 g) per day
Dried fruit and cookies ("slower-acting carbohydrate")	Several individually wrapped packages per day
Glucagon kit (this must be protected from breakage and from freezing of the vehicle)	Two kits
Intravenous set up	One complete kit
Single-use sterile needles and syringes	Several 18-g and 10-cm^3 syringes, respectively, in the event that medical treatment is required in a hospital or clinic with limited resources
Insulated packs	Enough to carry all supplies
Letter from physician	Listing supplies and their necessity, for international border crossings

Supplies should be packed and carried in a minimum of two independent sites (e.g. carried personally at all times by two people, or by one person with the second set in a separate travel bag and/or at a nearby hotel or embassy/consulate).

meters, including meters that use photometric versus electrochemical methods, as well as glucose oxidase–versus glucose dehydrogenase–based technology. The majority of studies indicate that high glucose levels are misreported to a greater extent at altitude than low-normal glucose levels. In the author's own experience (Fig. 1), six different glucose meters have been tested at altitudes of 0–4,800 m, with two glucose meters giving falsely high and four giving falsely low readings using control glucose solutions, by as much as 37%. A significant reduction in the readings obtained for control glucose solutions was found at altitudes between 3,000 and 5,000 m compared with readings taken <3,000 m ($P < 0.05$). Interestingly, one meter failed to function >5,000 m, presumably because of the low temperature, and several meters required warming by hand before obtaining any readings at all. Although this can be caused by battery failure at cold temperatures, many meters have also been reported to perform poorly at cold temperatures (3–5,51), and most manufacturers indicate a lower limit for meter function on the product information sheet and/or have built-in a low-temperature alarm. Overall, therefore, meter reliability at altitude must be considered suspect unless proven otherwise. The use of multiple meters with control glucose solutions can lend some confidence to the individual with type 1 diabetes traveling at altitude, whereas carrying glucose monitoring equipment next to the skin may prevent the problems associated with meter and battery malfunction at low temperatures (Table 1).

ALTITUDE-INDUCED ANOREXIA — Many studies have shown that prolonged travel at high and, in particular, extreme altitude is associated with significant loss of body weight (rev. in 53). Both fat mass and fat-free mass are lost at extreme altitude, at a rate that can reach 1–2 kg/week in total weight lost. The available data suggests that this occurs because of negative energy balance (by up to 30%) in association with decreased food intake and increased basal metabolic rate at extreme altitudes (53–56), the latter likely consequent to the hormonal changes discussed above. Malabsorption of ingested nutrients does not appear to be a significant factor (53,55). Importantly, although body weight can be maintained if energy intake is adequate (54), there appears to be a dissociation between feelings of hunger and actual food intake at extreme altitudes. Although this may be consequent to central nervous system changes associated with low-grade cerebral edema (15), several recent studies have also provided intriguing evidence for a role of the anorexigenic hormone leptin in altitude-induced loss of appetite. Acute exposure to high altitude (4,559 m) was found to be associated with increased leptin levels in individuals experiencing reduced appetite, but not in those with normal appetites (57,58). However, several more recent studies have challenged this notion, demonstrating parallel reductions in leptin levels and body weight after prolonged exposure to altitudes of up to 5,050 m (59–61). In one study, a negative correlation was found between norepinephrine and leptin levels at extreme altitude (60), consistent with in vitro data demonstrating that norepinephrine can inhibit the leptin response to insulin in adipocytes (62). Because norepinephrine levels remain elevated at altitude, even after prolonged exposure (see above), these findings are consistent with a role for adrenergic overdrive in the leptin secretory response to altitude. However, these data still do not provide a mechanistic explanation for the loss of appetite and ensuing decline in energy balance that occurs at extreme altitudes. When taken together, therefore, it is clear that ascent to altitude is associated with loss of appetite; however, the mechanisms underlying this change remain unclear. Nonetheless, for individuals with type 1 diabetes, negative energy balance can clearly make maintenance of glycemic control more difficult, and insulin injections should be carefully timed and titrated to ensure that they are matched to actual nutrient ingestion. Indeed, mild postprandial hypoglycemia has been noted in several individuals with type 1

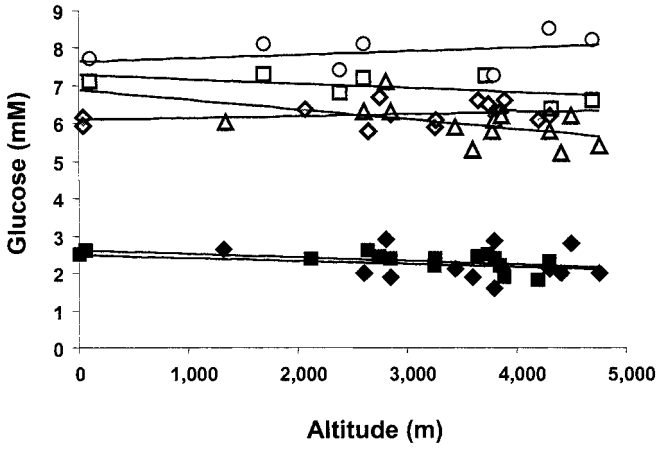

Figure 1—*Blood glucose meter testing with control glucose solutions at altitudes ranging from sea level to 4,800 m. All meters were tested by the same individual, and the meters included were One Touch Basic (LifeScan Canada, Burnaby, BC, Canada), Accu-Chek Advantage (Roche Diagnostics Canada, Laval, QC, Canada), and One Touch Ultra (LifeScan Canada, Burnaby, BC, Canada), with the numbers indicating pairing of meters on separate treks. A best-fit regression line is plotted for each meter. Control glucose solutions in the range of 5–8 mmol/l (open symbols) and 2–4 mmol/l (closed symbols) were supplied by the manufacturer. Temperature was not controlled and hence several meters failed to function at very low temperatures until prewarmed by hand. One meter failed to perform at all >5,000 m, likely because of freezing temperatures. As compared with the measurements taken <3,000 m, values obtained >3,000 m were significantly reduced (by 7 ± 2%, P < 0.05). ◇, One Touch Basic 1; ■, Accu-Chek Advantage 1; △, One Touch Basic 2; ◆, Accu-Chek Advantage 2; □, One Touch Basic 3; ○, One Touch Ultra 3.*

diabetes at extreme altitude, which was prevented by insulin administration after food intake (6,7). Although this was attributed to an altitude-induced delay in carbohydrate absorption, most studies have shown that nutrient absorption is not significantly affected by altitude (53,55). However, an alternative possibility is simply a mismatch between anticipated and actual food intake due to altitude-induced anorexia.

ALTITUDE AND TEMPERATURE

— In addition to the metabolic challenges imposed by travel at high altitude, the individual with type 1 diabetes must be particularly cognizant of the impact of the environment on his/her ability to maintain glycemic control. Average temperatures decrease by 2°C for every 300 m in elevation; hence, temperatures at the freezing point can be expected >3,000 m, dropping to the −15 to −30°C range or even lower at extreme altitudes. These temperatures do not include the additional impact of wind chill. Thus, frostbite can be a real possibility during travel at altitude, and care to protect the extremities should be taken, particularly by those with impaired circulation and/or neuropathy (63). However, additional considerations for individuals with type 1 diabetes are the impact of low temperatures on glucose monitoring equipment (as discussed above) and on insulin storage. All major producers of insulin (Aventis, Eli Lilly, and Novo Nordisk) recommend that insulin not be exposed to temperatures that are <2°C because of potential loss of bioactivity (64). Thus, particular care must be taken by anyone carrying insulin to prevent its freezing, such that insulin should be carried next to the skin in all situations in which temperatures already are or are likely to fall below freezing. The author has particular experience in this regard, having failed to take the necessary precautions while climbing Mt. Kilimanjaro; the temperature on the summit was −15°C (not including significant wind chill) and, despite being carried inside two layers of thermal packing with two packages of activated chemical hand-warmers, the author's insulin froze inside her knapsack within 2 h of leaving base camp. When taken in combination with concomitant glucose meter failure, the author's blood glucose levels were 25 mmol/l upon returning to base camp 10 h later. Fortunately, injection of insulin that had been left properly stored at base camp rapidly restored normoglycemia. Finally, at least one report has indicated that high temperatures can pose similar problems for mountain climbers carrying insulin (3). In this case, a climber on Mt. Rainier developed severe hyperglycemia (>33 mmol/l) consequent to exposure of his insulin pump to bright sunlight and therefore, presumably, high temperatures for a prolonged period of time; again, replacement of the insulin with a nonexposed fresh supply restored normoglycemia. It should also be noted at this point that no particular difficulties in trekking to altitude with insulin pumps have been reported in the literature, with the single exception of one pump that was never released in the U.S. and that has since been corrected to allow pressure equilibration; this does not appear to be an issue with other pumps currently on the market (65,66). In summary, therefore, in addition to adequate protection of insulin from extremes of temperature, ensuring that additional supplies of insulin are available in the event of an emergency is absolutely essential to the traveler with type 1 diabetes (Table 1).

ADDITIONAL CONSIDERATIONS

— There are a number of additional challenges that must be considered by all those undertaking adventure travel at any altitude but, in particular, by individuals with type 1 diabetes. In addition to appropriate vaccinations, as advised by a travel clinic (Table 2) (67), these include the impact of long-distance travel, poor hygiene, gastrointestinal disturbances, food supplies, and isolation.

Due to a relative paucity of suitable destinations in North America, high and extreme altitude adventure travel can involve long-duration flights across multiple time zones (e.g., 24- to 36-h flying time over 11–13 time zones to travel from Toronto, Canada, to Kathmandu, Nepal). The individual with type 1 diabetes therefore needs to be aware of the difficulties imposed by prolonged physical inactivity during such travel, as well as understand the impact of time zone changes on self-medication. Although frequent blood glucose monitoring and insulin dose adjustments are clearly de rigueur for such travel, the current American Diabetes Association position statement also recommends that patients obtain counseling regarding adjustments to the timing of insulin administration during travel through three or more time zones (68), which may be particularly important if multiple types of insulin with different durations of action are being used.

Proper hygiene may be difficult at al-

Table 2—*General travel supplies*

Eyes, skin, lips protection	Gastrointestinal, genitourinary infections	Respiratory symptoms	Pain	Vaccinations	Other
UV protection (used prophylactically)	Oral rehydration salts (e.g., Gastrolyte)	Cough drops (sugar-free)	Tylenol 2	Diphtheria, polio, and tetanus	All other medications normally taken
Bandages (a variety of sizes)	Bismuth subsalicylate (e.g., Peptobismol; used prophylactically)	Cough suppressant (sugar-free)	Tylenol 3	Hepatitis A and B	Antinausea (e.g. Gravol, oral or suppository; as necessary)
"Second skin" blister pads	Loperamide hydrochloride (Imodium)	Antihistamines	Ankle braces, knee braces and/or elastic bandage	Encephalitis, Meningococcal, Typhoid, Yellow Fever (where required or if advisable; as determined by geographic location)	Sleep aid (sleeping pills or hypnotics, as advised by physician; as necessary)
Antibiotic ointment	Broad spectrum antibiotic (e.g., a quinolone)			Rabies (only if bitten)	Water purification tablets/iodine (as necessary)
Fluconazole/topical	Metronidazole				Acetazolamide (for altitude; used prophylactically) Antimalarial (used prophylactically as required for side-trips and/or for jungle travel to remote mountain locations; as determined by geographic location)

All medications should be in appropriately labeled (e.g. dose information, patient's name), waterproof, and unbreakable containers, when possible.

titude because water sources may be either unavailable (due to total absence or subzero temperatures) or contaminated (see below). Additionally, bathing may be largely precluded by low temperatures, whereas toilets may consist of a hole in the ground, if they exist at all. Finally, skin abrasions in the form of blisters are common during trips involving prolonged periods of walking. Minor bacterial and/or fungal infections, including urinary tract and foot/skin infections, as well as vaginal infections in women, can thus be difficult to prevent and can lead, in the case of urinary tract and foot infections, to more serious complications in individuals with type 1 diabetes, including pyelonephritis and gangrene, respectively (69–72). The person with type 1 diabetes should therefore be fully prepared to care for such minor infections, should they occur (Table 2). However, more serious infections may necessitate medical care, as discussed in more detail below.

Diarrhea is extremely common during travel to developing countries, with ~20–50% of travelers being affected (67,73). The Food and Drug Administration (FDA) defines traveler's diarrhea as "a subset of diarrhea occurring in travelers that is most commonly caused by an infectious agent" (74). Although prevention through appropriate dietary hygiene is the best prophylactic, clinical trials have demonstrated that over-the-counter bismuth subsalicylate is effective in >60% of individuals (67,73), and the FDA has recently approved the use of this product for the treatment of travelers' diarrhea (74). Oral rehydration may be necessary in severe cases of diarrhea, as may be the use of antibiotics and/or antimotility agents (Table 2) (67,73,75). Although there is no evidence that individuals with type 1 diabetes are at increased risk for traveler's diarrhea, infection and dehydration in diabetic individuals increases blood glucose levels and more commonly results in hospitalization than in normal individuals (76). Furthermore, it has been reported that many diabetic people inappropriately refrain from treating their diarrhea with oral rehydration solutions that contain carbohydrate (75), a widely used substrate to enhance sodium absorption (77). However, one very small study on this topic demonstrated only nonsignificant increases in blood glucose levels in patients taking oral rehydration solutions that contained either glucose or rice, suggesting that such preparations can be safely used by patients with type 1

Table 3—*General recommendations for individuals with type 1 diabetes trekking at altitude*

Pretravel preparation		During travel	
General	Diabetes related	General	Diabetes related
Get a general physical check-up, as well as a dental check-up, to prevent any unnecessary health problems whilst traveling	Get a diabetes-specific check-up; if complications are present, discuss the advisability of travel at altitude with your physician, based on the severity of the complication and any contraindications for travel (depending on the nature of the complication; see text)	Maintain a good level of hygiene	Monitor blood glucose levels frequently (a minimum of 6–8 measurements/day is recommended, or more as appropriate) and adjust insulin doses appropriately
A good level of physical training is an asset	Ensure that you are capable of self-management of your diabetes, including the ability to adjust insulin doses based on exercise, food intake, and/or the results of glucose monitoring	Maintain adequate levels of hydration and nutrition	Monitor ketone bodies, as appropriate, and adjust insulin doses appropriately
Pack appropriate clothing, as well as a suitably rated sleeping bag and other appropriate outdoor gear, as recommended by travel companies	Consult your physician regarding prevention and treatment of hypoglycemia, ketoacidosis, illness, and infection	Take all possible proactive measures to prevent illness and/or infection	Insulin doses may be need to be reduced by 50% or more if exercise intensity or duration is high
Pack appropriate supplies, as outlined in Tables 1 and 2	Know how your body normally reacts to different types of stresses, particularly exercise		Insulin doses may need to be increased above normal levels at high or extreme altitudes, despite increased levels of exercise and/or decreased food intake
Obtain emergency evacuation and medical insurance			Insulin doses may need to be adjusted in the event of illness, particularly nausea
Be prepared for the unexpected!			Insulin doses may need to be adjusted in the event of anorexia; do not inject preprandial insulin until food intake is assured
			Use a new source of insulin if unexplained hyperglycemia cannot be corrected with the bottle currently in use, as both freezing and high temperatures can reduce activity

diabetes (75). Nonetheless, advice from a physician on prevention and care of infections, as well as on maintenance of glycemic control under such conditions, should be obtained as part of appropriate travel planning.

The sage traveler should be aware that neither food supply nor food choices can be guaranteed in developing countries, and in remote locations or at altitude, the only food available is often that which is carried by the traveler or his/her trekking crew. The experienced travel company can normally advise on types and quantities of food that should be available at any given time of year. However, the traveler with type 1 diabetes should be prepared to adapt insulin-dosing regimens to food availability and should also carry both short- and long-acting carbohydrate so as to prevent hypoglycemia and ensure adequate nutrition (Table 1).

All travelers to remote locations, either in first world or developing countries, must be prepared for the probable lack of immediate or more than basic medical attention. Travel at extreme altitudes often results in significant delay in transport to a hospital because of nonaccessibility of helicopters, and in many developing countries, medical care may be days or even weeks away due to lack of transport (e.g., travel by foot or mule only). Travelers should therefore ensure that they have appropriate medical insurance, including emergency evacuation coverage, before any such trips. In addition, particularly in developing countries, medical care may not be available in state-of-the-art hospitals, but rather is found in local clinics with limited resources. Given the potential risk for life-threatening illness in travelers with type 1 diabetes due to ketoacidosis or severe infection, individuals should be encouraged to take appropriate personal medical supplies, including an intravenous set-up and needles/syringes of different sizes (Table 1). A letter from the travelers' physician should also be carried to facilitate passage with these supplies across international borders.

Finally, it must be acknowledged that although this review has focused on the adventure traveler with type 1 diabetes,

much of the discussion is also relevant to those with type 2 diabetes, particularly those that are insulin requiring. Similar considerations should be given to children with diabetes who attend summer camps at high altitude (78) as well as tourists at relatively lower altitudes, such as in the American Midwest (1,500–2,500 m), where AMS has also been documented in some individuals (11,15,21).

THE GLORIES OF SUCCESS AND THE CONSEQUENCES OF FAILURE

— It seems clear that there are no absolute contraindications to travel at high or extreme altitudes for the knowledgeable individual with type 1 diabetes who is free of complications. However, there is some risk, including the possible consequences of hypoglycemia, illness, or injury, and this should be considered seriously when planning travel. Individuals should therefore be encouraged to let their travel companions know about their condition (9) as well as the minimum necessary procedures in the event of a problem (as also discussed above). Specific recommendations for individuals with type 1 diabetes traveling at altitude are summarized in Table 3. In her own high- and extreme-altitude travels over the course of nearly a decade, the author has only encountered one other individual with type 1 diabetes. Regrettably, this person failed to plan appropriately for travel with diabetes, resulting in an unhappy outcome. In this particular case, the individual did not feel it necessary to inform the travel company that he had type 1 diabetes, and he did not take a single glucose meter with him on his 20-day trip to extreme altitude. After developing severe gastroenteritis, the travel company felt that he was not sufficiently competent to care for himself, and they took the decision to medically evacuate him (by donkey!); he and his wife ruined their trip, although, fortunately in this instance, nothing worse happened. This case, along with others discussed in this review, highlights the necessity for informed self-management on the part of the adventure traveler with type 1 diabetes. However, the sense of accomplishment in crossing a high pass or in reaching the summit of even a small mountain cannot be surmounted, and, with appropriate caution, individuals with type 1 diabetes should not be discouraged from attempting to achieve their ultimate goal.

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