Journeys to High Altitude—Risks and Recommendations for Travelers with Preexisting Medical Conditions

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Search Strategy and Selection Criteria

A literature review was completed using Ovid/ Medline (1950–Present) and Pubmed databases. The following search terms were employed: preexisting medical conditions and altitude, each individual condition and altitude, air travel and preexisting medical conditions, and high altitude medicine. Published articles were used as a source of further references not yielded by the primary search. Textbooks written by recognized experts in the field of high altitude medicine were consulted to source information not available elsewhere.

Introduction

The demographics of adventure travel are shifting. Expanding road, rail, and air networks as well as mechanized mountain lifts have rendered it increasingly possible for people of varying levels of health and fitness to reach remote high altitude destinations (Table 1). High altitude cities and employment sites also attract holidaymakers, workers, and business travelers (Figure 1). Passive ascent to altitude by airplane, automobile, train, hot air balloon, or cable car may result in sudden exposure to altitude without adequate time for acclimatization.

The environmental conditions at altitude and the associated hypobaric hypoxia pose a significant physiologic challenge to the human body (Figure 2). Furthermore, many high altitude sojourns include strenuous physical activities such as skiing, hiking, and climbing. Emergencies in remote locations demand that the sick or injured rely on their companions or on their own compromised abilities to access the medical help they need. The conscientious traveler will take steps to gain the knowledge and skills necessary to minimize personal risk. However, many at-risk travelers remain naive to the health risks of high altitude travel. Similarly, physicians should prepare themselves with the knowledge required to advise their patients on safe travel to altitude (Table 2). The need for knowledge and preparedness is especially critical in the case of individuals with preexisting medical conditions. These patients may be at increased risk for developing altitude-related illness or decompensation of their underlying disease with altitude-related changes in physiology.

This article reviews the effects of altitude in relation to a selection of common medical conditions and gives recommendations for how people with these disorders can protect their health at altitude.

Cardiovascular Disorders

Hypertension

There is a significant amount of individual variability in the effects of altitude on blood pressure. In the majority of people there is a small alpha adrenergic-mediated increase in blood pressure proportional to elevation gain, the effect of which is not clinically significant until above 3,000 m. However, in some people, there is a pathological reaction to high altitude which results in large blood pressure increases. A work by Häsler and colleagues suggests racial differences in the blood pressure response to altitude. Black mountaineers experienced a progressive decrease in systolic blood pressure (SBP) with increasing altitude whereas the matched white subjects experienced increasing SBP. Furthermore, bilanders who divide their time between sea level and high altitude residences experience significantly higher mean arterial pressure at their high altitude dwelling compared to sea level. In all people, the extent of pressure change depends on the degree of hypoxic stress, cold, diet, exercise, and genetics. Over-reactive sympathetic responses during sleep may cause periodic breathing which increases the risk of exacerbating hypertension and causing cardiac arrhythmias. Hypertension is also an independent risk factor for sudden cardiac death (SCD) during mountain sports.

Despite these risks, well-controlled hypertension is not a contraindication to high altitude travel or physical activity performed at altitude. Aneroid sphygmomanometers have been validated for use at high altitude (4,370 m). Patients with poorly controlled blood pressure should monitor their blood pressure...
Table 1  Altitude definitions

<table>
<thead>
<tr>
<th>Altitude level</th>
<th>Meters</th>
<th>Feet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate altitude</td>
<td>1,500–2,500</td>
<td>4,921–8,202</td>
</tr>
<tr>
<td>High altitude</td>
<td>2,500–3,500</td>
<td>8,202–11,483</td>
</tr>
<tr>
<td>Very high altitude</td>
<td>3,500–5,800</td>
<td>11,483–19,029</td>
</tr>
<tr>
<td>Extreme altitude</td>
<td>&gt;5,800</td>
<td>&gt;19,029</td>
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while at altitude and be made aware of the potential for sudden, large fluctuations in blood pressure. A plan for medication adjustments should be prepared in advance and should include increasing the dose of the patient’s usual antihypertensives as a first-line strategy for uncontrolled hypertension. Alpha-adrenergic blockers and nifedipine are the drugs of choice if hypertension remains severe. The development of hypotension may necessitate a later medication reduction with acclimatization to altitude. Patients taking diuretics should exercise caution in avoiding dehydration and electrolyte depletion. Furthermore, beta-blockers limit the heart rate response to increased activity and interfere with thermoregulation in response to heat or cold.

Coronary Artery Disease

There is no evidence to date linking coronary artery disease (CAD) to either a higher incidence or severity of altitude illness. There are also no data to suggest that exposure to altitudes up to 2,500 m increases the incidence of SCD or myocardial infarction (MI) in patients with CAD. However, a theoretical potential for increased risk exists in that both myocardial oxygen delivery and requirements are altered with exposure to high altitude. CAD is associated with an increased risk of SCD during skiing and hiking in the mountains.

Acute hypoxia, physical activity, dehydration, and cold cause sympathetic activation at altitude, the results of which include vasoconstriction and an increase in heart rate, blood pressure, and cardiac output. This increase in cardiac workload and oxygen demands is most notable in the first 3 days of altitude exposure. People with CAD have significantly reduced capacity to compensate for the increased demands on the heart, even at moderate altitude. Diseased arteries have impaired endothelial vasomotor control, and thus alkalosis, cold, and unopposed sympathetic activity may cause constriction of the coronary arteries and reduced myocardial perfusion. Levine and colleagues noted a 5% decrease in the angina threshold for people with CAD in the pre-acclimatization period at 2,500 m. Wyss and colleagues demonstrated an 18% decline in exercise-induced coronary flow reserve in patients with stable obstructive CAD at 2,500 m. Additionally, at altitude, myocardial...
Increasing altitude results in a decrease in inspired PO2 (P{subscript}I{subscript}O{subscript}2), arterial PO2 (P{subscript}a{subscript}O{subscript}2), and arterial oxygen saturation (S{subscript}a{subscript}O{subscript}2). (Adapted with permission from Hackett and Roach, 2007.)

**Table 2** Review articles on altitude travel with preexisting medical conditions

<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Review article</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular diseases</td>
<td>Hultgren{superscript}5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Luks{superscript}6</td>
</tr>
<tr>
<td>Respiratory diseases</td>
<td>Cogo and colleagues{superscript}7</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>Luks and Swenson{superscript}8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Brubaker{superscript}10</td>
</tr>
<tr>
<td>Neurological conditions</td>
<td>Baumgartner and colleagues{superscript}11</td>
</tr>
<tr>
<td>Elderly travelers</td>
<td>Cooper{superscript}13</td>
</tr>
<tr>
<td>Women and pregnancy</td>
<td>Jean and colleagues{superscript}14</td>
</tr>
<tr>
<td>Ocular conditions</td>
<td>Mader and Tabin{superscript}16</td>
</tr>
<tr>
<td>Medication considerations</td>
<td>Luks and Swenson{superscript}17</td>
</tr>
<tr>
<td>Air travel</td>
<td>Gendreau and DeJohn{superscript}19</td>
</tr>
</tbody>
</table>

Oxygenation in areas supplied by stenotic arteries is significantly reduced relative to areas supplied by healthy vessels.{superscript}40 Patients with CAD may be at significant risk of life-threatening ventricular arrhythmias at altitude due to the combined effects of pulmonary hypertension and myocardial ischemia.{superscript}41,42

Patients with exertional angina at their resident altitude will likely experience a worsening of their symptoms at higher altitude. Thus, travel to high altitude is not recommended and exercise at altitude is generally contraindicated in this cohort.{superscript}5,31,41 However, Morgan and colleagues proposed that patients are safe to exert themselves at altitudes up to a target heart rate which is 70% to 80% of their low altitude ischemic endpoint.{superscript}44 Patients with well-controlled CAD who participate in unrestricted physical activity at sea level are probably safe to travel up to 2,500 m.{superscript}31,36,38,40 However, it is recommended that physical exertion should be avoided for the duration of a 3- to 5-day acclimatization period.{superscript}26,27,30 Adequate nutrition and hydration should be maintained at all times to minimize the risk of adverse events.{superscript}26 Wyss and colleagues{superscript}40 recommend further caution, stating that people with CAD should avoid physical exertion even at moderate altitudes. Travel to high altitude is contraindicated for 6 months following an MI. After 6 months, a normal exercise stress test should be a prerequisite to travel.{superscript}39,43 Non-MI patients
who have undergone coronary artery bypass grafting or coronary angioplasty may be limited in their exercise potential at high altitude but there is no evidence to suggest that altitude exposure increases the risk of graft closure or stent restenosis.41

Heart Failure

There is very little research to guide recommendations for patients with heart failure wishing to travel to altitude. However, experts have frequently observed that people with congestive cardiac failure tend to quickly decompensate with high altitude exposure due to the effects of acute mountain sickness (AMS)-related fluid retention.2,22,27,29 High altitude travel is therefore contraindicated in people with symptomatic heart failure at their resident altitude.27 Patients with clinically stable, asymptomatic heart failure have been shown to tolerate exertion at simulated altitudes up to 2,500 m without decompensation. However, this study was limited to only a few hours of observation and thus the generalizability of the results is limited. Should they decide to travel to altitude, patients can expect a decrease in work capacity proportional to the altitude gained and their sea level exercise capacity.45 Acetazolamide prophylaxis or an increase in the dose of the patient’s regular diuretic should be considered.2,27 Furthermore, particular attention must be paid to fluid balance. Patients should be monitored closely for signs of fluid retention while avoiding dehydration due to exertion and use of diuretics.22,27,29

Congenital Heart Disease

Exposure to hypobaric hypoxia results in pulmonary vasoconstriction, excessive amounts of which result in high altitude pulmonary edema (HAPE).2 Patients with congenital heart disease (CHD) including tetralogy of fallot, ventricular septal defect, atrial septal defect, patent ductus arteriosus, or absence of a pulmonary artery have an exaggerated pulmonary arteriolar vasoconstrictor response to hypoxia which makes them more susceptible to the development of pulmonary hypertension and HAPE.2,5,50 The extent of this risk is not well understood or easily predicted. Some individuals have demonstrated the ability to function well at high altitude whereas others suffer the consequences of increased pulmonary hypertension, HAPE, or right heart failure even at moderate altitudes.50–56 Symptoms with ascent may include dyspnea, weakness on exertion, and syncope.5

For people with symptomatic pulmonary hypertension at sea level, altitude exposure is contraindicated.2 Asymptomatic patients with CHD should be warned of the potential for developing HAPE and take nifedipine prophylactically to reduce their risk. Travelers with a brisk hypoxic pulmonary vasoconstrictor response may be identified in the clinic by observing their response to inhalation of a low oxygen mixture.3 These recommendations equally apply to patients with primary or secondary pulmonary hypertension.5

Respiratory Disorders

Chronic Obstructive Pulmonary Disease

People with chronic obstructive pulmonary disease (COPD) may be hypoxemic at sea level and thus may develop altitude-related symptoms at lower elevations than healthy people (Figure 2).2,3,27 Blunted carotid body response due to chronic hypercapnia may reduce their ability to produce a hypoxic ventilatory response, thus further exacerbating the hypoxia.7 Breathing cold air results in pulmonary vasoconstriction and increased pulmonary artery pressure.6,52 Elevated levels of carboxyhemoglobin due to smoking may further compromise oxygen-carrying capacity in this cohort.58 Depending on baseline oxygen saturation and the pathologic condition of the lungs, risks associated with altitude exposure include profound hypoxemia, pulmonary hypertension, disordered ventilatory control, impaired respiratory muscle function, and sleep-disordered breathing.2

No studies have been conducted on patients with COPD at high altitude. However, studies of patients with mild to moderate COPD at 1,920 m concluded that it is safe for such patients to travel to intermediate altitude.33,58 Altitude exposure is contraindicated for patients with severe COPD who have dyspnea at rest or on mild exertion at sea level. Patients with moderate disease should undergo individualized risk assessment and ascend with caution.2,7 Hypoxic challenge, spirometry testing, and the British Thoracic Society's
To minimize the risk of adverse effects, patients with COPD should avoid strenuous exercise at altitude and ensure optimal health prior to ascent. Maintenance of hydration at altitude is important to avoid problems associated with thickened mucosal secretions.

Bronchial Asthma

Altitude can influence bronchial hyperresponsiveness, and thus, the likelihood of an acute asthma attack. Possible aggravating factors at altitude include physical exertion, hypoxia, cold air, decreased air density, and decreased humidity. Furthermore, bronchoconstriction at low barometric pressure exacerbates hypoxia and thus theoretically predisposes asthmatics to HAPE and AMS. At altitudes up to 2,000 m, asthmatic travelers receive the benefits of decreased airborne allergens and reduced resistance to airflow. At altitudes above 2,500 m, conditions may be more conducive to induce an asthma attack due to the cold, dry air. Travelers at highest risk are those who use inhaled bronchodilators more than three times per week at their living altitude and those who participate in strenuous aerobic activity at altitude. Between 3,500 and 5,000 m, it has been shown that asthmatics have a reduced risk of suffering an asthma attack. Whereas the cold, dry air provides a stimulus for an asthma attack, changes in physiologic mediators that occur with acclimatization are thought to exert a modulatory effect over airway hyperresponsiveness.

While at altitude, use of volumetric spacers is recommended for metered dose inhalers, and the mouth should be protected against cold and wind. It is notable that high altitude natives routinely use silk scarves to protect their airways from exposure to cold air. Exertion at altitude should be moderate to avoid excessive hyperventilation and passive ascent to high altitude should be avoided as sudden exposure to hypoxia can increase airway irritability. Peak expiratory flow rate is a practical method for monitoring asthmatic status at altitude.

Obstructive Sleep Apnea

Hypobaric hypoxia associated with high altitude is likely to exacerbate the effects of obstructive sleep apnea (OSA). Richalet and colleagues suggest that individuals with Down syndrome and OSA have significantly impaired chemoreceptor sensitivity to hypoxia and are thus at increased risk of HAPE with exposure to even moderate altitudes. Thus, high altitude travel is contraindicated for people with OSA who demonstrate arterial oxygen desaturation at sea level. It is of interest that acetazolamide has been shown to reduce the apnea–hypopnea index in patients with OSA. Should a patient with OSA choose to travel to altitude, it is reasonable to prescribe acetazolamide prophylaxis in an effort to improve the symptoms of OSA and reduce the risk of developing AMS. Patients who travel with their continuous positive airway pressure machine may need to adjust the pressure setting to accommodate for the decrease in barometric pressure at altitude.

Pleural and Interstitial Lung Disease

No baseline data exist to help the physician predict which patients with interstitial lung disease (ILD) are most likely to suffer deterioration in their respiratory status at high altitude. It is recommended that patients with ILD in whom the presence of pulmonary hypertension has not been confirmed should undergo echocardiography before traveling to high altitude. Symptomatic pulmonary hypertension is a contraindication to high altitude travel. If patients with secondary pulmonary hypertension wish to travel to high altitude, they should use supplemental oxygen and nifedipine for HAPE prophylaxis. According to the Aerospace Medical Association, patients should wait for a minimum of 2 weeks following resolution of a pneumothorax before high altitude ascent, including commercial air travel.

Gastrointestinal Conditions

High altitude exposure is associated with a risk of gastrointestinal (GI) bleeding that increases with altitude and is thought to be related to hypoxia and cold. Wu and colleagues report that bleeding generally appears within 3 weeks of altitude exposure and includes hematemesis, melena, or hematochezia. Endoscopic examination of affected patients revealed a number of pathologies including hemorrhagic gastritis, gastric ulcer, duodenal ulcer, and gastric erosion. A history of peptic ulcer disease, high altitude polycythemia, alcohol consumption, use of non-steroidal anti-inflammatories (NSAIDs) and dexamethasone increase the risk of high altitude GI bleeding. Patients with a history of peptic ulcer disease should avoid alcohol, NSAIDs, smoking, and caffeine at altitude. Dexamethasone should only be used in cases of high altitude cerebral edema or HAPE. Should GI bleeding develop at altitude, the treatment of choice is twice the normal dose of omeprazole twice daily. The patient should be evacuated as quickly as possible. Patients with active inflammatory bowel disease should avoid remote travel during active phases of the disease and avoid long-term wilderness travel even in a quiescent stage.

Chronic Kidney Disease

Depending on the extent of the kidney disease, impaired renal function could alter an individual’s ability to maintain fluid, electrolyte, pH, and blood pressure homeostasis at high altitude. Furthermore, Quick and colleagues demonstrated that patients with renal anemia
do not compensate for hypobaric hypoxia by increasing erythropoietin secretion which could limit their acclimatization and increase susceptibility to AMS.\textsuperscript{9,72} The mild metabolic acidosis associated with chronic renal insufficiency is theoretically protective against AMS due to increased ventilatory drive. However, the metabolic acidosis also causes pulmonary vasoconstriction and thus may increase susceptibility to HAPE. Impaired fluid regulation could further contribute to the development of pulmonary edema and exacerbate hypoxemia. Chronic hypoxia may accelerate the progression of chronic kidney disease (CKD) in patients who remain at high altitude for extended periods.\textsuperscript{9}

The limited available evidence suggests that people with CKD are able to safely tolerate short trips to high altitude, albeit with caution. In the excellent review by Luks and colleagues,\textsuperscript{9} a number of helpful recommendations are made for patients with CKD planning a trip to high altitude. Patients on diuretics should monitor their weight daily and adjust their medication dose if fluid retention develops. Non-steroidal anti-inflammatory medications should be avoided as they have the potential to exacerbate renal hypoxia by inhibiting renal vasodilatation and increasing renal oxygen consumption. Angiotensin-converting enzyme inhibitors should be prescribed to minimize altitude-related proteinuria. Doses of some medications for AMS treatment and prophylaxis may need to be adjusted for patients with CKD (Table 3).\textsuperscript{9}

### Diabetes Mellitus

A single case-control study concluded that diabetes represents a risk factor for SCD during mountain hiking.\textsuperscript{34} Type 1 diabetics acclimatize well and there is no evidence to date indicating that they are at increased risk of developing altitude illness.\textsuperscript{73–76} Altitude exposure, including intensive exercise, is not contraindicated for diabetics with good glycemic control and no vascular complications.\textsuperscript{10,11,43,74,77} However, the unpredictable high altitude environment is far from the ideal milieu for maintaining effective glycemic control.

With increasing altitude, diabetic mountaineers report a reduction in metabolic control,\textsuperscript{11,75} as demonstrated by elevated HbA1c, insulin requirements, and capillary blood glucose.\textsuperscript{76,77} Reduced insulin sensitivity, altered carbohydrate intake, and exercise are thought to be the major factors contributing to these effects.\textsuperscript{10,11,78,79} Nutrition and exertion while trekking or mountaineering are variable, and at times

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### Table 3  Cautions and contraindications in the use of medications to treat high altitude illness in patients with preexisting medical conditions\textsuperscript{37}

<table>
<thead>
<tr>
<th>Medication</th>
<th>Contraindications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamide</td>
<td>Hepatic insufficiency, Patients on long-term high doses of aspirin.</td>
<td>Renal failure, Sulf allergy</td>
</tr>
<tr>
<td></td>
<td>Ventilatory compromise (FEV &gt; 25%)</td>
<td>Concurrent use of topiramate, potassium-wasting diuretics, and ophthalmic carbonic anhydrase inhibitors</td>
</tr>
<tr>
<td></td>
<td>GFR &lt; 10 mL/min</td>
<td>Diabetics</td>
</tr>
<tr>
<td></td>
<td>Metabolic acidosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypercalcemia</td>
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<tr>
<td></td>
<td>Hyperphosphatemia</td>
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</tr>
<tr>
<td></td>
<td>Recurrent nephrolithiasis</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>First trimester and beyond 36 wk of pregnancy\textsuperscript{44}</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Hepatic insufficiency (no data)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients on beta-blockers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients on monoamine oxidase inhibitors or tricyclic antidepressants</td>
<td></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Patients taking nitrates or alpha-blockers esophageal or gastric varices</td>
<td>Healthcare insufficiency, GFR &gt; 30 mL/min</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>Patients taking nitrates or alpha-blockers</td>
<td>Healthcare insufficiency, GFR &gt; 50 mL/min</td>
</tr>
</tbody>
</table>

GL, gastrointestinal; FEV, forced expiratory volume; GFR, glomerular filtration rate.

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unpredictable (e.g., the need to wait out or outrun bad weather). Furthermore, illness, cold, stormy weather, stress, fear, fatigue, and altitude-related cognitive impairment may present major challenges to diabetes self-management.7,8

Strenuous physical activity, hypothermia, and GI symptoms of AMS predispose diabetic mountaineers to hypoglycemia, requiring adjustments in insulin dose10,11. Physically fit diabetics appear to have improved glycemic control at altitude when compared to less fit diabetics.11 Early recognition of poor glycemic control is difficult at altitude, as symptoms of hypoglycemia may be confused with AMS or paresthesia associated with acetazolamide prophylaxis. HAPE has also been reported as a trigger for diabetic ketoacidosis in a previously undiagnosed diabetic.80 Furthermore, inappropriate insulin dose reduction, decreased caloric intake and absorption, metabolic acids produced during exercise, and acetazolamide prophylaxis may result in the development of ketoacidosis.77 Dexamethasone also rapidly increases insulin resistance and is only recommended for emergency use in diabetics.10,11,81

To maximize glycemic control, precise tracking of energy intake and expenditure, frequent blood glucose monitoring, and flexible insulin dosing are imperative.10,43,74 However, some blood glucose monitors are unreliable at moderate to high altitude due to the combined effects of elevation, temperature, and humidity.77,82,83 Exogenous insulin may be sensitive to heat and cold and thus should be stored carefully in an inside pocket to prevent it from freezing.10,11,18

Diabetic retinopathy is a relative contraindication for travel to high altitude, as hypoxemia frequently causes retinal hemorrhage in healthy mountaineers at an altitude above 5,500 m.2,11,16 Travel to altitude could have more severe consequences for diabetic patients with complications or poor metabolic control, and they should be evaluated and counseled accordingly. All diabetic patients should be carefully screened for complications that could increase their risk associated with exercise or exposure to altitude.11 The Web site www.mountain-mad.org is an excellent resource for people with diabetes who are interested in mountain pursuits.84

**Obesity**

Ri-Li and colleagues found that obese people had worse AMS scores than non-obese counterparts at a simulated altitude of 3,658 m.85 This effect is attributed to nocturnal desaturation associated with periodic, apneic breathing.85,86 Furthermore, excess abdominal weight increases the likelihood of OSA and obesity–hypoventilation syndrome.8 These factors can exacerbate both hypoxemia and pulmonary hypertension which may increase an individual’s risk for developing HAPE.8,43 Excess body weight may also complicate or preclude stretcher rescue from remote locations. Obesity–hypoventilation syndrome is a contraindication to high altitude travel. If such travel is necessary, supplemental oxygen and prophylactic acetazolamide are recommended.8

**Neurological Disorders**

**Epilepsy**

The effect of altitude on the seizure threshold has not been studied in depth. However, many well-controlled epileptics safely travel to altitude and are at no known increased risk for development of altitude-related illness or seizures.43,87 There have been multiple case reports of seizures occurring in non-epileptic individuals at altitude, including one fatal case.12,87 – 91 Daleau and colleagues reported a case where previously undiagnosed hyperventilation-induced seizures were unmasked in a patient with a positive family history for epilepsy.92 Basnyat also reported a single case of grand mal seizures at high altitude in a well-controlled epileptic patient on anticonvulsant medications.87

Seizures at high altitude are believed to be provoked by a number of potential factors including respiratory alkalosis, hypocapnia, hypoxia, or sleep deprivation.12,87 Fluoroquinolone antibiotics prescribed for gastroenteritis have also been implicated in two case reports87,88 because of their potential for lowering the seizure threshold.93 Lastly, although the potential for having a seizure may not be greatly elevated at altitude, consideration must be given to the additional potential for harm, should a seizure occur in a remote location or while performing high risk technical mountaineering maneuvers.

**Cerebrovascular Disease**

The risk of stroke at altitude may be increased due to hyperviscosity secondary to polycythemia, dehydration, cold exposure, and forced inactivity. Ischemic stroke and cerebral artery thrombosis are potential complications of high altitude cerebral edema.12 Jha and colleagues document 30 cases of stroke in young (≥48 y) individuals working at high altitude for a number of months. Ischemic strokes were the most common type, and altitude-related polycythemia was identified as the most significant risk factor.94 Travel to high altitude is contraindicated for a 90-day period post stroke or transient ischemic attack. Following this period, decisions about the safety of high altitude exposure and/or necessary treatment at altitude must be made based on each individual’s clinical situation and the physician’s estimation of stroke risk.12

**Migraine**

Migraine sufferers do not appear to be at increased risk of developing altitude sickness.95 However, altitude exposure is a clinically recognized trigger for migraines and the severity of headaches may increase at altitude.12,22,95,96 Furthermore, Murdoch described a
migraine sufferer whose migraine presentation changed drastically at altitude to include focal neurological deficits. Migraine sufferers can safely travel to high altitude, albeit with the caution that migraine frequency, severity, and character may be altered.

Hematological Conditions

Iron Deficiency Anemia

There is little information available on the effects of anemia at altitude, and the risk of altitude-related illness in this cohort has not been established. Hackett states that patients with iron deficiency anemia appear to acclimatize well to high altitude. Pollard and Murdoch report that hemoglobin concentrations of 14 to 18 g/dL are optimal for high altitude acclimatization. Patients with anemia can expect to have reduced exercise capacity at altitude. Anemia should be corrected prior to high altitude travel and premenopausal women may benefit from iron supplementation while at altitude if their ferritin stores are low.

Sickle Cell Anemia

Exposure to altitudes above 2,000 m has been associated with a high incidence of vaso-occlusive sickle cell crisis or splenic infarcts in patients with sickle cell disease (HbSS or HbSC) or sickle cell trait (HbAS), and sickle cell disease. Travel to altitude is contraindicated for people with sickle cell disease. Splenic crisis is the most frequent risk associated with exposure to hypobaric hypoxia in people with sickle cell trait. Furthermore, severe exertion has been associated with sickle cell crisis and sudden death in this patient cohort. Thriet and colleagues suggest that although individuals with sickle cell trait are capable of intense exercise at high altitude, their performance is diminished.

Although some experts do not recommend absolute activity or altitude restrictions in patients with sickle cell trait, others have advised that altitude should be avoided. Should they decide to travel at altitude, people with sickle cell trait should be informed of the risks and instructed to avoid over-exertion, to maintain adequate hydration, and to minimize heat stress. Individuals who are deconditioned should be exceptionally cautious in exerting themselves at altitude. Patients may be unaware of their sickle cell status prior to traveling. Should sickle cell crisis develop, appropriate treatment includes immediate descent, oxygen, fluids, and analgesics.

Psychiatric Conditions

It is well documented that high altitude expeditions may elicit alterations in both emotional and cognitive functioning. These changes are likely due to the cumulative effects of hypoxia, high altitude deterioration, physical exhaustion, fluid and electrolyte disturbances, and preexisting psychological morbidity. Cultural and interpersonal challenges are additional stressors likely to be encountered on a high altitude sojourn. Ryn documented profound psychological changes in a large portion of a cohort of healthy Polish mountaineers traveling in the Andes. With increasing altitude, the symptoms progressed from neurasthenic syndrome to cyclothymic disorder to acute psychotic disturbances. New onset anxiety disorders or exacerbations of diagnosed anxiety are also common at altitude and are thought to predispose people to AMS.

Safety, positive group interactions, and success at mountain travel demand a high degree of skill, cognitive flexibility, and emotional control. While at altitude, dramatic changes in a traveler’s psychiatric status should be considered a medical emergency and supervised descent should follow without delay. Patients with preexisting psychiatric disorders should undergo careful psychiatric assessment prior to embarking on a high altitude sojourn. Patients taking psychotropic drugs should ensure that they are compliant with their prescribed medication at high altitude.

Pregnancy

Pregnant women are not believed to be at increased risk of altitude-related illness. However, hypoxic conditions have the potential to compromise the uteroplacental circulation and cause placental hypoxia. The fetal circulation is further compromised when the mother exerts herself and the skeletal muscle competition for blood supply increases. Susceptibility to dehydration increases as a result of the additive effects of pregnancy and altitude-related hyperventilation. Women staying at altitudes over 2,500 m for weeks to months have an increased rate of antenatal complications including bleeding, hypertension, preeclampsia, abruptio placenta, preterm labor, intrauterine mortality, and intrauterine growth retardation. Isolation from medical care and the potential for physical trauma inherent in many outdoor pursuits present additional challenges. Pregnant women are also more prone to serious complications of certain travel-related infections and may be limited in their treatment options.

According to a recent consensus statement, travel to high altitude is contraindicated in the first trimester of pregnancy in women at increased risk of spontaneous abortion. Beyond the first trimester, low risk pregnant women can safely enjoy short sojourns up to 2,500 m. Moderate physical exertion at these altitudes is acceptable following 2 to 3 days of acclimatization. Strenuous exercise should be avoided at altitude. Contraindications to altitude exposure beyond 20 weeks of gestation include co-existing hypertension, preeclampsia, intrauterine growth restriction, anemia, and maternal smoking. Acetazolamide is also contraindicated in pregnant women. An extended stay at altitude be necessary for a pregnant woman, extra vigilance in the form of frequent prenatal checks is necessary to promptly identify problems that may arise.

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Other Conditions

Raynaud’s Phenomenon

Little is known about the specific effects of altitude on patients with Raynaud’s phenomenon (RP). However, it is well known that patients with RP are at increased risk of cold injury. Because the high altitude environment may include extremes of cold, these patients should travel to altitude during warmer months or to high altitude destinations with less severe climates. However, should they travel in winter climates, these individuals should take extra precautions to maintain the warmth of their extremities. High quality boots and mittens are essential; disposable chemical handwarmers are also recommended. Calcium channel blockers (eg, nifedipine) are the drugs of choice for the treatment of RP and should be considered in patients with RP who wish to participate in cold weather recreation at altitude.

Ophthalmologic Conditions

Patients who have undergone radial keratotomy to correct their myopia are at risk of significant visual deterioration at high altitude. The incisions made during this procedure weaken the cornea and cause it to deform with exposure to hypoxic conditions. Progressive hyperopic shift with deterioration in both near and far vision has been reported in a number of mountaineers at high altitude. Patients who have undergone radial keratotomy should travel to altitude with multiple pairs of corrective spectacles with varying degrees of correction for hyperopia.

Some people who have undergone myopic laser in situ keratomileusis (LASIK) also experience significant visual changes with high altitude exposure. The visual changes correct with descent to low altitude or with prolonged altitude exposure but can persist for a number of weeks following descent. It is recommended that patients allow a minimum of 6 months following LASIK before traveling to altitude. Patients who have undergone myopic LASIK should carry spectacles with myopic corrective power while at altitude.

Damage to the Carotid Bodies

The carotid bodies provide the stimulus for the hypoxic ventilatory response to hypoxia and thus their function is key to high altitude acclimatization and prevention of AMS. Neck irradiation or surgery involving one or both of the carotid arteries can potentially damage or ablate the carotid bodies, and thus alter their function. Roeggla and colleagues analyzed blood gas samples taken at moderate altitude from four patients before and after unilateral carotid endarterectomy. Following endarterectomy, the patients had a suboptimal ventilatory response, and thus significantly decreased $P_2O_2$. Patients with a history of neck surgery should be warned of their potentially limited capacity to acclimatize and should ascend with caution.

Medication

The drugs most commonly used to treat or prevent altitude-related illness are acetazolamide, nifedipine, and dexamethasone. Salmeterol, sildenafil, and tadalafil are occasionally used in the treatment and prevention of HAPE. Patients with preexisting medical conditions or those who are taking other medications may have fewer medication options or elevated risk of experiencing adverse drug reactions. Luks and Swenson provide an excellent review of these issues, the main points of which are summarized in Table 3.

Tissot and colleagues found that patients taking warfarin were 2.7 times more likely to have a subtherapeutic international normalized ratio (INR) following ascent to altitude greater than 2,400 m. This risk is doubled in patients with atrial fibrillation. Thus, INR should be monitored closely following altitude travel to facilitate early detection and compensation for subtherapeutic INR values. In patients with atrial fibrillation, it would be prudent to measure INR after arrival at altitude if this is practicable. Warfarin dosing and monitoring may be hindered by extended periods of remote travel, alterations in eating habits, travel-related illness, and physical exertion. Although it comes with the added inconvenience of carrying and disposing of injection paraphernalia, low molecular weight heparin should be considered in patients where adherence to a warfarin regime is not practical but stable anticoagulation is critical. An additional, albeit expensive, option is a portable INR monitor which a suitably trained patient could use in conjunction with a nomogram for adjusting warfarin doses.

Cortisol demands will increase in response to the hypobaric hypoxia at altitude. Patients taking glucocorticosteroids should adjust their dose accordingly. It is recommended that the maintenance dose be doubled at altitudes above 3,000 m and tripled above 4,000 m. Supplemental injectable corticosteroids should also be available for administration in case of unexplained deterioration. Medications with a narrow therapeutic index that require toxicity monitoring (eg, lithium and certain anticonvulsant drugs) pose an additional limitation to prolonged remote travel at altitude.

Medical Issues on Commercial Flights

Passive ascent to altitude may result in sudden exposure to altitude without adequate time for acclimatization. This rapid change poses an additional physiologic challenge to people with compromised health and affects the safety of some medical devices. Cabin pressure in commercial aircraft is regulated at barometric pressures equivalent to altitudes between 1,500 and 2,500 m. In patients with reduced partial pressure of arterial oxygen at sea level, blood oxygen saturation can fall drastically at normal cabin pressures. Even healthy passengers may be uncomfortable in these conditions.
and symptoms of subacute mountain sickness have been reported in flight.\textsuperscript{143} Physicians should refer to the BTS guidelines for recommendations on predicting and preventing respiratory decompensation during air travel.\textsuperscript{57}

As gas expands with decreasing barometric pressure, pneumatic splints are disallowed in most flights and plaster casts should be bivalved if applied within the previous 48 h to avoid circulatory compromise.\textsuperscript{19}

**Table 4** Summary of recommendations

<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Recommendations regarding altitude exposure</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Ascend with caution</td>
<td>Case series</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Contraindicated if symptomatic at resident altitude. Ascend with caution if asymptomatic at resident altitude</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Contraindicated</td>
<td>Multiple small case-control studies</td>
</tr>
<tr>
<td>• Unstable angina</td>
<td>Ascend with caution</td>
<td></td>
</tr>
<tr>
<td>• Exertional angina</td>
<td>Contraindicated for 6 mo after MI</td>
<td></td>
</tr>
<tr>
<td>• Myocardial infarction</td>
<td>No contraindication if asymptomatic at resident altitude</td>
<td></td>
</tr>
<tr>
<td>• CABG, angioplasty</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>Individual cardiology risk assessment needed</td>
<td>Small cohort studies</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>Ascend with caution</td>
<td>Case series, multiple case reports</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>Ascend with caution, individual risk assessment needed</td>
<td></td>
</tr>
<tr>
<td>• Mild</td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td>• Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>Ascend with specific precautions</td>
<td>Multiple case series</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>Contraindicated if oxygen desaturation occurs at sea level</td>
<td>Case report, expert opinion</td>
</tr>
<tr>
<td>Pleural and interstitial lung disease</td>
<td>Ascend with caution</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>• Secondary pulmonary hypertension</td>
<td>Contraindicated for 3 wk post resolution</td>
<td>Clinical guidelines</td>
</tr>
<tr>
<td>• Pneumothorax</td>
<td>Contraindicated in active PUD</td>
<td>Larger cohort study</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Contraindicated in active disease; travel with limitations in quiescent disease</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Ascend with specific precautions</td>
<td>Two case-control studies</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Ascend with precautions</td>
<td>Case reports</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>Contraindicated if oxygen desaturation occurs at sea level</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>PE</td>
<td>Contraindicated if symptomatic</td>
<td>Case-control study</td>
</tr>
<tr>
<td>• Pulmonary hypertension</td>
<td>Contraindicated for 3 wk post resolution</td>
<td>Case series</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>Contraindicated in active PUD</td>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Specific precautions if history of PUD</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Ascend with specific precautions</td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>Relaxation with specific precautions</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>Contraindicated in obesity—hyponoventilation syndrome</td>
<td></td>
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<tr>
<td>Epilepsy</td>
<td>Ascend with caution</td>
<td></td>
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<tr>
<td>Cerebrovascular disease</td>
<td>Contraindicated for 90 d post CVA/TIA</td>
<td></td>
</tr>
<tr>
<td>Migraine</td>
<td>Ascend with caution</td>
<td></td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>Correct prior to ascent</td>
<td></td>
</tr>
<tr>
<td>Sickle cell anemia</td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td>• Sickle cell disease</td>
<td>Ascend within limitations</td>
<td></td>
</tr>
<tr>
<td>• Sickle cell trait</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric conditions</td>
<td>Ascend with caution</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Contraindicated in the first trimester if high risk of spontaneous abortion</td>
<td>Cohort studies, expert consensus report</td>
</tr>
<tr>
<td>• Contraindicated beyond first trimester in the presence of certain co-morbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>Ascend with specific precautions</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Radial keratotomy</td>
<td>Ascend with precautions</td>
<td>Case-control study</td>
</tr>
<tr>
<td>LASIK</td>
<td>Ascend with precautions</td>
<td>Case series</td>
</tr>
<tr>
<td>Damage to carotid bodies</td>
<td>Ascend with caution</td>
<td>Case series</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; LASIK, laser in situ keratomileusis; CABG, coronary artery bypass graft; PUD, peptic ulcer disease; CVA, cerebral vascular accident; TIA, transient ischemic attack.
• Seek medical advice before booking the trip.
• Avoid travel if a medical condition is not stable.
• Purchase travel insurance including coverage for remote evacuation.\textsuperscript{11}
• Ensure optimal physical fitness prior to travel.
• Understand airline restrictions and requirements for travel with medication or medical devices. Request necessary documentation from a physician.
• Consult a physician and/or pharmacist in relation to regular medications as follows:
  – Potential interactions with medications commonly used to treat altitude-related illness\textsuperscript{37}
  – Potential respiratory depressant effects\textsuperscript{43}
  – Medications that can affect exercise tolerance, thermoregulation, acclimatization, or cognition
  – Considerations for transport and storage of medications (ie, temperature and ultraviolet sensitivity)\textsuperscript{18}
  – Understand the effect of time zone changes on medication schedules.\textsuperscript{31}
• Continue with regular treatments unless otherwise instructed by a physician.
• Bring extra doses of regular medications.\textsuperscript{7,144}
• Carry emergency supplies of medications separate from the main supply.\textsuperscript{7,144}
• Travel with a partner or group.
• Inform and educate team leaders or travel companions about relevant medical conditions. If necessary, provide verbal and/or written instructions\textsuperscript{26} with regards to:
  – The nature of existing medical conditions
  – How to recognize symptoms
  – How to intervene in the case of an emergency
  – The location of key items (eg, medication, syringes, blood glucose monitor).
• Wear Medic Alert\textsuperscript{®} identification (eg, bracelet) at all times.
• Maintain nutrition and hydration.\textsuperscript{26}
• Allow extra time for acclimatization (eg, an extra night around 2,000 m) and restrict activity during this period.\textsuperscript{31}
• Descend to lower altitude immediately with the onset of symptoms.\textsuperscript{31}

Table 5 Checklist of recommendations for people traveling to altitude with preexisting medical conditions

\begin{itemize}
  \item Seek medical advice before booking the trip.
  \item Avoid travel if a medical condition is not stable.
  \item Purchase travel insurance including coverage for remote evacuation.\textsuperscript{11}
  \item Ensure optimal physical fitness prior to travel.
  \item Understand airline restrictions and requirements for travel with medication or medical devices. Request necessary documentation from a physician.
  \item Consult a physician and/or pharmacist in relation to regular medications as follows:
    – Potential interactions with medications commonly used to treat altitude-related illness\textsuperscript{37}
    – Potential respiratory depressant effects\textsuperscript{43}
    – Medications that can affect exercise tolerance, thermoregulation, acclimatization, or cognition
    – Considerations for transport and storage of medications (ie, temperature and ultraviolet sensitivity)\textsuperscript{18}
    – Understand the effect of time zone changes on medication schedules.\textsuperscript{31}
  \item Continue with regular treatments unless otherwise instructed by a physician.
  \item Bring extra doses of regular medications.\textsuperscript{7,144}
  \item Carry emergency supplies of medications separate from the main supply.\textsuperscript{7,144}
  \item Travel with a partner or group.
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  \item Allow extra time for acclimatization (eg, an extra night around 2,000 m) and restrict activity during this period.\textsuperscript{31}
  \item Descend to lower altitude immediately with the onset of symptoms.\textsuperscript{31}
\end{itemize}

Recommendations

All people traveling to altitude should know the precise details of their planned trip, train for physical demands, be familiar with standard ascent and acclimatization protocols, and recognize the symptoms of altitude-related illness. For people with preexisting medical conditions, the risks of altitude exposure and removal from potential medical support are significant and must be taken seriously (Table 4). On the other hand, with proper planning and precautions, many people with preexisting medical conditions can safely take part in outdoor adventures at high altitude (Table 5). Ultimately, avoidance of potential risk must be carefully weighed against an individual’s desire to achieve personal goals. Physician and patient must work together to plan a rational and informed approach.

Declaration of Interests

The authors state they have no conflicts of interest to declare.

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