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Metabolic disorders confronted in high-altitude regions.
Trastornos metabólicos enfrentados en regiones de gran altitud.

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ABSTRACT

There are various metabolic disorders that occur in non-acclimatized person after rapid ascent to high altitude. People permanently residing at elevations are adapted to this habitat by birth but many issues are faced by lowlanders who ascend to higher terrains for orology, sports, photography, tourism or other recreational activities, reason being differences in the environmental conditions like the air density, oxygen level, UV exposure, hardness of water etc. It usually begins within a few hours of ascent and takes few days to weeks (subjective from person to person) to get acclimatized to such conditions. The major as well common disorders include acute mountain sickness (AMS), gastrointestinal symptoms (nausea, anorexia), tachycardia, high-altitude pulmonary edema (HAPE) presenting with dyspnea cyanosis, blood pressure fluctuation, high-altitude cerebral edema (HACE) skin irritation, epiphora (eye watering) etc. Ascending steadily is the safest way to avoid altitude sickness. Pre-travel assessment and other components of high-altitude patient management should be taken care of. In addition to this dietary intake such as antioxidants, carbohydrates and iron-rich foods often play a significant role in prevention of such diseases at high-altitudes.
Keywords: acclimatization, AMS, HAPE, HACE.

RESUMEN

Hay varios trastornos metabólicos que ocurren en personas no aclimatadas después de un rápido ascenso a gran altura. Las personas que residen permanentemente en las elevaciones se adaptan a este hábitat por nacimiento, pero los habitantes de las tierras bajas enfrentan muchos problemas que ascienden a terrenos más altos para la orología, los deportes, la fotografía, el turismo u otras actividades recreativas, debido a las diferencias en las condiciones ambientales como la densidad del aire, el oxígeno. nivel, exposición a los rayos ultravioleta, dureza del agua, etc. Por lo general, comienza a las pocas horas de ascenso y toma de días a semanas (subjetivo de persona a persona) para

aclimatarse a tales condiciones. Los trastornos principales y comunes incluyen mal de montaña agudo (AMS), síntomas gastrointestinales (náuseas, anorexia), taquicardia, edema pulmonar de gran altitud (HAPE) que se presenta con disnea cianosis, fluctuación de la presión arterial, edema cerebral de gran altitud (HACE) cutáneo. irritación, epífora (ojos llorosos), etc. Ascender de manera constante es la forma más segura de evitar el mal de altura. Se debe tener en cuenta la evaluación previa al viaje y otros componentes del manejo de pacientes a gran altitud. Además de esta ingesta dietética, como los antioxidantes, los carbohidratos y los alimentos ricos en hierro a menudo desempeñan un papel importante en la prevención de este tipo de enfermedades en las altitudes elevadas.
Palabras clave: aclimatación, AMS, HAPE, HACE.

INTRODUCTION

Every year, thousands of people travel to high-reaching mountains for tourism, montology, or to train and participate in various adventure sports. Unfortunately, the consequences of acute altitude sickness affect their expedition, but the presenting clinical symptoms differs among the population. To explain why people are affected differently, we have discussed a few aspects that will clear up the disparities of how high-altitude atmospheric conditions (mainly hypobaric and hypoxic conditions) affect different individuals in one’s own way. With the increase in elevation above sea level, environmental conditions change, which affects various factors like habitat, climate, nutritional patterns and food consumption trends, body metabolism and many more. The regional population where people’s ancestors have lived for thousands of years is genetically adapted to survive in these conditions but for the visitors like tourists or army troops deployed at these areas, it takes time for getting acclimatized to these conditions. However, complete acclimatization of the body is not possible in a short period of time. This can be seen in given figure 1(Brendan Scott, 2018) which express that after the human body reaches around 2,100 m (7,000 feet) above sea level, the percent saturation of oxy haemoglobin begins to decrease rapidly. Air always contains about 21% oxygen but its partial pressure decreases i.e., it is thinner at high altitudes leading to high altitude sickness.

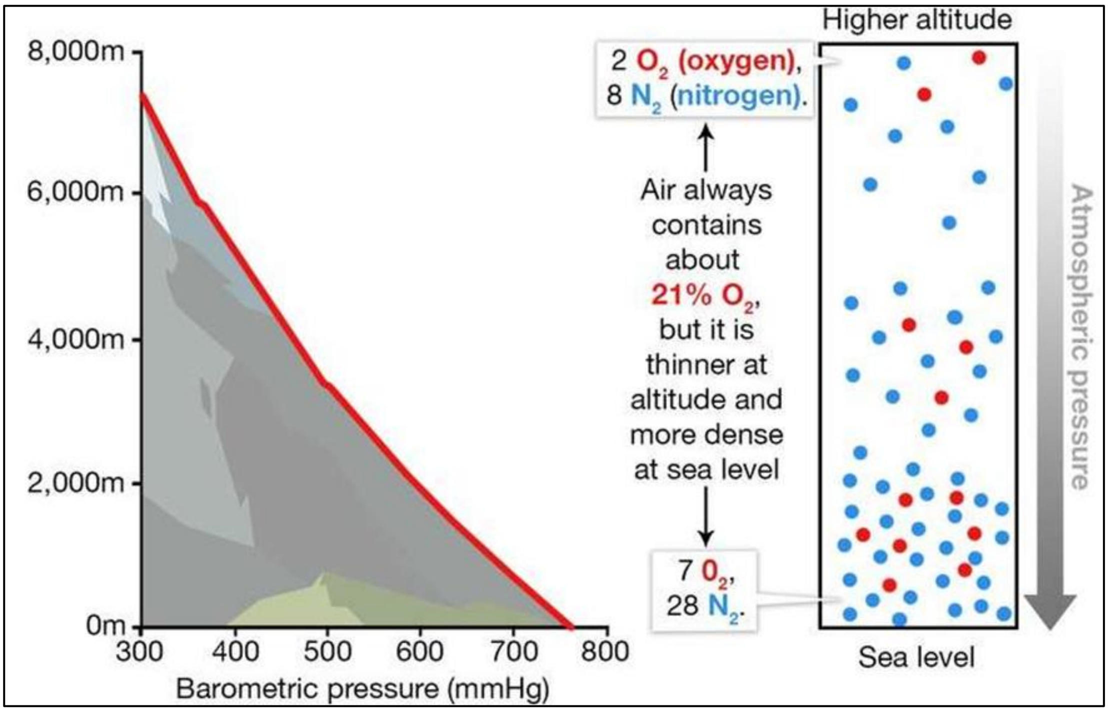

Fig. 1: Relation between higher altitude and sea level in terms of O2 concentration

METABOLIC DISORDERS

People who are travelling to higher altitude having certain diseases like cardiovascular diseases, asthma, diabetes etc. are more prone to AMS, HAPE, HACE and elevation more than a limit can be fatal. In this review we have discussed some common diseases in relation with high altitude sickness.

1. Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. Symptoms include breathing difficulty, cough, mucus (sputum) production and wheezing. Of all the patients traveling to high altitude, patients with pulmonary disorders face some of the greatest challenges in this environment due to the potential for worsening hypoxemia and the ventilator demands that may be placed on patients with altered lung mechanics. Several of the most common disorders are considered in the space that follows. Patients with pulmonary disease who are planning travel to high altitude should give consideration to monitoring oxygenation with pulse oximetry using a small handheld device. Only a single study has examined COPD patients in an actual high-altitude environment. Graham and Houston (Graham et al., 1978) studied 8 patients with COPD (mean FEV 11.27 L) and found that resting PaO_2 fell from a sea level baseline of 66 to 54 mmHg after 3 h at 1,920 m. Further data on COPD patients during commercial flight consistently demonstrates that PaO_2 often falls below 50 mmHg when patients with FEV 1 between 1 and 1.5 L are exposed tohypobaric or normobaric hypoxia simulating altitudes between 2,348 and 3,050 m (Akero et al., 2005 and Christensen et al., 2000) Mild exercise leads to further declines in arterial oxygen tension (Seccombe et al., 2004), while supplemental oxygen administration rapidly reverses hypoxemia (Berg et al., 1992).

2. Interstitial Lung Disease (ILD)

Interstitial lung disease (ILD) is an umbrella term used for a large group of diseases that cause scarring (fibrosis) of the lungs. The scarring causes stiffness in the lungs which makes it difficult to breathe and get oxygen to the bloodstream. Only two studies have evaluated the effect of simulated high altitude on patients with interstitial lung diseases such as pulmonary fibrosis. Seccombe et al. (2004) studied 15 patients with unspecified forms of interstitial lung disease at a simulated altitude of 2,440 m (8,000 ft) and found that resting PaO_2 fell from 84 to 51 mmHg after 20 min at rest and to 41 mmHg after walking 50 m. The decreased oxygenation was associated with increased Borg dyspnea scores. The clinical implications of worsening hypoxemia at high altitude in interstitial lung disease patients are not clear. Increased hypoxemia increases the risk of AMS in patients without lung disease (Burtscher et al., 2004 and Roach et al., 1998), but studies that specifically examined patients with lung disease have reported varying results.

3. Asthma

Asthma is a chronic lung disorder that can make breathing difficult. It features narrow, inflamed airways (bronchial tubes). "Asthma" is an ancient Greek word meaning "short breath," and as the name implies, it can leave individual gasping for air. The impacts of high altitude on asthma are multiple. On the one hand, lower air density and decreased dust mites (Spieksma et al, 1971) benefit asthma patients, while hypoxia, hypocapnia, and decreased air temperature and humidity may trigger increased airway reactivity (Boner et al., 1993). Epidemiologic studies have documented increased incidence of asthma or exercise induced bronchoconstriction (EIB) among cross country skiers and ski mountaineers, individuals whose activity requires very high ventilation in cold environments; many had no history of EIB at lower altitude (van den et al., 1991). Overall, the number of studies of asthma patients during actual acute high-altitude exposure is limited, making it difficult to draw firm conclusions.

4. Pulmonary Hypertension

Pulmonary hypertension is a type of high blood pressure that affects the arteries in your lungs and the right side of your heart. In one form of pulmonary hypertension, called pulmonary arterial hypertension (PAH), blood vessels in your lungs are narrowed, blocked or destroyed. The damage slows blood flow through your lungs, and blood pressure in the lung arteries rises. Your heart must work harder to pump blood through your lungs. The extra effort eventually causes your heart muscle to become week and fail. An important factor in HAPE pathogenesis is exaggerated pulmonary vascular response to hypoxia, which leads to elevated pulmonary arterial and capillary pressures that promote the transit of red blood cells, protein, and fluid from the vascular space into the pulmonary interstitium and alveolar space (Maggiorini et al., 2001).

5. Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea (OSA) is highly prevalent in the general population, in particular in men and women of older age. In OSA patients sleeping near sea level, the apneas/hypopneas associated with intermittent hypoxemia are predominantly due to upper airway collapse. The lower air density at high altitude may lead one to expect a decrease in the severity of obstructive sleep apnea with high-altitude exposure. This hypothesis was investigated by Burgess et al. (2006) who performed sleep studies at sea level and high altitude on patients with baseline moderate OSA. A similar decrease in the obstructive apneahypopnea index with increasing altitude was seen in an earlier study on normal individuals with low baseline obstructive sleep apnea indices (Burgess et al., 2004). In both studies, however, the decrease in obstructive events was offset by a marked increase in central apnea. In moderate OSA patients, for example, the RDI for central events rose from 0.4 events/h at 60 m to 78.8 events/h at 2,750 m, much higher than the sea level obstructive RDI (Burgess et al. 2006).

High-altitude periodic breathing in healthy mountain travellers and in patients with pre-existing obstructive sleep apnea can be prevented or treated with acetazolamide, a drug that is also used for acute mountain sickness. Use of acetazolamide in these patients decreased the number of central events but had no significant effect on the number of obstructive events in these patients (Nussbaumer-Ochsner et al., 2012)

6. Coronary Artery Disease (CAD)

In response to both exercise and hypoxemia, coronary arteries dilate in an effort to preserve myocardial blood flow and oxygen delivery. Individuals with coronary artery disease (CAD) may have impaired coronary vasodilation and thus may be at risk for adverse cardiac events at high altitude. Resting hypoxemia alone does not appear to unmask CAD, while exercise in acute hypoxia may provoke ischemic changes on electrocardiography in persons with CAD (Khanna et al., 1976).

Patients who have undergone revascularization following a myocardial infarction tolerate exertion at high altitude; a recent study demonstrated that 6 months after revascularization for acute coronary syndrome, patients with normal left ventricular function and no evidence of ischemia on exercise testing at low altitude could perform maximal, symptom-limited exercise tests after rapid ascent to 3,454 m without electrocardiographic evidence of myocardial ischemia or significant arrhythmia.

There is no evidence of life-threatening arrhythmias in patients with CAD at high altitude. Several studies have documented cases of sudden cardiac death at high altitude in a general population, but whether high altitude increases the risk of this problem specifically in CAD patients is unknown (Burtscher et al., 2007).

7. Hypertension

In hypertensive patients ascending to high altitude, systolic blood pressure rises to a modest extent (10–15 mmHg on average) but then declines over a period of days to weeks (Palatini et al., 1989). There is no evidence that hypertension increases risk of AMS. Although there are theoretical reasons to support the use of alpha-blockers and calcium channel blockers for control of elevated blood pressure at high altitude, no systematic studies have been conducted to evaluate their utility in this regard. After adjustments, patients should continue monitoring and alter medications accordingly. Patients should return to their original regimen upon descent to lower elevation. Nocturnal oxygen can be considered to help stabilize blood pressure at high altitude.

8. Polycythemia Vera

Little is known about the response of individuals with polycythemiavera (PV) to high altitude. While a higher hematocrit could theoretically improve oxygen delivery in acute hypoxia, dehydration due to either inadequate fluid intake or altitude-induced diuresis could lead to increased blood viscosity and worsening symptoms of their disease. PV patients are also at risk for gastrointestinal complications such as gastroduodenal erosions and peptic ulcer disease (Torgano et al., 2002)

A final question for these individuals is whether acute hypoxia will lead to a rise in serum erythropoietin levels and, therefore, hematocrit, in the days following ascent. These individuals typically have been shown to have low serum erythropoietin levels at baseline (Carneskog et al., 1989), but no studies have examined whether these levels change in response to acute hypoxia.

9. Hemoglobinopathy

High-altitude travel should be avoided in patients with sickle-cell anemia, as hypoxia predisposes to sickling and vaso-occlusive crises. Sickle-cell disease patients are also at risk for developing pulmonary hypertension (Lee et al., 2007). The incidence of problems in patients with sickle-cell trait has not been well established, but two recent reports suggest these patients may also be at risk for splenic crises. Tiernan described two Caucasian men with sickle-cell trait who developed splenic crises at elevations between 2,700 and 2,900 m, while Franklin and Compeggie describe four cases of splenic syndrome that occurred during moderate exercise at altitudes between 1,675 and 3,660 m (Franklin et al., 1999).

10. Chronic Liver Disease

In chronic liver diseases two group of liver diseases patients might have problem. First, Hepatopulmonary syndrome is marked by intrapulmonary shunts and affects up to 47 % of patients with cirrhosis (Hopkins et al., 1992). These individuals have increased alveolar-arterial oxygen difference at baseline, which worsens with upright positioning. Given that intrapulmonary shunting is the reason for baseline hypoxemia, one would predict exaggerated hypoxemia at high altitude, which would not improve with supplemental oxygen.

Second, Portopulmonary hypertension is a form of pulmonary arterial hypertension that occurs in up to16% of patients with cirrhosis and portal hypertension (Benjaminov et al., 2003). Given the numerous case reports and case series suggesting that patients with underlying pulmonary hypertension are at risk for HAPE at high altitude, there is reason to suspect portopulmonary hypertension patients might be at risk as well.

11. Gastrointestinal Bleeding

Reports from construction of the Qinghai-Tibet Railroad suggest an increased risk of gastrointestinal bleeding at altitude. Wu et al., (2007) found a 0.49 % incidence of hematemesis, melena, or hematochezia among 13,502 railroad workers between 3,500 and 4,900 m. Eighty-four percent of cases occurred within 3 weeks of arrival at high altitude, and the greatest incidence was seen at the highest elevations. Endoscopy performed on all affected individuals revealed gastric and duodenal ulcers, gastric erosions, and hemorrhagic gastritis.

A few other reports have also documented GI bleeding at high altitude. Saito (Saito A., 1989), for example, noted upper gastrointestinal bleeding in 5 of 52 Mt. Everest climbers, while Liu (Liu MF., 1995) reported that among Chinese soldiers stationed between 3,700 m and 5,380 m for 1 year, the incidence of GI bleeding was 0.8 % among all patients and 1.5 % among those patients with AMS.

Studies do not establish a definitive link between hypoxia and gastrointestinal bleeding, but do suggest that patients with poorly controlled esophagitis, gastritis, or peptic ulcer disease or those taking long courses aspirin or other nonsteroidal anti-inflammatory medications may be at risk for problems at high altitude.

PREVENTION

The best way to prevent altitude disease is to ascend slowly. The altitude at which a person sleeps is more important than the maximum height reached during the day. Control of the rate of ascent (called graded ascent) is essential for activity any higher than 8,000 feet (2,500 meters). Above 3,000 meters (10,000 feet), climbers or trekkers should not increase their sleeping altitude by more than 300 to 500 meters per day and should include a rest day (sleep at the same altitude) every 3 to 4 nights before they sleep at any higher altitudes. If people cannot limit each day's ascent to less than 500 meters, they should limit their average ascent over the entire ascent to less than 500 meters per day. During rest days, day hikes to higher elevations are acceptable as long as people return to the lower level for sleep. People vary in their ability to ascend without developing symptoms. Thus, a climbing party should be paced for the member who acclimatizes to high altitude the slowest. Acclimatization reverses quickly. If acclimatized people have descended to low levels for more than a few days, they must once more follow a graded ascent when they come back. In addition, Table 1 (Andrew et al., 2013) provides recommendations for pre-travel evaluation and other aspects of patient management at high altitude.

Table 1: Recommendations for pre-travel evaluation.

Sr. No.	Name of disease	Recommendations
1.	Chronic obstructive pulmonary disease	-Avoid travel above 2,000 m without supplemental oxygen in patients with pulmonary hypertension -Travel with supply of rescue inhalers and oral steroids in event of exacerbation
2.	Interstitial Lung Disease	-Avoid high-altitude travel with TLC < 40 % predicted or supplemental oxygen requirement at home elevation -Patients with less severe disease: assess for supplemental oxygen and travel with portable oxygen or prescription to fill at destination if predicted P_aO_2< 50 mm
3.	Asthma	-Avoid high-altitude travel in patients with moderate persistent or severe asthma -Patients with mild- persistent asthma can ascend to high altitude and should remain on pre-existing medications and carry a supply of rescue in halers and steroids for exacerbations - Patients traveling in cold environments must keep inhalers warm and be aware that the number of puffs per inhaler may be decreased at elevations above 3,000 m
4.	Pulmonary Hypertension	-Patients with moderate to severe pulmonary hypertension (mean PA pressure .35 mmHg or systolic pressure .50 mmHg) should avoid high-altitude travel without supplementary oxygen -Patients should be counselled regarding recognition and management of HAPE and monitor oxygen saturation during their high-altitude stay
5.	Obstructive Sleep Apnea	-Patients with moderate to severe obstructive sleep apnea should travel to high altitude with their CPAP machine if reliable power access can be assured -Acetazolamide should be used in addition or as an alternative to CPAP to decrease the incidence and severity of central sleep apnea
6.	Coronary Artery Disease	-Patients with stable CAD should avoid exertion during the first several days after arrival -Should reduce exercise levels to slightly lower than at sea level -Should avoid heavy exertion in cold temperatures
7.	Hypertension	-Patients with poorly controlled or labile hypertension at sea level should monitor blood pressure

		-After adjustments, patients should continue monitoring and alter medications accordingly -Nocturnal oxygen can be considered to help stabilize blood pressure at high altitude
8.	Polycythemia Vera	- Patients should maintain adequate hydration and mobility and consider low-dose aspirin to decrease risk of thrombotic events -PV patients with history of gastrointestinal complications should avoid high-dose aspirin
9.	Hemoglobinopathy	-Patients with sickle-cell disease should avoid travel to high altitude without supplemental oxygen -Patients with sickle-cell trait may travel to high altitude but should maintain adequate hydration
10.	Chronic Liver Disease	-Chronic liver disease patients should be screened for portopulmonary hypertension and hepatopulmonary syndrome, and high-altitude travel should be avoided in people with those conditions -Portopulmonary hypertension patients who must travel to high altitude should travel with supplemental oxygen and use nifedipine or a phosphodiesterase inhibitor -Hepatopulmonary syndrome patients who must travel to high altitude should monitor oxygen saturation following ascent
11.	Gastrointestinal Bleeding	-No data indicate that travellers with history of upper GI bleeding should use ulcer prophylaxis during ahigh-altitude sojourn -Travelers with history of upper GI bleeding should avoid nonsteroidal anti-inflammatory medications and aspirin and rely on acetaminophen to treat headaches or musculoskeletal pain

PREVENTION THROUGH CONSUMPTION OF FOOD

- Maintain Hydration

It is easy to become dehydrated in high-altitude environments. Dehydration increases the risk of frost bite and worsens the fatigue, impaired judgment and apathy of hypoxia. The body's requirement for fluids is very high at altitude; often exceeding 4 litters of water per day. Altitude increases water losses from the lungs due to the cold, dry air. There is also increased urinary loss of water because altitude and cold have diuretic affect. Sweating adds to the water loss. Drink a minimum of 1 quart of water every three hours. I recommend putting a pinch of salt in plain water of using a sports drink. Make sure the sports drink has sodium listed on the label. You can also make your own sports drink by adding 1/2 tsp sea salt, three tablespoons of sugar or honey and a ¼ cup of fresh lemon or orange juice to one quart of water.

- Antioxidants

Free radical damage to cells increases with altitude because anaerobic metabolism predominates and ultraviolet exposure increases. Free radical damage is a main cause of aging. Humans make their own natural protective antioxidants but these levels can go down when exercising intensely at high altitude unless the individual is "trained." Trained athletes are able to counteract the damaging effects of free radicals because they produce more natural antioxidants.

Vitamin E supplementation at high altitude has shown positive effects in mountain climbers working at 1600 ft. Tests showed lower levels of oxidative damage as well as a higher exercise performance capacity. Other studies show no effect. A more recent study published in the August 2006 edition of "Medicine and Science in Sports and Exercise" demonstrated that prior treatment with antioxidants could improve ventilatory threshold. This is the point at which your breathing rate really goes up or what skiers sometimes call "busting a lung".

- Carbohydrates intake for energy

When it comes to nutrition, training at altitude increases the use of carbohydrates for energy compared to training at sea level. Your body is just going to be a bit less efficient and will therefore need more readily-available sources of energy.
This means you may need to put more of an emphasis on carbohydrates in your pre-race or training meal and your overall diet. Inadequate intake of carbohydrates may hinder performance and decrease the time by which you can exercise before bonking or reaching exhaustion.

Focus on good quality carbohydrates, such as Dates, Bananas, Sweet Potatoes & Oats rather than sugary foods and refined white grains. Avoid increasing carbohydrates from sugary foods and refined white grains. In other words, skip the candy bars, gels and sports drinks and focus on real food. Vegetables are carbohydrates as well; increasing your intake can be a decent way to get additional nutrients in as well as healthy carbs. Our favourite clean carb source before a day of skiing is a baked sweet potato with butter or coconut oil melted on it, with a dash of cinnamon. It'll give you some quick carbs plus it's a warm breakfast.

- Iron-rich foods

In addition, exposure to altitude increases the production of red blood cells to help carry oxygen around the body, which increases the need for iron. Animal foods contain iron that's well absorbed by the body. Animal foods such as:

- Lean Beef
- Pork
- Chicken
- Eggs
- Tuna
- Salmon

Avoid combining these foods with calcium-rich foods like milk, or tea, coffee, and cocoa as they can inhibit absorption of the iron. Plant foods, such as leafy greens (spinach, chard, beet, collard, etc.), dried fruit, tofu, lentils, oatmeal, beans, and fortified grains also provide iron but it's not absorbed as well as animal iron. That's ok though; to increase the absorption of iron from plant foods, combine it with a vitamin C source such as tomato sauce, peppers, oranges, strawberries, or pineapple.

- Protect your immune system

Lastly, being at altitude puts additional stress on your body and your immune system. Before you ascend and while you are at altitude, be sure to eat foods that are anti-inflammatory, antioxidant and support a healthy immune system. Think vegetables and fruits of all colours of the rainbow.

- Red Strawberries
- Orange Carrots
- Yellow Bell Peppers
- Green Leafy Vegetables
- Blueberries
- Purple Eggplant
- Brown Mushrooms
- White Cauliflower

Include at least a serving of vegetables with lunch and dinner and a serving of fruit with breakfast, snack, and/or dessert. Dried fruit is an excellent, portable way to get iron, anti-oxidants, vitamins, and minerals.

- Avoid Alcohol

The effects of alcohol are enhanced at altitude. In the bloodstream, alcohol interferes with hemoglobin's ability to carry oxygen. Coupled with less oxygen availability that's normally at altitude, you'll really be low on oxygen if you drink. Also, the diuretic (water-losing) effects of it will be accentuated, and dehydration is always a big risk at altitude. And, getting dehydrated will really sap your energy and contribute to headaches (Jason Barker., 2020).

CONCLUSION

Adequate acclimatization via controlled ascent remains the most important factor in preventing altitude sickness, although prophylactic pharmacotherapy also may be useful. Some disorders are usually short timed and the most important aspect in the treatment of worsening AMS, or development of HACE is early identification and descent. Use of sunglasses in order to prevent the UV exposure to the eyes is advisable. Also, a healthy diet with iron, vitamin C supplements is must during the stay. Long distance walking, running or any vigorous exercise must be prevented to avoid breathlessness.

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