



CRACKCast Episode - High Altitude Medicine (Ch. 136 – 9th)

Episode Overview

Key Concepts:

- **All forms of altitude illness can be treated with oxygen and rapid descent.**
- The diagnosis of AMS requires the presence of **headache** in the setting of recent **elevation change** to greater than 8000 feet. Additional nonspecific symptoms may include nausea, anorexia, fatigue, and insomnia.
- Patients with AMS should not ascend further until symptoms improve. Patients with mild HAPE may be treated in place if experience providers and treatment options exist. Patients with moderate HAPE or HACE should descend immediately.
- **Dyspnea at rest is an early symptom of HAPE.** More advance findings of HAPE include marked rest tachypnea, cough productive of frothy sputum, and altered mentation. Immediate treatment with oxygen and descent are recommended.
- **Altered consciousness and cerebellar ataxia are early signs of HACE.** Failure to initiate immediate treatment with oxygen, descent, and dexamethasone can result in permanent disability or death.
- AMS may be prevented by using acetazolamide or dexamethasone. Symptoms can be controls with analgesia (ibuprofen and antiemetics). HAPE may be prevented using nifedipine, inhaled salmeterol, and phosphodiesterase type 5 inhibitors (sildenafil [40 mg every 8 hours] and tadalafil [10 mg every 12 hours]).
- Temazepam (7.5 mg qhs) can safely improve sleep quality.
- We will accidentally talk in both feet and meters because Canadian are a weird hybrid bunch. To convert multiple meters by 3.3



Core questions

1. Describe the physiologic process of acclimatization to high altitude. List at least three responses.
2. What is the pathophysiology of AMS, HACE and HAPE?
3. Describe the risk of high altitude in the following patient groups:
 - a. Coronary artery disease
 - b. Pulmonary hypertension
 - c. COPD
 - d. Asthma
 - e. Sickle cell disease
 - f. Pregnancy
 - g. Children
4. How do you calculate the alveolar partial pressure of oxygen?
5. Describe the clinical presentation of acute mountain sickness, HAPE and HACE.
6. How do you treat acute mountain sickness?
7. How do you treat HAPE?
8. How do you treat HACE?
9. How do carbonic anhydrase inhibitors prevent and treat acute mountain sickness?

Wisecracks

- 1) List 6 factors contributing to the incidence of high-altitude illness
- 2) Define moderate altitude, high altitude and severe altitude
- 3) Describe 5 options for prevention of altitude illness
- 4) List 4 systemic diseases for whom high-altitude travel is contraindicated
- 5) What are the causes of hypoxemia?
- 6) What are the causes of tissue hypoxia?

Rosens in Perspective

- *Acute high altitude illnesses*, are completely preventable illnesses in impatient, rushed altitude seekers. They result from exposure to low oxygen states caused by low atmospheric pressure. Aka: hypobaric hypoxia
- *Although the percentage of atmospheric oxygen is a constant 20.9%, as elevation increases, atmospheric pressure decreases and with it, oxygen availability. (Dalton's law of partial pressures)*



- *Human physiology is remarkably adaptable when given sufficient time to acclimatize by gradual ascent. A classic example is the over 40 million people that live at elevations greater than 2500 meters. However if those of us living at sea level were to rapidly ascend that height we would become very ill or die.*
- *On the summit of Mt. Everest (8848 m, 29k feet), the partial pressure of inspired oxygen (PiO_2) is only 29% of the sea level value. Although gradual ascents (over weeks) of Mt. Everest without oxygen are not uncommon, a rapid, unacclimatized ascent to the same summit would result in rapid loss of consciousness and death.*

Gradual ascent reduces symptoms and can save lives.

*Cerebral forms of altitude illness occur as a continuum, from common and benign **acute mountain sickness (AMS)**, to rare, but potentially lethal **high-altitude cerebral edema (HACE)** and **High altitude pulmonary edema (HAPE)***

For the sake of comparison - AMS occurs very commonly with rapid ascents > 2500 meters (a rapid ascent (1 or 2 days) to 4400 meters feet on Mt. Rainier has rates as high as 67%; or 50% for those who fly to the Khumbu region vs. 25% in those who walk up). **HACE is much less common < 1% with rapid ascents > 4300 meters.**

High-altitude pulmonary edema (HAPE) is the primary lung syndrome. HAPE is the leading cause of death from altitude illness.

- *It's incidence ranges from 0.01% to 15% with rapid ascents (as cited in Rosen's from Auerbach 2012)*
- *The pathophysiologic effects of high altitude begin when the oxygen saturation of the arterial blood begins to fall below the 90% level.*
- *The sigmoidal shape of the oxyhemoglobin dissociation curve prevents a significant fall of arterial oxygen saturation (SaO_2) in most individuals until an altitude of approximately 3000m.*
- *At this altitude, the steep portion of the curve is encountered, and marked oxygen desaturation may occur with relatively small increases in altitude (See Fig. 136.1 in 9th edition for more detail).*
- ***Some predisposed individuals may desaturate to less than 90% at altitudes as low as 2500m.***

Core Content Questions

[1] Describe the physiologic process of acclimatization to high altitude. List at least three responses.

Hypobaric hypoxia stimulus leads to your body working hard to improved oxygenation.

Acclimatization is both immediate (within minutes the carotid bodies sense hypoxemia) and continuous over months (hemoglobin increases may continue over more than 6 weeks). It involves multiple systems from protein synthesis to respiratory, cardiovascular, renal, and hematologic responses.

*Acclimatization begins as the oxygen saturation of arterial blood falls below sea-level values. The altitude at which this occurs depends on the rate of ascent, the duration of exposure, and the individuals physiology e.g. **preexisting disease that limits cellular oxygen delivery (such as cardiomyopathy) or decreased pulmonary reserves.***

Here's the list:

Acute (minutes to hours):

1.1 Increase in minute ventilation = hypoxic ventilatory response (HVR)

- *Within minutes of exposure to high altitude, the peripheral chemoreceptors in the carotid bodies sense the decrease in the partial pressure of oxygen in alveolus (P_{aO_2}) and signal the respiratory control center in the medulla to increase ventilation.*
- *The magnitude of the HVR varies among individuals and may be genetically predetermined. HVR may also be inhibited or stimulated by numerous factors, including ethanol, sleep medications, caffeine, coca, prochlorperazine, and progesterone.*

1.2 Catecholamine response to acute hypoxia:

- *increased cardiac output and elevations in heart rate, stroke volume, blood pressure, and venous tone. Except at extreme altitudes, acclimatization over weeks results in the gradual return of the resting heart rate to near sea-level values. Continued resting tachycardia is evidence of poor acclimatization.*

1.3 Release of erythropoietin (in hours: but the response is delayed)

- *Leading to new circulatory red blood cells in 4 or 5 days. During the next 2 months, red blood cell mass increases in proportion to the degree of hypoxemia.*



Delayed (days to weeks)

1. Renal excretion of bicarbonate to adapt to the respiratory alkalotic state induced by the HVR, Maximum rate/amount by 6-8 days
- 2.
3. Hematopoietic responses
 - Increase in hemoglobin
 - Increase in number of red blood cells
 - Increase in MCV
 - Increased plasma volume
 - Increase total blood volume

Other responses (shownotes)

Hypoxemia also results in an increase in 2,3-diphosphoglycerate, causing a rightward shift of the oxyhemoglobin dissociation curve, which favors a release of oxygen from the blood to the tissues.

This is counteracted by the leftward shift of the oxyhemoglobin dissociation curve caused by the respiratory alkalosis from hyperventilation. The result is a net null change in the oxyhemoglobin curve and an increase in oxygen-hemoglobin binding in the lung, which raises Sao₂. Some individuals with mutant hemoglobin and high oxygen-hemoglobin affinity are found to acclimatize more efficiently than their normal counterparts at moderate altitudes.

[2] What is the pathophysiology of AMS, HACE and HAPE?

All comes down to a combination of: inadequate adaptation both due to environmental pressures and personal genetic limitations. The big end-organs that fail - are the brain and the lungs.

Hypobaric hypoxia's effects on central nervous system homeostasis give rise to AMS and HACE. AMS is the common, benign form that unheeded, can develop into rare, but potentially lethal HACE.

AMS can develop within 4 to 8 hours of acute exposure to hypobaric hypoxia. HACE and HAPE typically occur 2 to 4 days after exposure to high altitude.

It's the hypobaric hypoxia that triggers a complex pathophysiologic response...follow in Fig 136.2

Let's talk through the pathophysiology (truncated) for these:

- **AMS → HACE**
 - **Exist on a spectrum**



- *The definitive etiology of the cerebral forms of altitude illness remains unclear. Evidence suggests that clinical manifestations of AMS and HACE result from the combined effects of altered cerebral hemodynamics and inflammatory mediators that damage the blood brain barrier*
 - *Hypoxia: cerebral vasodilation occurs with increased arterial blood velocity and volume.*
 - *Hypocapnia: cerebral vasoconstriction*
 - *Impaired cerebral autoregulation*
 - *Systemic hypertension (from strenuous exercise)*
 - *Vasogenic edema from multiple mediators and damage to the blood brain barrier*
 - *Failure of CSF buffering*
- **HAPE:**
 - *HAPE results from overly exuberant increases in pulmonary arterial pressures (hypoxia-induced acute pulmonary hypertension) that lead to stress failures of the delicate pulmonary capillary beds → progressing to alveolar and interstitial edema.*
 - **It's this hypoxic pulmonary vasoconstriction response (HPVR) that leads to blood "backup" in the lungs.**
 - **There is a wide variation in both individual HPVR due to epigenetic reasons as well as UNEVEN vasoconstriction leading to patchy pulmonary edema.**
 - **Proposed reasons? (shownotes)**
 - *decreased nitric oxide bioavailability at the pulmonary tissue level.*
 - *Acute inflammatory mediators post lung injury*
 - *Sodium channel-mediated alveolar fluid clearance changes (inhaled beta-adrenergic agonists, which have been proven to decrease risk of HAPE.)*
 - *Sensitized lung due to ongoing pulmonary infection*

See Figure 136.2 in Rosens 9th Edition, Chapter on High Altitude Medicine



[3] Describe the risk of high altitude in the following patient groups:

1. Coronary artery disease

- a. ***In theory, (no studies on this) people with diseased myocardium should be advised to avoid high altitude because of decreased environmental oxygen availability.***
- b. ***Due to the hypoxic response travelers will have increased sympathetic activity, increase in their cardiac work demands and increased myocardial oxygen consumption***
- c. ***increase angina symptoms and dysrhythmias.*** Although both cardiac rhythm abnormalities and ST segment and T wave electrocardiographic changes are reported, none of these changes are associated with clinical evidence of myocardial ischemia. Limited data suggest no increased risk for sudden cardiac death or myocardial infarction at altitudes up to 8000 feet. When individuals with stable angina are exercised, there is conflicting evidence for the probability of inducing malignant dysrhythmias. Travelers with heart disease who ascend to moderate altitudes do not appear to have an increased incidence of AMS.
- d. ***Travelers with mild stable CAD should be advised to ascend gradually, to limit activity especially in the first few days at elevation, and to continue anti-anginal and antihypertensive medications.*** Individuals who have more severe, symptomatic coronary disease or those in a high-risk group (low ejection fraction, abnormal stress test results, and high-grade ventricular ectopy) should avoid travel to high altitudes. Ascent to moderate elevations can be suggested on an individual basis with the previously mentioned precautions. ***Individuals with heart failure who travel to altitude may require increased use of diuretics to promote diuresis and acclimatization. Acetazolamide prophylaxis may be useful to speed acclimatization and to prevent AMS and its accompanying fluid retention.***

2. Pulmonary hypertension

- a. ***At increased risk for HAPE - they should be advised AGAINST travel to higher elevations***
- b. ***If travel necessary use oxygen, nifedipine, PDE5 inhibitors, steroids***

3. COPD

- a. ***predispose them to development of hypoxemia, sleep apnea, pulmonary hypertension, and ventilation disorders at even moderate altitudes.***
- b. ***COPD is a risk factor for the development of AMS.***
- c. ***Although oxygen saturation remains more than 90% in a healthy, awake individual until an altitude of 8000 feet, patients with COPD may desaturate below 90% at lower altitudes. High altitude increases hypoxic pulmonary vasoconstriction and may potentiate the development of cor pulmonale, which is known to adversely affect***



*survival at sea level. **Individuals with chronic COPD should be advised of the potential need for oxygen supplementation when traveling to moderate altitude, especially if they are already using oxygen at sea level or if dyspnea or fatigue becomes worse. Use of a pulse oximeter can guide the need for increased oxygen supplementation.***

4. Asthma

- a. **May actually do better at higher altitude - fewer allergens, pollutants**
- b. *Even those with exercise induced bronchospasm do not have worsening symptoms while exercising at 5000 feet. In addition, AMS incidence is not increased in asthmatics. **People with asthma traveling to higher elevations should continue their usual medications and carry a rescue supply of bronchodilators and steroids.***

5. Sickle cell disease

- a. **At increased risk for pain and ischemic crises even at low altitude**
- b. *In patients with sickle cell disease, exposure to even low to moderate altitudes (4000 to 6500 feet) will provide additional hypoxia stress. **Up to 20% of patients with hemoglobin sickle cell and sickle cell-thalassemia disease may experience a vaso-occlusive crisis, even under pressurized aircraft conditions. Oxygen is therefore advised for air travelers who have sickle cell disease.***

6. Pregnancy

- a. **an increased incidence of complications in maternal, fetal, and neonatal life.**
- b. **Lower birth weight, increased premature birth**
- c. **Increased risk of gestational hypertension, preeclampsia**
- d. **Travel above 13000 ft is not advised**

7. Children

- a. **Most healthy children do well, those at higher risk:**
 - i. **< 6 weeks old, those with a history of pulmonary HTN, premature infants, children with Down syndrome, CHD, CF or neuromuscular problems**
- b. **Symptoms of AMS are difficult and non-specific in preverbal children**
- c. **Lower risk of HAPE < 2 yrs**
- d. **Symptoms and signs of most other high altitude illness approaches that in adults as the child gets older**

8. Patients post radial keratotomy (shownotes)

Patient with a history of radial keratotomy may experience hyperopic (farsighted) visual changes with ascent above 9000 feet.



This results from corneal swelling from ambient hypoxia because the cornea is markedly sensitive to both systemic and ambient oxygen tension.²³ In normal corneas, this swelling is uniform. After radial keratotomy, the swelling is exacerbated and inconsistent secondary to the pattern of the incisions.

Photorefractive keratotomy and LASIK, which use laser techniques that do not produce incisions but instead shave the cornea and corneal stroma, respectively, do not result in similar problems.

[4] How do you calculate the alveolar partial pressure of oxygen?

As described by the alveolar gas equation, for any given inspired oxygen tension, the level of ventilation determines alveolar oxygen: as the P_{aCO_2} decreases, P_{aO_2} correspondingly increases.

The factors that determine the values for alveolar pO_2 and pCO_2 are:

- *The pressure of outside air*
- *The partial pressures of inspired oxygen and carbon dioxide*
- *The rates of total body oxygen consumption and carbon dioxide production*
- *The rates of alveolar ventilation and perfusion*

-- From Wikipedia

See Box 136.1 in Rosens Chapter 136 9th Edition

Respiratory quotient = the ratio between the amount of CO_2 produced in metabolism and the oxygen used (usually ranges from 0.8 - 1)

[5] Describe the clinical presentation of acute mountain sickness, HAPE and HACE.

Common theme - consider your ddx! (See box 136.3 and 136.5 in Rosens 9th Edition)

	Clinical presentation	Key points
AMS	<p>Lake Louise Criteria:</p> <ul style="list-style-type: none"> • Recent ascent to 8k ft (2400 m) • Headache PLUS one of <ul style="list-style-type: none"> ○ GI: <ul style="list-style-type: none"> ■ Anorexia, nausea, vomiting ○ General: <ul style="list-style-type: none"> ■ Weakness, fatigue, dizziness, lightheadedness, difficulty sleeping <p>Symptoms onset within a few hours of altitude and maximize at 24-48 hrs (and then usually resolve)</p>	<ul style="list-style-type: none"> • Symptoms can range from mild to incapacitating • Clinical diagnosis, no objective hx or physical findings requires a broad ddx (including CO poisoning!)



		<i>The headache may vary from mild to severe, is generally bitemporal and throbbing in nature, and is worse during the night and on awakening or on suddenly becoming upright.</i>
HACE	<ul style="list-style-type: none"> <i>The symptoms of severe AMS (headache, fatigue, and vomiting) as well as those of HAPE (cough and dyspnea) are often present.</i> <i>ataxia, slurred speech, and altered mental status</i>, which can range from mild emotional lability or confusion, to hallucinations and worsening obtundation that may advance to coma and death. Less commonly, generalized seizures and rarely, focal neurologic deficits may occur. 	<p>Evidence of CNS dysfunction:</p> <ul style="list-style-type: none"> Ataxia Altered mentation <p>Worsening AMS over hours to days</p> <p>Consider ddx</p>
HAPE	<ul style="list-style-type: none"> <i>Insidious onset 2-4 days after arrival at high altitude (but can come on rapidly)</i> <i>Marked dyspnea on exertion, fatigue with minimal-to-moderate effort, prolonged recovery time, and dry cough</i> <i>Cough may become productive; may develop blood</i> <i>Can rapidly progress to hypoxemia, CNS dysfunction, coma and death</i> <i>Exam = tachypnea, tachycardia, rales (patchy), rhonchi, gurgles, cyanosis</i> 	<ul style="list-style-type: none"> Dyspnea at rest Dry cough Concurrent AMS symptoms Be sure to think through the wide DDX of acute dyspnea

[6] How do you treat acute mountain sickness?

*Management of AMS must adhere to the axiom,
“After the symptoms of altitude illness occur, further ascent to a higher sleeping altitude is contraindicated.”*

SEE ROSENS BOX 136.2 9th Edition

1. Mild
 - a. Do NOT ascend to higher sleeping altitude
 - b. Wait for symptom resolution and acclimatization (usually 3-4 days)
 - c. Consider pharmacology
2. Moderate
 - a. Rest
 - b. Descent (even 150m makes a difference!)
 - c. Pharmacology
 - i. *Aspirin, ibuprofen, and acetaminophen are useful for the treatment of high-altitude headache.*



1. *Narcotic analgesics should be avoided because of depression of the hypoventilation response (HVR) and respiratory drive during sleep.*
 - ii. **Antiemetics**
 1. *for nausea and vomiting, prochlorperazine unlike other antiemetics, stimulates the HVR.*
 - iii. **Acetazolamide = respiratory stimulant** (*prevents periodic breathing which worsens insomnia*)
 1. *Also enhances renal bicarbonate diuresis, improves*
 2. **62.5 mg - 125 mg BID**
 - a. *Avoid Benzo's or other respiratory depressants especially alcohol*
 - iv. *Consider dexamethasone*
- 3. Severe**
- a. **Rest**
 - b. **Descent**
 - c. **Pharmacology**
 - i. **As above**
 - ii. **Consider adding:**
 1. **Dexamethasone 8 mg po; then 4 mg po q6hrs for 3 days**
 - a. *Euphoric effects*
 - b. *anti-inflammatory properties, possibly to reduce cerebral blood flow, and to block the action of vascular endothelial growth factor.*
 - d. **Oxygen / hyperbaric oxygen therapy**

[7] How do you treat HAPE?

This is the #1 fatal form of high altitude illness. See Box 136.4 in Rosens 9th

- Usually occurs at 2500-3000m (but can occur at lower elevations)
- Investigations usually helpful to work-up other causes of acute dyspnea at altitude (u/s, CXR, ECG)

Viagra: consider as prophylaxis in those who have had HAPE before: 50mg q8h

Treatment:

1. Stop ascending, rest, keep warm
2. Oxygen (or hyperbaric/normobaric oxygen via gamow)
3. Descent (usually at least ~1000m, but as much as practically possible)
4. Nifedipine
 - a. *Unlike pulmonary edema secondary to acute CHF, HAPE does not result from excessive intravascular volume or failed cardiac pump function. As such, diuretic therapy has no role in the treatment of*



HAPE and may further exacerbate volume loss in patients who are already intravascularly depleted.

- b. lowers pulmonary artery pressure, pulmonary blood volume, and pulmonary vascular resistance or enhance alveolar fluid clearance*
- c. Works well for prophylaxis and treatment*
- d. **good therapy to have on hand if descent is impossible or no oxygen is available***
- e. Treatment with 30 mg of a slow-release nifedipine preparation administered twice daily is effective. Patients should be monitored for the development of hypotension during nifedipine administration.*

5. Other medications

- a. Unstudied for acute treatment, may be helpful for prevention
 - i. phosphodiesterase type 5 inhibitors (including tadalafil and sildenafil)
 - ii. Beta-adrenergic agonists to help with alveolar fluid clearance (salmeterol 125 µg inhaled twice daily)

The mainstay of HAPE treatment remains immediate oxygen (if it is available) and descent. Should these treatments not be available, nifedipine should be initiated. No compelling evidence suggests the concurrent use of these medications with oxygen has additional benefit beyond the use of oxygen alone.

Of note, the radiographic findings of cardiomegaly, bat-wing distribution of infiltrates, and Kerley B lines, which are typical of cardiogenic pulmonary edema, are absent in cases of HAPE.

Patients may be able to re-ascend (generally in 2 to 3 days) when symptoms resolve and oxygen levels remain acceptable off supplemental oxygen at rest and with mild exercise. Re-ascent with pulmonary vasodilator medication may be considered.

Other prevention therapies:

- PDE5 inhibitors
- Dexamethasone
- Salmeterol
- Acetazolamide (to help with acclimatization, prevent HAPE, and reduce pulmonary vasoconstriction)

[8] How do you treat HACE?

HACE is the least common but most severe form of high-altitude illness. Death from HACE at as low as 2500m is reported, although most cases occur above 3000m. Mild AMS can progress to severe HACE with coma in as few as 12 hours.

Although severe symptoms usually develop within 1 to 3 days, they may not occur until 5 to 9 days.

Treatment:

- DESCENT
- High fio2 oxygen
- Dexamethasone 8 mg IM or PO, then 4 mg q6 hrs.
- ABCD's
 - Some may require intubation
 - Management of increased ICP in extreme cases

Early treatment of HACE generally results in good outcomes, but after coma is present, the mortality rate exceeds 60%.

See HACE DDx in Box 136.7 Rosens 9th Edition

[9] How do carbonic anhydrase inhibitors prevent and treat acute mountain sickness?

Acetazolamide has myriad beneficial effects.

By acting as a carbonic anhydrase inhibitor, it:

- *enhances renal bicarbonate diuresis*
 - *and so improves renal correction of the ventilation-related respiratory alkalosis encouraging increased ventilation and arterial oxygenation.*
- *It decreases nocturnal period breathing and so improves sleep.*
- *It acts as a diuretic and so attenuates fluid retention common in patients with AMS. [although dehydration is risk factor for AMS]*
- *It lowers CSF volume and pressure, which may play an additional role in its therapeutic effect.*

In addition, it has positive effects beyond its role as a carbonic anhydrase inhibitor, with beneficial chemoreceptor effects on ventilatory drive, alterations of cerebral blood flow, relaxation of smooth muscles, and upregulation of fluid resorption in the lungs.

Adverse reactions:

- **Paresthesias**
- Polyuria
- Nausea
- Diarrhea
- Drowsiness
- Tinnitus
- Myopia
- Change of taste in foods
- Sulfa medication cross reactivity



Wisecracks

1) List 6 factors contributing to the incidence of high-altitude illness

The incidence and severity of altitude illness are directly related To:

1. *elevation*
2. *rapidity of ascent.*

Other variables influencing AMS development include:

3. *prior acclimatization,*
4. *Individual genetic susceptibility,*
5. *sleeping elevation,*
6. *duration of stay*

2) Define moderate altitude, high altitude and severe altitude

- **Mod**
 - 1500 m - 2400 m (5k - 8k ft)
 - ***Rapid ascent to this altitude may result in mild, transient symptoms, but severe altitude illness is uncommon.***
- **High**
 - 2400 m - 4200 m (8k - 14k ft)
 - **High altitude illness is common with rapid ascent to this height, especially in anyone with pre-existing medical illness**
- **Severe**
 - 4200 m - 5400m (14k - 18k ft)
 - **High risk for altitude illness with rapid ascent - including the severe forms: HACE and HAPE**
- **Extreme altitude**
 - 5400m (18k ft and up)

*Although climbers using careful acclimatization schedules can **transiently tolerate this height**, complete acclimatization generally is not possible and long visits above this level result in progressive deterioration. Given limitations in physiologic reserves, climbers who become incapacitated at this elevation typically are dependent on others to survive.*

3) Describe 5 options for prevention of altitude illness

1. Gradual / staged ascent that allows for acclimatization
 - a. Limit sleeping height to less than 1000-1600 ft gain/day

Interestingly, you can also affect the relative altitude effects by watching the seasonal variations in barometric pressure. *In the winter, barometric pressures tend to be lower making “relative altitudes” physiologically higher. Local weather can also significantly affect the barometric pressure. A low-pressure front can reduce the barometric pressure 12 to 40 mm Hg and so increase the “relative altitude” by 500 to 2500 feet. At extreme elevations this can be physiologically relevant.*

4) List 4 systemic diseases for whom high-altitude travel is contraindicated

- Sick cell disease (with hx of crises)
- Severe, symptomatic CAD (or other severe CHF - low EF, high grade ventricular ectopy)
- Severe COPD
- Symptomatic pulmonary hypertension
- Uncompensated CHF

5) What are the causes of hypoxemia?

Acute hypoxemia:

- **Low inspired FiO2**
- **Inadequate tidal volume (hypoventilation)**
- **Diffusion limitation**
- **V/q Mismatch**
- **Right to left shunt**



Chronic mild hypoxemia causes a chronic mild acid load on the respiratory, renal, and blood buffer systems; acute illness such as a respiratory infection can rapidly cause a decompensation in this fragile balance, resulting in a worsening acidosis.

6) What are the causes of tissue hypoxia?

From UpToDate

Cellular hypoxia is a state in which there is insufficient oxygen to meet the metabolic demands of a given tissue. It can result from impaired perfusion (ischemia) and/or diminished arterial oxygen content (due to anemia or hypoxemia).

Cellular tolerance of hypoxia is variable. As examples, skeletal muscle cells can recover fully after 30 minutes of hypoxia, but irreversible damage occurs in brain cells after only four to six minutes of similar hypoxic stress. Therefore, life-threatening hypoxemia needs to be treated with the administration of oxygen (and sometimes with red cell transfusion) while measures are being initiated to treat the primary cardiopulmonary insult.

Cellular mechanisms that contribute to hypoxic cell injury include depletion of ATP, development of intracellular acidosis, increased concentrations of metabolic by-products, generation of oxygen free radicals, and destruction of membrane phospholipids. There is also a dramatic increase in intracellular calcium concentration, contributing to cellular injury via a variety of mechanisms, including direct damage to the cytoskeleton and induction of genes that contribute to apoptosis.

Hypoxia also induces an inflammatory reaction characterized by neutrophilic infiltration, thus augmenting cellular damage via release of cytokine mediators, oxygen free radicals, and by intensifying ischemia due to disruption of the microcirculation.