CHAPTER 10

High-Altitude Travel

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Increasing numbers of people are traveling to high altitude for work or pleasure. While the rewards of such travel are often great and include opportunities to see places of great beauty or historical and cultural significance, to accomplish lifelong objectives, or to simply have an enjoyable vacation, there are risks associated with such travel. Unacclimatized lowlanders are at risk for one of several forms of acute altitude illness within the first several days of ascent, while individuals with underlying medical problems may be at risk for worsening control of those problems or other complications.

This chapter provides information for counseling individuals seeking advice about how to prevent such problems. After defining the term "high altitude" and describing features of the high-altitude environment and the physiologic responses to hypobaric hypoxia, the chapter describes a general approach to three types of patients who may present for evaluation: the traveler who has never been to high altitudes before and seeks advice on ensuring a safe trip, the returning traveler who had a problem on a prior trip and seeks advice on how to avoid repeating such problems in the future, and the potentially at-risk traveler with underlying medical problems that may be exacerbated by hypobaric hypoxia or may predispose to acute altitude illness.

WHAT CONSTITUTES "HIGH ALTITUDE"?

Although there are no firm definitions, the term "high altitude" generally refers to regions located above 1500 m (~5000 ft) in elevation. While some physiologic responses to hypoxia begin just above this threshold, acute altitude illness does not generally occur until an individual ascends above 2340 m (~8000 ft). For most healthy individuals, it is only when traveling above this latter threshold that the altitude should be taken into account with trip planning. For individuals with underlying medical conditions, however, the effect of the altitude may need to be considered at lower elevations. Regardless of underlying health status, the further an individual travels above these thresholds, the greater the potential for altitude-related problems.

The majority of high-altitude travelers will not ascend above 5500-6500 m, a range that includes common trekking destinations such as Mt. Kilimanjaro (5895 m) and Everest base camp (5350 m). Select individuals, typically those engaged in mountaineering expeditions, do ascend above this range and are exposed to extreme degrees of hypoxia that pose significant physiologic challenges and markedly increase the risk of acute altitude illness if proper acclimatization measures are not undertaken.

THE ENVIRONMENT AT HIGH ALTITUDE

The defining environmental feature at high altitude is the nonlinear decrease in barometric pressure with increasing elevation. This change, which is more pronounced at higher latitudes and during the winter months, leads to decreased ambient partial pressure of oxygen

(PO_2) that, in turn, lowers the PO_2 throughout the body and triggers several important physiologic responses (described later).

Other important environmental changes include lower air density, increased ultraviolet (UV) light exposure, decreased humidity, and decreased ambient temperature. The lower air density is likely too small to be of clinical significance, while the increased UV exposure decreases the time necessary to develop sunburn and ultraviolet keratitis ("snow blindness"), particularly with travel on snow-covered terrain. The decrease in humidity increases insensible water losses through the respiratory tract and the risk of dehydration, particularly when individuals engage in physical exertion, while the decrease in temperature may increase the risk of hypothermia and frostbite depending on the full range of environmental conditions at the time of travel.

Air quality often improves in the mountains, but this is not always the case. Greater solar radiation increases smog potential, while extensive valley systems can trap pollutants during temperature inversions, particularly when near urban centers. Finally, wood and yak-dung stoves are common heat sources in rural areas of the Himalaya and elsewhere, leading to poor air quality when these stoves are in high use.

PHYSIOLOGIC RESPONSES TO HYPOBARIC HYPOXIA

The decrease in PO_2 at all points along the oxygen transport cascade from inspired air to the alveolar space, arterial blood, and tissues causes physiologic responses across multiple organ systems, which facilitates adaptation to the hypobaric hypoxia (**Table 10.1**). Some of the responses, such as the increase in minute ventilation, start within minutes of exposure, while other responses, such as erythropoiesis, take several weeks before their full effect is realized. The magnitude of these responses varies considerably between individuals, and this

TABLE 10.1 Physiologic Responses to Hypobaric Hypoxia

System	Responses
Pulmonary responses	Arterial hypoxemia triggers increased peripheral chemoreceptor output, leading to an increase in minute ventilation and a respiratory alkalosis.
	The respiratory alkalosis blunts the initial ventilatory responses.
	With continued time at high altitude, minute ventilation rises further due to renal compensation for the respiratory alkalosis and increased sensitivity of the peripheral chemoreceptors.
	Alveolar hypoxia triggers hypoxic pulmonary vasoconstriction, leading to an increase in pulmonary vascular resistance and pulmonary artery pressure.
Cardiac responses	Cardiac output increases, largely due to an increase in heart rate.
	Stroke volume declines due to a decrease in plasma volume.
	Myocardial contractility is preserved.
	Systemic blood pressure increases to a variable extent.
Renal responses	Variable increase in diuresis and natriuresis following ascent leads to a decrease in circulating plasma volume.
	Arterial hypoxemia triggers increased secretion of erythropoietin (EPO) within 24-48 hours of ascent.
	There is an increase in bicarbonate excretion, as compensation for the acute respiratory alkalosis.
Hematologic responses	There is an initial increase in hemoglobin concentration and hematocrit due to reduction in plasma volume.
	Over days to weeks, there are further increases in red blood cell mass, hemoglobin concentration, and hematocrit due to increased EPO concentrations.

variability plays a large role in determining tolerance of hypobaric hypoxia and susceptibility to acute altitude illness.

Because of these environmental changes and physiologic responses to hypobaric hypoxia, high-altitude travelers are at risk for a range of problems they might not experience at lower elevations and may present for evaluation with one of several possible concerns:

- **The altitude-naïve traveler** who has never ascended to high altitude before and seeks advice on how to ensure a safe trip
- **The returning traveler** who had problems on a prior high-altitude trip and seeks information about what happened and how to prevent such problems in the future
- **The potentially at-risk traveler** who has underlying medical problems that may worsen at high altitude or predispose to acute altitude illness.

The remainder of this chapter describes an approach to each of these situations.

THE ALTITUDE-NAÏVE TRAVELER

Many travelers have never been to high altitude and seek advice about what to expect in this environment and how to prevent problems. Alternatively, individuals who have traveled to high altitude before without difficulty may be going to significantly higher elevations and are now concerned about similar issues. Effective counseling of such travelers encompasses a range of topics described in detail below.

Normal Responses to High Altitude

Even if they avoid acute altitude illness, individuals feel different at high altitude than at lower elevations as a result of the environmental changes and physiologic responses to hypobaric hypoxia. These differences (**Table 10.2**) should be reviewed as part of pre-trip counseling, as this can prevent misinterpretation of normal responses as evidence of illness and facilitate identification of those individuals who are truly becoming ill.

High-altitude travelers who are otherwise well commonly report poor sleep quality, insomnia, vivid dreams, and frequent awakenings. A major contributor to these problems is periodic breathing, in which periods of crescendo-decrescendo breathing movements are punctuated by apneas lasting from 5 to 20 seconds. While overall sleep quality tends to improve over time, periodic breathing can persist or worsen during long stays at high altitude.

Exercise is also challenging at high altitude. At any given level of work, heart rate and minute ventilation are higher than at sea level, and, unlike at sea level, arterial oxygen saturation decreases with progressive exercise. Even following extensive pre-trip physical training, individuals experience more intense breathlessness during exertion, particularly during the first few days at altitude. Importantly, however, on stopping to rest, dyspnea typically resolves within a short time (~1-2 min).

Recognition of Acute Altitude Illness

All high-altitude travelers should be able to recognize the three main forms of acute altitude illness: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and

TABLE 10.2 How Travelers Feel Different at High Altitude Compared with the Altitude of Residence

- Heart rate at rest and with any level of exertion higher than at altitude of residence
- Increased respiratory rate and tidal volume
- More frequent sighs
- Increased frequency of urination
- Dyspnea on exertion that resolves quickly with rest
- Difficulty sleeping, including frequent arousals, insomnia, vivid dreams
- Transient lightheadedness on rising to a standing position

high-altitude pulmonary edema (HAPE). The clinical features of these diseases are described in **Table 10.3**, while information about their underlying pathophysiology is described in several excellent reviews listed at the end of this chapter. Of these entities, AMS is by far the most common and the most likely to be encountered during high-altitude travel. HACE and HAPE are uncommon but potentially fatal if not recognized promptly and warrant attention in pre-travel counseling.

For individuals ascending to and remaining at a given elevation, the risk for these problems lasts up to 5 days following ascent. Individuals ascending to steadily higher elevations, as on a climbing expedition, remain at risk until they begin to descend from their maximum elevation, at which point the risk of illness decreases significantly and eventually disappears entirely as descent continues.

A challenge in recognizing AMS is the nonspecific nature of the symptoms, as headache can be seen as a result of dehydration, carbon monoxide intoxication from cooking in a poorly ventilated tent, and other causes. Similarly, symptoms of HAPE can be present in other respiratory disorders such as pneumonia and pulmonary embolism. However, while it is always important to consider a broad differential diagnosis, compatible symptoms and signs arising following ascent should be considered altitude illness until proven otherwise.

Risk Factors for Acute Altitude Illness

The primary reason individuals develop acute altitude illness is they ascend too high, too fast, where "fast" refers to the number of meters ascended per day rather than the walking pace itself. For example, an individual ascending to 5000 m over 3 days and remaining at that elevation is more likely to get sick than an individual completing the same ascent over 7 days.

There is an important interaction between the altitude attained and the time spent at that altitude that affects risk; individuals who ascend rapidly but descend quickly after reaching the summit may avoid altitude illness, whereas individuals who complete the same ascent at the same rate but remain on the summit for many hours face a higher risk of problems.

There is considerable inter-individual variability in susceptibility to acute altitude illness, such that some individuals acclimatize well and tolerate seemingly fast ascents while others develop problems even with appropriate ascent profiles. While susceptibility to altitude illness is likely a multigenetic trait, the specific genetic polymorphisms have not been identified, and we lack a simple, reliable means of predicting which travelers face risk following ascent.

A common misperception is that being in good physical condition protects against acute altitude illness. To the contrary, highly fit endurance athletes are just as susceptible to AMS, HACE, and HAPE as unconditioned individuals and must adhere to the same principles of altitude illness prevention.

Prevention of Acute Altitude Illness

Effective prevention relies on a combination of both nonpharmacologic and pharmacologic measures.

Nonpharmacologic Measures

Because the primary risk factor for acute altitude illness is an overly rapid ascent, the single best preventive measure is to undertake an adequately slow ascent to the target elevation. In particular, once above 3000 m, individuals should not increase their sleeping elevation by more than 300-500 m per night and, every 3-4 nights, should take a rest day and remain at the same elevation for a second night. While simple in its prescription, this rule of thumb can be hard to follow, as the logical stopping points on most major trekking or climbing routes are not spaced at 500 m intervals. In such situations, rather than focusing on the elevation gain for each day of the trip, one can focus on the overall rate of gain for the entire trip. If excessive gains in elevation are necessary on particular days, rest days can be added to the itinerary to decrease the overall ascent rate. As individuals gain experience traveling at high altitude they can deviate from these guidelines based on their personal

TABLE 10.3 Clinical Features and Management of Acute High-Altitude Illnesses

Acute Altitude Illness	Timing and Altitude of Onset	Clinical Features	Prevention	Treatment
Acute mountain sickness (AMS)	Seen at altitudes ≥2340 m Altitude of onset varies significantly between individuals Subacute onset of symptoms within 6-10 hr of ascent to a given elevation	Headache plus one or more of the following: nausea, vomiting, lethargy, sustained light-headedness Normal neurologic exam and normal mental status	Slow ascent (above 2500 m, limit increases in sleeping elevation to 500 m/day) Avoid overexertion Acetazolamide or dexamethasone with moderate- to high-risk ascent profiles	Stop ascending Acetaminophen or NSAIDs for headache Antiemetics Mild to moderate illness: acetazolamide Severe cases: dexamethasone Descend if symptoms do not improve in 1-2 days or worsen on appropriate treatment Further ascent possible if symptoms resolve
High-altitude cerebral edema (HACE)	Seen at altitudes ≥3000 m, with increasing incidence at higher elevations Subacute onset of symptoms. Sudden onset of symptoms should prompt search for alternative causes	Preexisting AMS or concurrent HAPE symptoms (not universally present) Ataxia, altered mental status Severe lassitude, somnolence, coma Focal neurologic deficits uncommon and should prompt consideration of other diagnoses Potentially fatal if not recognized and treated promptly	Slow ascent Avoid overexertion Acetazolamide or dexamethasone with moderate- to high-risk ascent profiles	Descend until symptoms resolve If descent not possible, supplemental oxygen or a portable hyperbaric chamber Dexamethasone
High-altitude pulmonary edema (HAPE)	Seen at altitudes ≥2500 m, with cases documented at lower elevations in patients with history of pulmonary vascular diseases Subacute onset within 2-5 days of ascent	Mild: dyspnea and arterial O_2 desaturation out of proportion to that seen in normal individuals with similar ascent rates at a given elevation; decreased exertional tolerance, dry cough Severe: dyspnea with mild exertion or at rest; cough with pink, frothy sputum; cyanosis May see concurrent signs or symptoms of AMS or HACE but not universally present Potentially fatal if not recognized promptly	Slow ascent Avoid overexertion Nifedipine for individuals with prior history of HAPE (alternative: phosphodiesterase inhibitors)	Descend until symptoms resolve Avoid heavy exertion on descent If descent not possible, supplemental oxygen or a portable hyperbaric chamber Nifedipine or phosphodiesterase inhibitor (may not be necessary if supplemental oxygen available) Avoid concurrent use of nifedipine and phosphodiesterase inhibitor

NSAIDs, Nonsteroidal anti-inflammatory drugs.

tolerances of hypobaric hypoxia, but for the altitude-naïve traveler, they represent the appropriate initial approach.

Travelers should also avoid overexertion, heavy alcohol consumption, and opiate pain medications. Forced hydration is often recommended as a tool for decreasing the risk of altitude illness but has never been shown to be of benefit. Constant vigilance to adequate fluid intake does, however, prevent dehydration, whose symptoms mimic those of AMS.

Pharmacologic Measures

Information about the medications used to prevent AMS, HACE, and HAPE are provided in **Tables 10.3** and **10.4**. Because AMS and HACE may have a common pathophysiology, medications used to prevent AMS should prevent HACE. Several options are available for HAPE prevention, but these are reserved for individuals with a history of HAPE and are not used in the altitude-naïve traveler. Despite recent attention in the literature, ibuprofen has not replaced acetazolamide or dexamethasone as the preferred option for pharmacologic prophylaxis.

Not all travelers require pharmacologic prophylaxis. Instead, the decision to use medications should be based on an assessment of the risk associated with a planned ascent profile (**Table 10.5**). Pharmacologic prophylaxis is not necessary with low-risk ascent profiles but should be strongly considered with moderate- to high-risk itineraries.

Treatment of Acute Altitude Illness

As with prevention, the therapeutic approach to altitude illness is based on a combination of nonpharmacologic and pharmacologic measures. The most important treatment principle is to stop ascending and, in some cases, to descend to lower elevation. Patients with mild to moderate AMS may remain at the same elevation while undergoing treatment, while those with incapacitating AMS, HACE, or HAPE should descend. Descent raises the barometric pressure and the PO_2 at each step of the oxygen transport cascade, thereby terminating the pathophysiologic processes contributing to these diseases. Five hundred to 1000 m of descent is usually sufficient in most cases, although more severely ill patients should be evacuated as to as low an altitude (and as quickly) as possible. When descent is not feasible due to weather or logistical factors, supplemental oxygen or portable hyperbaric chambers are suitable alternatives, if available.

A general treatment approach for each disease, including pharmacologic measures, is described in **Table 10.3**, while the appropriate doses for the medications used in treatment are provided in **Table 10.4**. Clinical experience suggests that dexamethasone is more effective than the acetazolamide for treating moderate to severe AMS. The use of medications in HAPE varies based on the clinical setting; travelers who access health facilities may only require supplemental oxygen, while those in more remote settings should receive either the nifedipine, tadalafil, or sildenafil. No further ascent should be undertaken until the individual is asymptomatic while off medications. Strong consideration should be given to adding pharmacologic prophylaxis with continued ascent following an episode of altitude illness.

THE RETURNING TRAVELER

Travelers returning from trips to high altitude often present for evaluation of problems that developed during their sojourn. The range of problems for which they may seek evaluation is broad and includes the acute altitude illnesses described above and a host of other problems that may or may not be related to the altitude, such as vision changes due to retinal hemorrhages or prior refractive surgery, neurologic disorders such as seizures or transient focal neurologic deficits, respiratory problems such as persistent cough or pneumonia, and chest pain on exertion. Depending on the problem, the common concerns in such evaluations are determining what happened, whether the individual can return to high altitude in the future, and what preventive measures would be useful on such trips.

TABLE 10.4 Doses and Other Considerations for Medications Used in the Prevention and Treatment of Acute Altitude Illness

Medication	Dose for Prevention	Dose for Treatment	Other Considerations
Acetazolamide	125 or 250 mg every 12 h	250 mg every 12 h	Contraindicated in patients with cirrhosis Avoid in patients with severe ventilatory limitation (FEV_1 <25% predicted) Avoid in patients on chronically high doses of aspirin Caution in patients with documented sulfa allergy
Dexamethasone	2 mg every 6 h or 4 mg every 12 h	AMS: 4 mg every 6 hr HACE: 8 mg once then 4 mg every 6 h	May increase blood glucose values in diabetic patients Avoid in patients at risk for peptic ulcer disease Caution in patients at risk for strongyloidiasis
Nifedipine	30 mg sustained-release version every 12 h	30 mg sustained-release version every 12 h	Caution in patients using medications metabolized by CytP450 system Caution with concurrent use with other antihypertensive medications
Sildenafil	50 mg every 8 h[a]	50 mg every 8 h[a]	Avoid concurrent use of nitrates and alpha-blockers Caution in patients taking medications metabolized by CytP450 system
Tadalafil	10 mg every 12 h	10 mg every 12 h[b]	Avoid concurrent use of nitrates and alpha-blockers Caution in patients taking medications metabolized by CytP450 system
Salmeterol	125 μg every 12 h[c]	Not used for treatment	Potential for adverse effects in patients with coronary artery disease prone to arrhythmia

[a]Clinical utility for prevention or treatment not demonstrated.
[b]Clinical studies have shown benefit only in HAPE prevention.
[c]Not used as monotherapy for HAPE prevention. Recommended only as adjunct to pulmonary vasodilator therapy.
AMS, Acute mountain sickness; *FEV_1,* forced expiratory volume in the first second; *HACE,* high-altitude cerebral edema; *HAPE,* high-altitude pulmonary edema.

Determining What Happened

A major challenge in these assessments is the fact the symptoms and signs have typically resolved by the time the patient presents for evaluation. If the traveler accessed medical care at the time of the problem, he or she may have medical records, including chest radiographs and laboratory studies, that can be used as part of the assessment. In many cases, however, individuals descend to lower elevation and return home without any formal evaluation at the time of their problem. All that is available in such situations is the individual's oral description of the events and perhaps an oxygen saturation value if someone on their trip

TABLE 10.5 Risk Categories for Acute Altitude Illness in Unacclimatized Individuals Ascending to High Altitude[a]

Risk Category	Description
Low	• Individuals with no prior history of altitude illness and ascending to ≤2800 m • Individuals taking ≥2 days to arrive at 2500-3000 m with subsequent increases in sleeping elevation <500 m/day and an extra day for acclimatization every 1000 m
Moderate	• Individuals with prior history of AMS and ascending to 2500-2800 m in 1 day • No history of AMS and ascending to >2800 m in 1 day • All individuals ascending >500 m/day (increase in sleeping elevation) at altitudes above 3000 m but with an extra day for acclimatization every 1000 m
High	• Individuals with a history of AMS and ascending to >2800 m in 1 day • All individuals with a prior history of HACE and HAPE • All individuals ascending to >3500 m in 1 day • All individuals ascending >500 m/day (increase in sleeping elevation) above >3000 m without extra days for acclimatization • Very rapid ascents (e.g., <7-day ascents of Mt. Kilimanjaro)

[a]Altitudes listed refer to the altitude at which the person sleeps. Ascent is assumed to start from elevations <1200 m. *AMS,* Acute mountain sickness; *HACE,* high-altitude cerebral edema; *HAPE,* high-altitude pulmonary edema.
Adapted from Luks, A.M., McIntosh, S.E., Grissom, C.K., et al., 2014. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Acute Altitude Illness: 2014 update. Wilderness Environ. Med. 25, S4–S14.

was carrying a pulse oximeter. The absence of corroborating data in such cases places a high premium on thorough history taking.

A key question is whether the problem was directly related to the hypobaric hypoxia at high altitude. A general rule of thumb is that symptoms and signs developing after ascent and resolving with descent are typically attributable to high altitude. There are exceptions to this rule, however, as vision deficits from symptomatic high-altitude retinal hemorrhages can persist for weeks following descent, while seizures associated with high altitude may terminate before descent. The timing of onset relative to the ascent can also be useful. AMS, HACE, and HAPE typically develop within 1-5 days of ascent to a given elevation, and, as a result, problems developing after that time period at a given altitude are more likely attributable to another issue. When available, pulse oximetry can aid in evaluating patients with respiratory issues. Patients with HAPE, for example, develop severe hypoxemia, and it is hard to ascribe respiratory problems at high altitude to HAPE if the individual had oxygen saturation values similar to those of healthy members of their trip.

Further Evaluation

For problems other than the acute altitude illnesses, the need for further evaluation depends on the particular problem. While individuals who developed chest pain on exertion at high altitude or those with symptomatic retinal hemorrhages, for example, warrant further evaluation by the appropriate specialist, other problems, such as persistent cough, may not warrant immediate assessment.

For individuals who developed acute altitude illness, a general principle is that prior performance at high altitude is a good but not perfect predictor of outcomes on subsequent trips. For example, an individual who developed AMS following a single-day ascent to 3000 m is likely but not guaranteed to develop AMS on a similar ascent in the future. Similarly, studies have shown that HAPE-susceptible individuals have about a 60% chance of recurrence on subsequent trips to the same elevation.

Individuals with AMS and HACE do not warrant any further testing to determine future risk, as there are no widely accessible means for this assessment. Because HAPE-susceptible individuals have a characteristic phenotype marked by excessive rises in pulmonary artery pressure in response to resting hypoxia and normoxic and hypoxic exercise, consideration can be given to evaluating for such responses in individuals with a concerning history. Such testing is not widely available, however, and, as a result, in individuals with a clear history of the diagnosis, it may be acceptable to forego such testing and just use pharmacologic prophylaxis on future trips.

Risk Mitigation for Future Trips

Individuals with a history of AMS, HACE, or HAPE can return to high altitude in the future. While those with AMS may not require pharmacologic prophylaxis with future ascents if they are going to lower elevations or using a slower ascent rate, individuals with HACE or HAPE should use pharmacologic prophylaxis, as the consequences of these illnesses are potentially great (**Tables 10.3** and **10.4**). Individuals should be counseled to ascend at a slower rate than on their prior trips.

When there is uncertainty about the likelihood of a problem recurring on future trips, consideration can be given to doing graded exposures to high altitude in more controlled settings. For example, prior to a committing trek into a distant, remote area, the individual can do a series of test trips to areas from which they can readily descend or access medical facilities in the event of problems.

THE POTENTIALLY AT-RISK TRAVELER

While many high-altitude travelers have no prior medical history, it is highly likely that some individuals who present for pre-travel counseling will have underlying medical conditions. Many of these travelers will have mild, well-controlled problems that pose little risk at high altitude, while others may have severe or difficult-to-control issues that could predispose to problems during the planned trip. Regardless of the severity of the condition, individuals with underlying medical issues warrant assessment to determine whether those issues will worsen at high altitude or affect the risk of acute altitude illness.

A Framework for Assessing Risk

A challenge of these evaluations is that, with the exception of several common conditions such as asthma, coronary artery disease, hypertension, and sleep apnea, the evidence base for pre-travel assessment of the full spectrum of problems with which patients may present is limited, and providers may find few, if any, studies that address risk for their patient's specific condition. In such situations, the assessment can be framed around four general questions.

Question 1: Is the Individual at Risk for Severe Hypoxemia or Impaired Tissue Oxygen Delivery?

While all individuals develop hypoxemia to varying degrees at high altitude based on how high they ascend, certain categories of patients, including those with moderate to severe chronic obstructive pulmonary disease, interstitial lung diseases, severe cystic fibrosis, and cyanotic congenital heart disease, will develop more severe hypoxemia than normal, particularly during exertion. This not only may lead to increased dyspnea and poor exertional tolerance but, in some studies, has been associated with an increased risk of AMS. With anemia, the arterial PO_2 will be the same at rest as in normal individuals, but oxygen carrying capacity and oxygen delivery are decreased, which may also lead to severe dyspnea and exercise limitation.

Question 2: Is the Individual at Risk for Impaired Ventilatory Responses to Hypoxia?

As described in **Table 10.2**, arterial hypoxemia normally triggers an increase in minute ventilation, whose role is to maintain the alveolar and arterial PO_2 at adequate levels. Individuals with severely impaired respiratory mechanics, as in severe chronic obstructive

pulmonary disease, obesity hypoventilation syndrome, and many neuromuscular disorders, or those with impaired respiratory drives may not be able to mount the expected ventilatory responses. This, in turn, will cause greater degrees of hypoxemia and, as a result, increased dyspnea, impaired exertional tolerance, and, possibly, an increased risk of AMS.

Question 3: Is the Individual at Risk Due to the Expected Pulmonary Vascular Responses to Hypobaric Hypoxia?

As noted in **Table 10.2**, decreases in the alveolar PO_2 at high altitude lead to an increase in pulmonary vascular resistance, which raises pulmonary artery pressure. This change is well tolerated in most individuals but could pose problems for patients with pulmonary hypertension or right heart disease, as the literature contains several reports documenting the development of HAPE or worsening right heart function in patients with underlying pulmonary hypertension exposed to ambient hypoxia during either travel to high altitude or commercial flight. How severe the underlying pulmonary hypertension or right heart dysfunction must be to predispose to problems remains unclear, as the patients in these reports had varying degrees of pulmonary hypertension, but the presence of this issue should raise concern in the pre-travel evaluation.

Question 4: Will Environmental Features of High Altitude or the Expected Physiologic Responses to Hypobaric Worsen the Underlying Medical Condition?

Certain features of the environment at high altitude or the expected physiologic responses to hypoxia can affect some medical conditions. For example, cold, dry air may adversely affect airway function in asthmatic individuals, particularly those with exercise-induced symptoms, while increased sympathetic nervous system activity can worsen blood pressure in hypertensive individuals. The expected hypoxemia at high altitude can trigger vaso-occlusive crises in sickle cell disease patients or potentially provoke myocardial ischemia in patients with inadequately controlled coronary artery disease. A complete discussion of how various diseases are affected by high altitude is beyond the scope of this chapter. The expected outcomes for several common diseases are described in **Table 10.6**, while more extensive reviews on this topic are listed at the end of the chapter.

If the answer to all of these questions is "no," the individual is likely safe to travel to high altitude without further evaluation or risk-mitigation strategies beyond the general prevention measures described above. Individuals with nonreassuring answers, however, may require further evaluation and one of several possible risk reduction measures.

Further Evaluation

For individuals deemed to be at risk based on nonreassuring answers to the first three questions noted above, the best way to evaluate potential outcomes at high altitude is to expose these individuals to hypoxia and monitor their responses. Because access to hypobaric chambers is limited, the most feasible approach is the hypoxia altitude simulation test, in which an individual breathes a hypoxic gas mixture while symptoms and physiologic responses such as heart rate, oxygen saturation, and blood pressure are monitored. The test can be supplemented with echocardiography to assess the pulmonary vascular responses to hypoxia. The test has advantages over published prediction rules designed to estimate the degree of hypoxemia experienced by lung disease patients at high altitude, as it allows direct measurement of oxygen saturation while breathing the gas mixture, but its utility is limited in several respects; it is hard to simulate the full duration of time and the full range of ambient hypoxia an individual may experience on his or her trip. An individual might not develop symptoms during the short duration of this test but could develop problems after several days at high altitude. For individuals planning trips to distant places such as the Himalaya or Andes Mountains, another option would be test trips under more controlled conditions prior to the intended trip by, for example, taking shorter trips to the Alps or Rocky Mountains, where symptoms and pulse oximetry can be monitored and the individual can easily descend or access health facilities in the event of problems. For nonreassuring answers to the fourth question above, the approach varies based on the clinical

TABLE 10.6 Common Medical Conditions and High-Altitude Travel

Disease or Condition	Key Issues for High-Altitude Travel
Asthma	Well-controlled patients can travel as high as 6000 m and possibly higher. Avoid travel with worsening asthma control or following an acute exacerbation. Continue inhaler regimen at high altitude and travel with an adequate supply of rescue medications.
Chronic obstructive pulmonary disease	Avoid high-altitude travel in patients with FEV_1 <1 L, CO_2 retention, pulmonary hypertension, or recent exacerbation. Assess the need for supplemental oxygen in patients with FEV 1.0-1.5 L. Monitor pulse oximetry following ascent. Continue inhaler regimen at high altitude and travel with an adequate supply of rescue medications.
Congestive heart failure	Avoid high-altitude travel with poorly compensated disease or following a recent exacerbation. Okay to ascend with well-compensated disease to altitudes <3000 m. Monitor weight and blood pressure following ascent and adjust medications according to pre-arranged plan.
Coronary artery disease	Avoid high-altitude travel with unstable angina, ischemia at low levels of exertion, or recent acute coronary syndrome (<3-6 months, no revascularization). Consider risk stratification with exercise treadmill test prior to planned travel. Reduce level of exertion to slightly lower than that done at sea level. No de novo exercise at altitude if not exercising at sea level. Continue existing medications at high altitude.
Diabetes mellitus	Increase frequency of blood glucose monitoring. Avoid overly strict glucose control early in the trip due to concerns about glucometer accuracy at high altitude. Evaluate for co-morbid conditions (e.g., coronary artery disease) that could worsen at high altitude. Avoid vigorous exercise at high altitude if not experienced with high-level exercise at sea level.
Hypertension	Mild or well-controlled disease: no indication for medication adjustments or routine blood pressure monitoring. Poorly controlled or labile hypertension: monitor blood pressure following ascent and adjust medications for severely elevated blood pressures (>180/120 with symptoms or >220/140 without symptoms).
Obstructive sleep apnea	Patients with moderate to severe disease should travel with CPAP machine if access to power can be assured. Consider adding acetazolamide to decrease the incidence of central sleep apnea.
Pregnancy	Evaluate pre-travel to ensure the pregnancy remains low risk. Avoid high-altitude travel with complicated or high-risk pregnancies (e.g., impaired placental function, chronic hypertension, intrauterine growth retardation, anemia). Exercise at levels lower than at home; avoid dehydration. Avoid travel into remote areas in the third trimester.

TABLE 10.6 Common Medical Conditions and High-Altitude Travel—cont'd

Disease or Condition	Key Issues for High-Altitude Travel
Pulmonary hypertension	Avoid high-altitude travel without supplemental oxygen with moderate to severe disease (mean PA pressure >35 mmHg or systolic PA pressure >60 mmHg). In less severe disease, consider adding pulmonary vasodilator therapy or supplemental oxygen.
Sickle cell diseases	Sickle cell anemia: avoid high-altitude travel due to increased risk of sickling and vaso-occlusive and splenic crises. Sickle cell trait: high-altitude travel likely okay, but patients should avoid heavy exertion and seek medical attention for left upper quadrant pain (possible splenic crisis).

CPAP, Continuous positive airway pressure; *FEV,* forced expiratory volume.

circumstances. Patients with coronary artery disease may require stress testing, for example, while patients with recent exacerbations of heart failure, asthma, chronic obstructive pulmonary disease, or recent stroke or myocardial infarction within the past 6 months may simply need to forego their planned trip.

Risk Mitigation Strategies

The most important principle of risk mitigation is to ensure the underlying medical problem is under good control at the time of the planned trip. Patients with evidence of worsening asthma, for example, should not embark on high-altitude travel, particularly into remote areas away from medical care. A second important principle is to ensure that patients remain on their baseline medications or therapies during their trip. Some individuals, such as those with diabetes, heart failure, or poorly controlled hypertension, should consider monitoring aspects of their disease more carefully during the trip and adjusting medications according to a pre-specified plan. Individuals at risk for disease exacerbations, such as those with asthma or chronic obstructive pulmonary disease, should travel with an adequate supply of rescue medications and a plan to access care in the event of symptoms that are difficult to control. Depending on their underlying medical condition, patients may need to adjust the dose or use alternative agents for acute altitude illness prophylaxis or treatment (**Table 10.4**).

Individuals at risk for severe hypoxemia or adverse consequences from the pulmonary vascular responses to hypoxia should consider using supplemental oxygen during the sojourn. In light of the logistical difficulties associated with air travel with supplemental oxygen, the best options for this would be to travel with a small, battery-powered portable oxygen concentrator, which is allowed on most commercial airlines, or to travel with a prescription for supplemental oxygen that can be filled at the destination if the patient has significant symptoms and/or severe hypoxemia. Patients with pulmonary hypertension may also need to add or augment pulmonary vasodilator therapy to blunt the expected pulmonary vascular responses at high altitude. Other disease-specific approaches are described in many of the references at the end of this chapter.

On returning to home at the conclusion of the trip, individuals who added or adjusted their medications should return to their baseline medication regimen.

RETURN TRAVEL TO HIGH ALTITUDE

Many of the issues described above are of greatest relevance to the first-time traveler to high altitude who has no prior sense of their susceptibility to acute altitude illness or how any underlying medical problems will be affected by this environment. As individuals make repeated trips to high altitude, however, they will gain greater understanding of their personal tolerances of hypoxia, which should carry several benefits. They will better understand

their ability to acclimatize to hypobaric hypoxia and, as a result, can adjust their ascent profiles and trip itineraries accordingly. The person who acclimatizes well, for example, may be able to move somewhat faster than the recommended rates, while highly susceptible individuals will learn they need to move slower than recommended and to consider pharmacologic prophylaxis. Individuals with underlying medical problems will also gain a greater understanding of how control of that problem is affected at high altitude and become better at adjusting their therapeutic regimen during their travels.

FURTHER READING

General High-Altitude Medicine

Bartsch, P., Mairbaurl, H., Maggiorini, M., et al., 2005. Physiological aspects of high-altitude pulmonary edema. J. Appl. Physiol. 98, 1101–1110.
This review provides a comprehensive overview of the clinical features and management of high-altitude pulmonary edema and the underlying pathophysiology of the disease.

Bartsch, P., Swenson, E.R., 2013. Clinical practice: acute high-altitude illnesses. N. Engl. J. Med. 368, 2294–2302.
This is a comprehensive review of the clinical aspects of the three main forms of acute altitude illness by leading experts in the field. It is a more up-to-date version of the review by Hackett and Roach below.

Hackett, P.H., Roach, R.C., 2001. High-altitude illness. N. Engl. J. Med. 345, 107–114.
This is a comprehensive review of the clinical aspects of the three main forms of acute altitude illness by leading experts in the field.

Hackett, P.H., Roach, R.C., 2004. High altitude cerebral edema. High Alt. Med. Biol. 5, 136–146.
This is a comprehensive review of the clinical aspects and underlying pathophysiology of high-altitude cerebral edema.

Hackett, P.H., Roach, R.C., 2012. High altitude medicine. In: Auerbach, P. (Ed.), Wilderness Medicine. Elsevier Mosby, Philadelphia, pp. 2–33.
This chapter is the most comprehensive overview of all aspects of high-altitude medicine, including the physiologic responses to hypoxia; the clinical features, management, and pathophysiology of the acute altitude illnesses; and other medical problems at high altitude and how to approach the high-altitude traveler with underlying medical conditions.

Luks, A.M., 2014. Physiology in medicine: a physiologic approach to prevention and treatment of acute high altitude illnesses. J. Appl. Physiol. (1985) 118 (5), 509–519. Epub ahead of print.
This review provides an overview of clinical high-altitude medicine with an emphasis on the physiologic basis for the approach to preventing and treating acute altitude illness.

Luks, A.M., Swenson, E.R., 2008. Medication and dosage considerations in the prophylaxis and treatment of high-altitude illness. Chest 133, 744–755.
This review describes the primary medications used in the prevention and treatment of acute altitude illness, including proper dosing, dose adjustments for patients with underlying liver and kidney disease, and other important issues to consider when placing travelers on these medications.

Luks, A.M., McIntosh, S.E., Grissom, C.K., et al., 2014. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Acute Altitude Illness: 2014 update. Wilderness Environ. Med. 25, S4–S14.
This is a widely read set of expert guidelines outlining the recommended approach to the prevention and treatment of AMS, HACE, and HAPE, with grading of the evidence for those recommendations.

Swenson, E.R., Bartsch, P., 2013. High Altitude: Human Adaptation to Hypoxia. Springer, New York.
This is a very comprehensive overview of high-altitude physiology and medicine that includes the physiology of hypoxia in all major organ systems as well as clinical aspects of acute and chronic altitude illness.

West, J.B., Schoene, R.B., Luks, A.M., et al., 2013. High Altitude Medicine and Physiology, 5th ed. CRC Press, Taylor & Francis Group, Boca Raton, FL.
This textbook is another comprehensive textbook on high-altitude physiology and medicine that contains information on the physiologic responses to hypobaric hypoxia and the clinical aspects of both acute and chronic forms of altitude illness.

Travelers with Underlying Medical Conditions

Bartsch, P., Gibbs, J.S., 2007. The effect of altitude on the heart and lungs. Circulation 116, 2191–2202.
This review describes the physiologic responses to hypoxia in the heart and lungs and describes an approach to patients with underlying coronary artery disease, heart failure, hypertension, and pulmonary hypertension who want to travel to high altitude.

Doan, D., Luks, A.M., 2014. Wilderness and adventure travel with underlying asthma. Wilderness Environ. Med. 25, 231–240.
This is a comprehensive review of the evaluation and management of individuals with asthma who want to participate in wilderness activities, with particular attention focused on high-altitude travel and diving.

Latshang, T.D., Bloch, K.E., 2011. How to treat patients with obstructive sleep apnea syndrome during an altitude sojourn. High Alt. Med. Biol. 12, 303–307.
Drawing on research data from their own research group, the authors provide practical recommendations for managing obstructive sleep apnea during travel to high altitude.

Luks, A.M., 2009. Do lung disease patients need supplemental oxygen at high altitude? High Alt. Med. Biol. 10, 321–327.
This review article considers the issue of hypoxemia in patients with lung disease traveling to high altitude and discusses tools for predicting the degree of hypoxemia at high altitude, logistical issues associated with travel with supplemental oxygen, and recommendations for assessing need and providing oxygen on a trip.

Luks, A.M., Hackett, P., 2014. High altitude and common medical conditions. In: Swenson, E.R., Bartsch, P. (Eds.), High Altitude: Human Adaptation to Hypoxia. Springer, New York, pp. 449–478.
This is one of the most comprehensive, up-to-date reviews of travel to high altitude with underlying medical problems. Building on an earlier review by the senior author, this chapter covers a broad range of diseases across multiple organ systems and provides practical recommendations for the approach to these patients.

Luks, A.M., Swenson, E.R., 2007. Travel to high altitude with pre-existing lung disease. Eur. Respir. J. 29, 770–792.
This is a comprehensive review of the issues associated with high-altitude travel in patients with a variety of lung diseases, including obstructive, restrictive, pulmonary vascular, and ventilatory control disorders.

Mieske, K., Flaherty, G., O'Brien, T., 2010. Journeys to high altitude—risks and recommendations for travelers with preexisting medical conditions. J. Travel Med. 17, 48–62.
This is a general review of high-altitude travel in patients with underlying medical problems across a variety of organ systems.

Richards, P., Hillebrandt, D., 2013. The practical aspects of insulin at high altitude. High Alt. Med. Biol. 14, 197–204.
This is a comprehensive review of travel to high altitude with diabetes mellitus that includes a lot of practical information on monitoring blood glucose and traveling with insulin.

Rimoldi, S.F., Sartori, C., Seiler, C., et al., 2010. High-altitude exposure in patients with cardiovascular disease: risk assessment and practical recommendations. Prog. Cardiovasc. Dis. 52, 512–524.
This is a comprehensive review of the challenges of high-altitude travel in patients with various forms of cardiovascular disease.