JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (JTS CPG)

Altitude Emergencies in the Prehospital Environment

This CPG provides an overview of prehospital management of an altitude emergent patient for point of injury (POI) and en route care that presents a standardized approach in the continuum of medical care for military operations. Primary areas of focus are POI up to Role 2 levels of care.

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ALTITUDE EMERGENCIES IN THE PREHOSPITAL ENVIRONMENT

AMS Prevention

- **Rapid ascents to 2500M** or less do not require prophylaxis.
- **Rapid ascents to 2500M-3500M** in less than 24 hours: Use acetazolamide 125mg PO BID starting at 8 hours and 24 hours prior to ascent.
- **Rapid ascents to 3500M** or higher results in a 70-100% incidence of AMS. Prophylaxis with dexamethasone 4mg q6h and acetazolamide 125mg PO BID should be used starting 24 hours prior to ascent.

Mild AMS

- Score 3-5
- Consider evacuation to 300 –1,000m lower altitude to speed recovery
- Titrate SpO2 >90% if available
- Administer ibuprofen or acetaminophen to treat headache.

Moderate AMS

- Score 6-9
- Consider evacuation to 300 –1,000m lower altitude to speed recovery
- Administer acetazolamide
  - Consider dexamethasone 4mg every 6 hours, max of 2 doses
  - No ascent until ≥24 hours after last dose

Severe AMS

- Score 10-12
- Evacuate 300–1,000m lower altitude
- Administer acetazolamide - 250mg every 12 hours
- Administer dexamethasone - 4mg every 6 hours, max of 2 doses
  - No ascent until ≥24 hours after last dose

STOP

STOP ASCENT IF PATIENT DISPLAYS

- Headache
- Dyspnea
- Nausea
- Anorexia
- Fatigue
- Dizziness
- Sleep difficulties

IF EVACUATION IS PROLONGED OR UNAVAILABLE

If immediate descent is not an option, individuals with severe AMS and risk of progression to HACE/HAPE should be treated with the following:

- HACE: administer dexamethasone - 8mg followed by 4mg every 6 hours.
- HAPE: administer nifedipine:
  - Extended release: 30mg orally every 12 hours
  - Immediate release: 20mg orally every 8 hours

If casualty is not a candidate for nifedipine, administer phosphodiesterase inhibitor.

- Tadalafil 10mg orally every 12 hours OR
- Sildenafil 50mg orally every 8 hours

Portable hyperbaric chambers can be used in conjunction with oxygen if available. It is a temporary stopgap pending descent.

AMS DX

Headache plus one of these:

- Weakness /lightheadedness
- Nausea/vomiting
- Anorexia
- Fatigue

HACE Dx

High-Altitude Cerebral Edema

- Ataxia
- Altered mental status

OR

- No pre-existing AMS
- Onset of ataxia AND altered mental status

HAPE Dx

High Altitude Pulmonary Edema

2 Signs from:

- Tachycardia
- Tachypnea
- Crackles or wheezing in at least 1 lung
- Central Cyanosis

2 Symptoms from:

- Dyspnea at rest
- Cough
- Decreased exercise tolerance
- Chest tightness or congestion

METRICS

- ✓ AMS patients are prescribed acetazolamide per protocol.
- ✓ HACE patients are prescribed acetazolamide per protocol.
- ✓ HAPE patients are prescribed nifedipine or phosphodiesterase inhibitors per protocol.

DHA Defense Health Agency JOINT TRAUMA SYSTEM ®

This information is pulled from the evidence-based Joint Trauma System (JTS) Altitude Emergencies in the Prehospital Environment Clinical Practice Guideline (CPG). JTS CPGs can be found at the JTS CPG website or the JTS Deployed Medicine site.

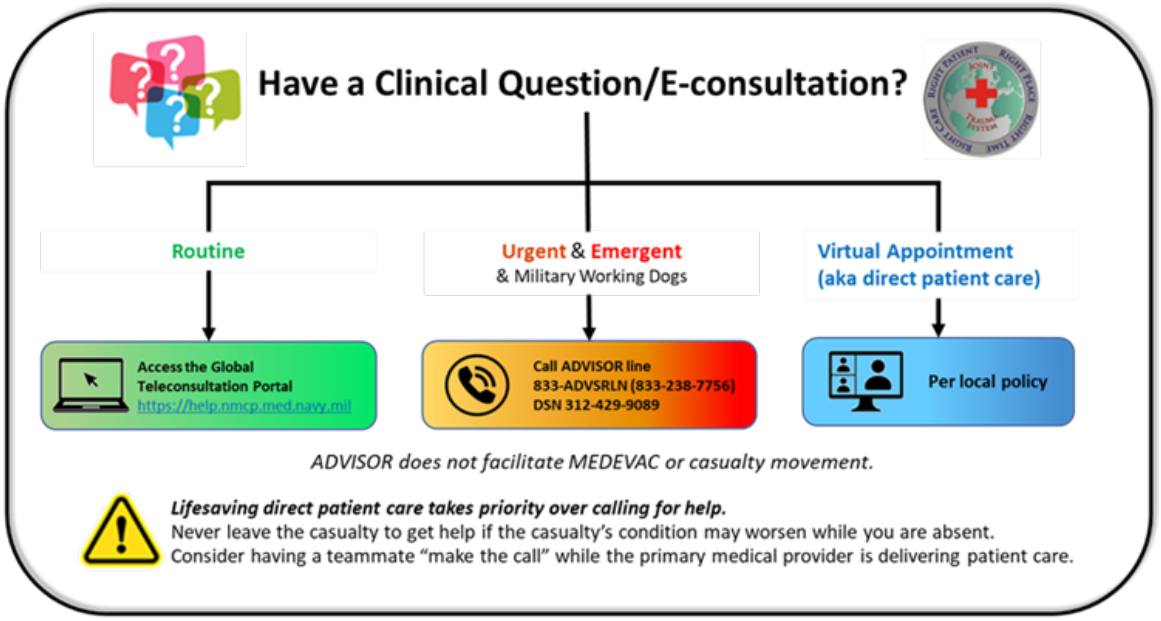


Illustration by Raymond Samonte

BACKGROUND

Ascending to, or being at, high altitude may cause high altitude illness (HAI). HAI includes acute mountain sickness (AMS), high altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE). HAI is caused by exposure to the hypobaric hypoxic environment, and it can lead to life-threatening physiologic changes.

Travel to high altitude may also exacerbate certain pre-existing medical conditions. It is often possible to prevent HAI by ascending slowly and allowing the body to adjust during a gradual ascent. Serious complications of high-altitude disease can be avoided by appropriate preparation, early surveillance of symptom onset, and aggressive treatment of disease. Normally, the most appropriate treatment in all altitude illnesses is to descend.

These clinical practice guidelines are adapted from the Wilderness Medicine Society (WMS) guidelines given that military operations may not allow forces to conduct the WMS recommended treatment. The WMS guidelines can be found at:
https://wms.org/magazine/magazine/1191/WMS_Clinical_Practice_Guidelines/Default.aspx

DEFINITIONS

Intermediate altitude: 1500-2500meters (m) (4921-8202feet (ft)): Decreased performance, no impairment of oxygen transport. No risk to low risk of severe HAI. There have been a few case series describing susceptible individuals getting AMS and HAPE at intermediate altitude; however, this is generally considered a rare occurrence. SpO2 expected to remain >90%. [1-3]

High altitude: 2500-4500m (8202-14,763ft): Decreased arterial oxygen saturations, hypoxemia during sleep/exercise. Moderate risk of severe HAI, including HACE and HAPE. SpO2 can drop below 80%. [3]

Very high altitude: 4500-5500m (14,763-18,044ft): Requires period of acclimatization. High risk of severe HAI. Prevalence of AMS is described as high as 70% in individuals ascending Mount Rainier (14,411ft). SpO2 at 17,500ft has been described as ranging from 65-81%. [3-4]

Extreme high altitude: >5500m (18,044ft): Severe hypoxemia/hypocapnia. Incompatible with prolonged human habitation. SpO2 on the peak of Everest Summit (29,000ft) is described as 54-62%.[3]

Rapid ascent for military operations: Ascent from sea level to high altitude 2500-4500m (8202-14,763ft) in less than 48 hours without proper pre-acclimatization or an ascent rate faster than 500m per day when above 3000m (9,842ft) altitude without proper pre-acclimatization.

PRE-MISSION PLANNING AND RISK MITIGATION

Risk factors for HAI include rapid ascent; highest altitude obtained; highest sleeping altitude; history of prior HAI; particularly a history of HACE and HAPE; obesity; recent acclimatization; overexertion; and cold weather exposure.[5]

PRE-MISSION EDUCATION

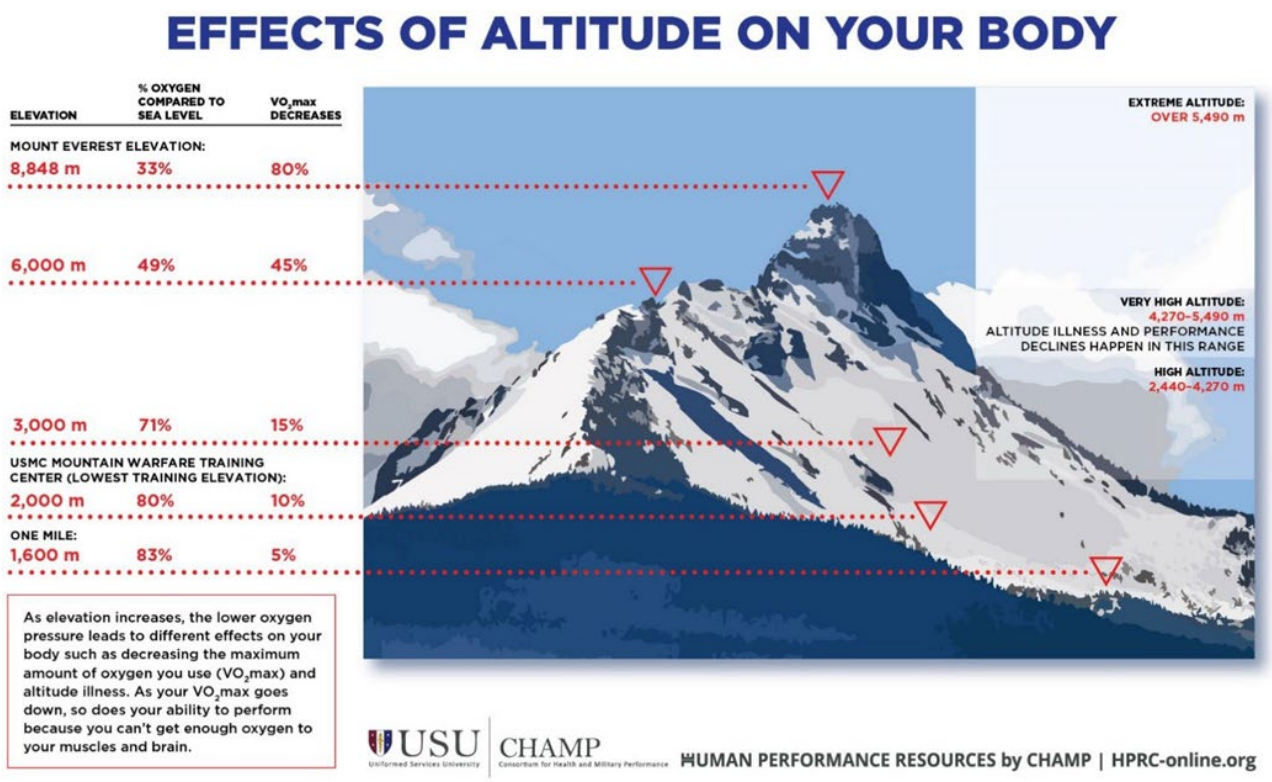
During pre-mission planning and briefings, it is imperative for supporting medical officers and medics who will be going on the mission to educate themselves on the signs and symptoms of altitude illnesses. Such education should focus on prevention, identification of other members on the mission, signs, symptoms, and treatments. Additional focus should be on teammate-to-teammate recognition with early identification the upmost importance.

Ascents should be limited to 500m for sleeping/camp each night past 3000m. This is important for mission planning and education for commanders. Ascending too rapidly will put forces at risk for non-acclimatization.

EFFECTS OF ALTITUDE ON PRE-EXISTING MEDICAL CONDITIONS

Though the military population does go through robust medical screenings, altitude exposure can significantly worsen many preexisting medical conditions. Current recommendations vary greatly depending on the specific condition, with minimal effect from altitude sojourns to strict contraindications with altitude exposures. A non-exhaustive list includes asthma, cardiovascular disease, pulmonary disease, hemoglobinopathies (including sickle-cell trait), pulmonary hypertension, obstructive/central sleep apnea and medications causing respiratory depression.[4,6-] See table of comorbidities and recommendations before altitude expositions.

Figure 1. Acclimatize for high-altitude-deployment



Source: HPRC-Online.org

PRE-ACCLIMATIZATION

Pre-acclimatization to high altitude environments describes exposures to altitude or hypobaric hypoxic conditions prior to actual high-altitude operations. Individuals pre-acclimatized to high altitude environments have a lower incidence of HAI.[7] Thus, if the mission requires rapid ascent to high altitudes, risk of HAI can be attenuated by pre-acclimatization strategies.

Pre-acclimatization success is proportional to length of exposure, altitude of pre-acclimatization, proximity in time from pre-acclimatization to re-exposure, and exercise capacity during pre-acclimatization periods.[8-11] Complete acclimatization can take weeks, but 70-80% of ventilatory acclimatization is achieved in 4-7 days. Benefits of pre-acclimatization have been shown to persist up to 2 months.[10] Methods of successful pre-acclimatization include staged ascent, gradual ascent, and daily intermittent hypoxic exposures (IHE).[12-14]

Staged ascent is the practice of spending a period of time at high altitude prior to a rapid ascent to very high or extreme altitude. Most studies have shown decreased symptoms of AMS with 3-7 days of prestaging at intermediate to high altitudes.[10,14-15] Personnel inserting at extreme high altitude will benefit from staging at the highest possible altitude for as long a duration as possible, prior to rapid ascent. If personnel experience AMS during staging, sleeping at a lower altitude while spending waking hours at a higher altitude will be beneficial.

Gradual ascent has been defined as increasing sleeping elevation by no more than 500m/day when ascending above 3000m. Daily exercises and activities may extend beyond 500m from the previous

night's sleep altitude. This strategy is the most conservative and probably the most effective method of acclimatization.

IHE refers to intermittent exposures to hypoxic environments in an attempt to pre-acclimate to high altitude. Numerous studies have had varying protocols ranging from 1-hour exposures daily for 1 week to greater than 4-hour exposures for greater than 1 week. Results have been mixed, with some studies showing decreased incidence of AMS and others showing no change.[12,16-19] Pre-acclimatization in a normobaric hypoxic environment does not appear to be as effective as the hypobaric hypoxic environment at preventing AMS.[16,20] For small unit special operations, IHE can be a second- or third-line method of pre-acclimatization, although not enough data exists to provide any meaningful strong recommendation on specific protocol. Following general principles of pre-acclimatization, noting that longer duration and higher simulated altitude exposure will likely prove to be more effective.

NUTRITION & HYDRATION

HYDRATION: Bicarbonate diuresis in response to respiratory alkalosis as well as venous constriction with suppression of antidiuretic hormone and aldosterone are normal physiologic responses to ascent, and the resulting hemoconcentration can increase blood oxygen carrying capacity.[3-4] These responses plus the lower humidity and the lower atmospheric pressure of higher altitude alpine environments predispose individuals to dehydration. Dehydration can be further exacerbated if patients are taking diuretic medications, such as acetazolamide. Signs and symptoms of dehydration can mimic those of AMS and HACE; however, dehydration itself has not been shown to increase the incidence of AMS.[21,22] Thus, dehydration should be avoided and guided by thirst and appropriate urine output. Overhydration and forced hydration has not been shown to be helpful.[7,23] Consider dehydration as a differential diagnosis or co-presentation when evaluating for AMS/HACE.

NUTRITION: Multiple studies have shown both men and women tend to reduce their energy intake after acute ascent to over 4,300m.[24-26] Acute high-altitude exposure alone has been demonstrated to increase basal metabolic rate and energy demand by 30%.[26] AMS can cause nausea, further exacerbating anorexia. One study showed that reduced calorie intake at altitude was independently associated with the presence of AMS symptoms.[24] Data on any specific type of diet having a benefit in performance or decreasing incidence of HAI are mixed.[28] Prolonged physical exertion at a caloric deficit will likely lead to performance deterioration. Considering the above, individuals should be encouraged to intentionally increase energy intake above sea-level when ascending to altitude; although the specific amount of caloric increase to optimize performance is likely determined by complex unique factors and there is not enough data to make a specific recommendation at this time.

IRON: Pulmonary hypertension from any cause is a strong risk factor for HAPE.[4] Iron infusions in healthy adult males lowered pulmonary artery systolic pressures by 6 mmHg 3 days after moving from sea level to 4340m as well as a separate study showing decreased pulmonary vascular reactivity in acute hypoxia.[29,30] Both those studies used one time dose of Iron Sucrose 200mg IV. Maximum oral iron absorption was shown to be limited at 25mg/day.[31] A small single randomized, double-blinded, placebo-controlled study did show a lower rate of AMS with iron infusions at 24hrs of altitude exposure, but it did not reach significance (P = .097).[21] Based on the above, consider screening personnel, especially those with a history of pulmonary arterial hypertension or HAPE, for iron deficiency prior to high altitude operations and treat iron deficiency with iron supplementation. Iron infusions are currently being studied at USAREIM at time of this CPG publication. Update required upon completion of their study.

ACUTE MOUNTAIN SICKNESS (AMS)

GENERAL APPROACH TO AMS

Acute Mountain Sickness Diagnosis Criteria at altitude (2500M or higher) Headache plus at least one of these:

- Weakness/lightheadedness
- Nausea/vomiting
- Anorexia
- Fatigue

During the mission planning phase, prioritize risk mitigation strategies. While at altitude, continue to reassess for AMS, considering differentials that may mimic AMS. Untreated AMS increases risk of HACE, whether AMS is diagnosed or not. Mild AMS can be treated in place with constant monitoring and re-evaluation. Higher risk AMS should be evacuated to lower altitude with repeat evaluations. Use pharmaceuticals and adjuncts listed above if the operational environment prevents rapid evacuation. More severe disease will require more aggressive therapy. There is an extreme risk to forces if AMS increases and or left untreated. Commanders should consider prophylaxis treatment, acclimatization, and if needed aggressive treatment.

AMS EVALUATION

AMS typically presents within 1-6 hours of altitude exposure although delayed presentations can occur at up to 48 hours. This is a clinical diagnosis of a syndrome consisting of headache, in addition to one or more additional symptoms including: lassitude/ fatigue/ weakness, nausea/ vomiting, anorexia, fatigue, and dizziness/ lightheadedness. Physical exam findings are nonspecific. See Appendix A for a scoring scale that can help with trending severity.[32] AMS generally does not occur below an altitude of 2000m. When diagnosing AMS, consider ruling out other differentials with similar presentations: dehydration, head trauma, caffeine withdrawal, migraine, alcohol hangover (veisalgia), carbon monoxide poisoning, viral syndrome, emotional stress, hyperthermia, and hypothermia.

AMS PREVENTION

Mission planning, pre-acclimatization strategy, nutrition, and hydration are discussed above and will mitigate incidence and severity of AMS. If the aforementioned risk mitigation approaches cannot be implemented due to mission constraints, consider pharmacologic therapy as described below.

Acetazolamide: There is strong evidence for the use of acetazolamide in preventing all HAI, including AMS. Reports on exercise performance deterioration at altitude secondary to acetazolamide are mixed, some reporting mild impairment and others reporting no change. A 2020 study done by the U.S. Army Research Institute of Environmental Medicine has shown no detrimental effect from acetazolamide at altitude.[33] The benefits of avoiding AMS and decreasing the likelihood of progression to HACE outweigh the risks of unlikely minor depression in exertional capacity.[33] For individuals with moderate to high risk of AMS, the recommended adult dose is 125 mg oral every 12 hours, and the pediatric dose is 1.25 mg/kg every 12 hours (max 125 mg/dose). Individuals should begin taking acetazolamide 24 hours prior to high altitude exposure and continue for 2 days at stable altitude if the rate of ascent was < 500m per day. If the rate of ascent was > 500m per day, then continue acetazolamide for 4 days once at stable maximum altitude. If symptoms of AMS return after acetazolamide has been stopped, then it can be restarted for an additional 2-4 days. Acetazolamide can be discontinued once steady descent has been initiated. (Luks AM, 2019, Davis C, 2020) For small units making rapid ascent to altitudes >3500 with high

risk of HAI and expectations of immediate execution of specialized tasks, increase the dosage of acetazolamide to 250 mg orally every 12 hours beginning 24 hours prior to exposure.[34]

Dexamethasone: There is strong evidence for the use of dexamethasone in preventing AMS.[17,34-35] However, given its significant side effect profile (ex. adrenal suppression) and ability to mask AMS symptoms without aiding in acclimatization it should be considered only as second line to acetazolamide, and/ or reserved as a treatment of severe AMS. It can also be used in addition to acetazolamide for otherwise unavoidable missions with a very high risk of AMS. For those at moderate to high risk of AMS, the recommended dose of dexamethasone is 4 mg orally every 12 hours starting the day of ascent and continuing until at a stable altitude for 2 days. Higher doses may be required by some individuals and units at very high-risk for AMS; increase dosing to 4 mg every 6 hours. If dexamethasone is used for greater than 10 days, consider a 7-day taper. There is no recommendation for use of dexamethasone for AMS in the pediatric population. [3-4,17]

AMS TREATMENT

Descent: This is the first line and the definitive treatment of nearly all HAI. Symptoms of AMS will typically resolve after descent of 300 - 1000 m from altitude of symptom onset. With increasing severity more urgent descent is advised. (See Appendix A.) With isolated AMS without progression to HACE or HAPE, individuals can be treated with arrest of ascent and rest at their current altitude for 1-2 days. Ascent may be resumed, at a rate no greater than 500m per day, once the individual is asymptomatic.

Oxygen: Oxygen is beneficial, titrate to SpO2>90%. Hypoxia reaches a peak during sleep; if possible, provide low flow oxygen (<2 L/min) by mask or nasal cannula during sleep to treat and prevent progression of AMS.[3,17] The logistics of carrying large amounts of oxygen are generally not feasible in the operational environment, thus oxygen should be reserved for severe AMS, HACE, and HAPE cases as an adjunctive therapy pending evacuation.

Portable hyperbaric chambers: Strong evidence exists for the effectiveness of portable hyperbaric chambers (PHCs) in treating severe HAI.[3,17,36] If immediate descent is not an option, individuals with severe AMS and at risk of progression to HACE should be treated with a PHC per the chamber's protocol. Descent and evacuation should be a priority for these individuals and the PHC should be viewed as a temporary stopgap.

Acetazolamide: Acetazolamide can be given to treat AMS in adults at a dose of 250 mg orally every 12 hours. In pediatrics, the dosing is 2.5 mg/kg orally every 12 hours (max 250 mg/dose).[17] In severe AMS, it should be used as an adjunct to dexamethasone.

Dexamethasone: There is strong evidence for the treatment of AMS with dexamethasone.[3,17] Dexamethasone should be given to individuals with severe AMS as well as moderate AMS who are at risk of progression towards HACE if descent is not an option. Although giving dexamethasone can improve symptoms of AMS, continuing altitude exposure can cause disease progression. Dosing for AMS treatment is 4mg every 6 hours until asymptomatic.[17]

If Dexamethasone is utilized for treatment of AMS, it should be limited to only a few doses and the individual should not ascend again until asymptomatic off dexamethasone for at least 48 Hours.

Ibuprofen/Acetaminophen: Ibuprofen and acetaminophen can be used to treat headache symptoms of AMS at their usual dosing for headache therapy.

HIGH ALTITUDE CEREBRAL EDEMA (HACE)

GENERAL APPROACH TO HACE

During the mission planning phase, prioritize risk mitigation strategies. Embedded providers should remain vigilant in surveillance of severe AMS and symptoms of HACE among their troops as well as themselves. Carefully monitor and treat those with severe AMS, watching for progression towards HACE. HACE is life- threatening; emergency evacuation should be a priority. Use pharmaceuticals and adjuncts listed above to begin treating HACE while coordinating evacuation. Do not delay evacuation for the aforementioned therapies. ***Treatment and evacuation efforts should be aggressive.***

HACE EVALUATION

Diagnostic Criteria for HACE

Presence of AMS and development of one of these:

- Ataxia
- Altered mental status

OR

- No pre-existing AMS
- The onset of ataxia AND altered mental status

HACE generally presents as a progression from AMS, although isolated HACE presentations have been reported. HACE is a clinical diagnosis and classically presents with headache, altered mental status and ataxia. The international criteria for HACE diagnosis are defined as the onset of ataxia OR altered mental status in the presence of acute mountain sickness; or the onset of ataxia AND altered mental status without the presence of acute mountain sickness. Symptoms are secondary to encephalopathy and can include behavioral changes, personality changes, apathy, drowsiness, confusion, social withdrawal, and stupor. Raised intracranial pressure can lead to cranial nerve three and six palsies. Other focal neurological deficits are rare and should prompt investigation towards other pathology. Differential diagnosis for HACE should include hypoglycemia, hyponatremia, hypothermia, hyperthermia, encephalitis/meningitis, postictal state, complex migraine, stroke, psychosis, intracranial hemorrhage, traumatic brain injury, shock, carbon monoxide poisoning, and toxidrome secondary to ingestion/exposure. An appropriate history, neurologic exam, and mental status exam are important for making this diagnosis.

HACE PREVENTION

Mission planning, pre-acclimatization strategy, nutrition, and hydration are discussed above and will mitigate the incidence and severity of HACE. The general approach to HACE prevention mirrors AMS prevention.

Acetazolamide: See AMS prevention recommendation.

Dexamethasone: See AMS prevention recommendation.

HACE TREATMENT

Descent: HACE leads to high mortality and morbidity. Descent to the lowest possible altitude in the most expeditious manner should be of the highest priority until symptoms fully resolve.[4,17]

Oxygen: If available, oxygen should be given continuously, titrating to an SpO2>90%. Rapid evacuation should not be delayed for oxygen therapy.

Portable hyperbaric chambers: Utilize a PHC to aggressively treat the patient in conjunction with oxygen if it does not delay evacuation or as a temporizing measure until evacuation becomes available. Compress chamber to the maximum pressure the chamber is designed to sustain. Continue to coordinate for emergent evacuation while the patient is in the hyperbaric chamber. Be aware that once a patient is in the chamber, there will be limited ability for repeat physical exams, additional treatments, and patient movement.[3,17,36]

Acetazolamide: In HACE, acetazolamide should be used as an adjunct to dexamethasone. Treat with acetazolamide at the same doses recommended for AMS therapy.[17]

Dexamethasone: Dexamethasone should be given to all individuals with HACE. Dosing for HACE treatment is 8mg IM/IV/orally followed by 4mg every 6 hours until asymptomatic. Given the high morbidity and mortality and lack of data on pediatric cases, dexamethasone is recommended for pediatric cases of HACE at a dose of 0.15mg/kg IM/IV/orally every 6 hours (max 4mg per dose).[17,37]

HIGH ALTITUDE PULMONARY EDEMA (HAPE)

GENERAL APPROACH TO HAPE

During the mission planning phase, prioritize risk mitigation strategies and identify individuals who are at high risk of HAPE. Identify HAPE early in the disease process, as early administration of oxygen and descent of 1000m can potentially resolve symptoms. Once diagnosed, evacuation to lower altitude should be the top priority. Use pharmaceuticals and adjuncts listed above to temporize HAPE pathophysiology while coordinating evacuation. Do not delay evacuation for the aforementioned therapies.

Once diagnosed with HAPE, the roles of acetazolamide and dexamethasone have not been shown to be beneficial in the treatment of HAPE. Treatment and evacuation efforts should be aggressive.

HAPE EVALUATION

HAPE is life threatening and early diagnosis is critical. The international diagnostic criteria for HAPE are a combination of two signs and two symptoms. The symptoms are dyspnea at rest, cough, decreased exercise tolerance or weakness, and chest tightness or congestion. The earliest symptoms are commonly decreased exercise tolerance and dyspnea at rest. Signs include crackles or wheezing in at least one field. Central cyanosis, tachycardia, and tachypnea.

Diagnostic Criteria for HAPE

2 Signs from:
- Tachycardia
- Tachypnea
- Crackles or wheezing in at least 1 lung field
- Central Cyanosis

2 Symptoms from:
- Dyspnea at rest
- Cough
- Decreased exercise tolerance or weakness
- Chest tightness or congestion

Risk factors for HAPE include pulmonary arterial hypertension, previous history of HAPE (50-60% risk of recurrence after a first HAPE episode), pulmonary infection, PFO, and use of respiratory depressants. HAPE presents in isolation from AMS/HACE in 50% of cases and will often present on the second night of higher sleeping altitude exposure.[3] Development of disease after 4 days of stable altitude exposure is unusual. Disease progression can present as fever, increasing tachycardia, tachypnea, fatigue, productive cough, hypoxia/cyanosis, and hypoxic encephalopathy. Physical exam findings can include rales, particularly in the right mid-lung fields. SpO2 readings will be lower than expected for a given elevation. Differential diagnoses to consider include

asthma, chronic obstructive pulmonary disease, heart failure, bronchitis, myocardial infarction, pneumonia, pulmonary embolism, pneumothorax, and trauma.[3,17]

HAPE PREVENTION

Mission planning, pre-acclimatization strategy, nutrition, and hydration are discussed above for all HAI and will mitigate incidence and severity of HAPE. Identify those at high risk of developing HAPE, particularly those with risk factors for HAPE participating in aggressive ascent profiles with limited pre-acclimatization.

Slow ascent rate is more critical for those at high risk of HAPE. These individuals should ascend no faster than 350M sleeping elevation per night.

Nifedipine: For individuals at high risk of HAPE, prophylaxis with nifedipine extended- release formulation 30mg orally every 12 hours or immediate-release formulation 20mg orally every 8 hours, beginning on the day of ascent is recommended. Prophylaxis should be continued for 7 days at maximum altitude and can be discontinued upon descent.[3,17]

Phosphodiesterase inhibitors: For individuals at high risk of HAPE who are not candidates for nifedipine, prophylaxis with tadalafil 10mg orally every 12 hours or sildenafil 50mg orally every 8 hours, beginning on day of ascent is recommended. Do not use phosphodiesterase inhibitors in combination with nifedipine due to risk of hypotension. Prophylaxis should be continued for 7 days at maximum altitude and can be discontinued upon descent.[3,17,38]

Dexamethasone: There is weak evidence showing benefit of dexamethasone in preventing HAPE and the mechanism is poorly understood. Thus, if patients are at high risk of HAPE and are not candidates for nifedipine or a phosphodiesterase inhibitor, consider prophylaxes with dexamethasone 8mg orally every 12 hours, beginning on day of ascent. Prophylaxis should continue until at a stable altitude for two days.[3,17,38]

Acetazolamide: No robust data exists supporting the use of acetazolamide in HAPE prevention; however, the physiologic response to acetazolamide and acclimatization likely leads to a benefit in reducing severity of HAPE.[17,39] Patients at risk of HAPE are probably also at risk of severe AMS/HACE. Thus, patients at high risk for HAPE should be on prophylactic acetazolamide. See AMS prevention recommendation.

Salmeterol: Inhaled salmeterol has been shown to decrease HAPE risk up to 50% in susceptible individuals. The studies utilized 250mcg doses which are not standard. Inhaled salmeterol should not be used for HAPE prevention.

HAPE TREATMENT

Descent: HAPE leads to high mortality and morbidity; thus, descent to lowest possible altitude in the most expeditious manner should be of the highest priority until symptoms fully resolve. Individuals suffering from HAPE should descend using as little exertion to themselves as possible, ideally via vehicle. If they must walk themselves, then remove any burdening load.[4,17]

Oxygen: If available, oxygen should be given continuously, titrating to an SpO2>90%. Rapid evacuation should not be delayed for oxygen therapy.

Portable hyperbaric chambers: See PHC recommendation for HACE.[4,17,40]

Nifedipine: In cases when evacuation to lower altitude is prolonged or unavailable, patients should be treated with nifedipine. Treatment dose of nifedipine is identical to prophylactic dose. If immediate evacuation is available, then nifedipine is not indicated.[3,17,41]

Phosphodiesterase inhibitors: In cases where the patient is not a candidate for nifedipine, consider treating with tadalafil or sildenafil at the prophylactic dose. See phosphodiesterase inhibitor recommendation for HAPE prevention.

ADDITIONAL CONSIDERATIONS

For air evacuation of HAI casualties, pilots should fly at the lowest allowable elevation possible. All efforts should be made to avoid flying at higher elevations than the point of injury unless the cabin is pressurized to an altitude lower than point of injury.

Individuals who conduct dive operations should refrain from flying and ascending to high altitudes for at least 12 to 24 hours after the last dive due to increased risk of decompression sickness.[42]

Underwater diving operations at altitude compound the inherent risks of diving operations at sea-level. These risks are beyond the scope of this guideline. Consult your Dive Medical Officer or Master Diver to discuss alternative decompression tables and considerations when executing dive missions at altitude.[43]

Physiologic changes that take place at altitude can unmask previously subclinical conditions, such as seizure disorders, brain masses, and vascular malformations. New onset focal neurologic deficits at altitude should be evaluated by a qualified medical provider for consideration of evacuation with further neurologic workup once at higher level of care.[3-4]

Sickle cell disease and sickle cell trait have not been described as risk factors for HAI; however, these individuals are at increased risk of vaso-occlusive crisis and splenic infarction at altitude.[3-4]

Pregnant women should not participate in non-routine high altitude military operations without first talking to a medical officer about the risks.

PORTABLE HYPERBARIC CHAMBER (PHC) USE

A PHC is not intended to be used as a cure for severe acute mountain sickness. They are designed to stabilize a patient only until they can descend. All patients with HAPE or HACE should descend as soon as possible after being initially stabilized in a PHC.[44]

PHC can decrease the altitude by approximately

- 2400m (7874ft) can be decreased to 1000m (3300ft) Δ Change (ft) 4574
- 4200m (13780ft) can be decreased to 2500m (8250ft) Δ Change (ft) 5530
- 5400m (17717ft) can be decreased to 3500m (11500ft) Δ Change (ft) 6217
- 9000m (29529ft) can be decreased to 61200m (20460ft) Δ Change (ft) 9069

For all PHC, the usual treatment protocol is to place the soldier into the bag, pump the bag up until the pressure-relief valve hisses, then keep the pressure up by occasional pumping for the duration of the treatment. Continuous pumping is required to ventilate the bag and remove CO2. PHC treatment durations are generally 1-2 hours every several hours for 4-6 treatments a day as tolerated by patients until symptoms improve or the patient can be evacuated as required. Prolonged care in a PHC is taxing for the provider and patient thus

the common use of intermittent therapy. Maximum therapeutic treatment is obtained by adding supplemental oxygen by nasal cannula or mask with the hyperbaric treatments. Hyperbaric treatments can be repeated as necessary until the casualty clinically improves or is able to descend.[45]

There is presently only anecdotal data to support PHC treatments in the setting of altitude emergencies.[45-46]

In individuals with AMS without HAPE or HACE The PHC can be used to relieve AMS until the patient can be evacuated or allowed more time for acclimatization. If the patient responds to the PHC, they may cautiously climb back up to the higher altitudes. The climber should be constantly monitored for any recurrence of symptoms of AMS.[45-47]

PLANNING CONSIDERATIONS

The PHC take approximately eight minutes to inflate and should be pumped 10-20 times per minute to maintain pressure and flush carbon dioxide The bags weigh 12-15lbs. Time in the PHC is dependent on the severity of AMS and how the climber responds to the treatment.

PHB at best generate 0.17ATM of pressure and thus have no utility in treatment of diving illness of any type.

RAPID ASCENT PROTOCOL FOR UNACCLIMATIZED

- Rapid ascents to 2500M or less do not require prophylaxis.
- Rapid ascents to 2500M to 3500M in less than 24 hours should utilize acetazolamide 125mg po BID starting at least 8 hours and ideally 24 hours prior to ascent.[48]
- Rapid ascents to 3500M or higher will result in a 70-100% incidence of AMS. Prophylaxis with dexamethasone 4mg q6h and acetazolamide 125mg PO BID should be utilized starting 24 hours prior to ascent.[49-50]

Operational requirements may dictate the need for unacclimatized individuals to rapidly ascend over the course of just a few hours to high altitude. A combination of acetazolamide and/or dexamethasone to decrease the risk of HAI and allow the service member to perform better physically and mentally is recommended. Several prophylaxis protocols for this situation have been studied both in chamber and field settings.

Studies utilizing the protocols that include dexamethasone have been of short duration, usually less than 48 hours. Therefore we recommend when utilizing rapid ascent protocols that include dexamethasone the individuals should complete the mission and return to lower elevation in 48 hours or less. If dexamethasone is discontinued while individuals are at these altitudes AMS symptoms may occur.[51-55]

PERFORMANCE IMPROVEMENT (PI) MONITORING

POPULATION OF INTEREST

Individuals and units traveling to high altitude locations 2500 meters (8202 feet) or above.

INTENT (EXPECTED OUTCOMES)

1. Conduct pre-mission planning and implement altitude illness risk mitigation strategies. This includes:
    - Implementation of pre-acclimatization strategies (staged ascent, gradual ascent, and daily intermittent exposures).
    - Screening of individuals for preexisting medical conditions listed in Table 1.
    - Education on signs and symptoms of altitude illnesses.
    - Plan for adequate nutrition and hydration.
    - Outfit unit with altitude illness-specific medications (ibuprofen, acetaminophen, acetazolamide, dexamethasone, nifedipine, phosphodiesterase inhibitors, salmeterol) and equipment (oxygen, PHC/Gamow™ bag).
    - When indicated, implement rapid ascent medication prophylaxis protocol using acetazolamide and/or dexamethasone.
2. Conduct surveillance of symptoms throughout expedition using Lake Louise AMS Score.
3. Apply recommended treatment to individuals exhibiting symptoms of HAI according to Altitude Emergencies Initial Management Algorithm.

PERFORMANCE / ADHERENCE METRICS

1. Number and percentage of patients in the population of interest diagnosed with AMS are prescribed Acetazolamide per protocol.
2. Number and percentage of patients in the population of interest diagnosed with HACE are prescribed Acetazolamide per protocol.
3. Number and percentage of patients in the population of interest diagnosed with HAPE are prescribed Nifedipine or Phosphodiesterase inhibitors per protocol.

DATA SOURCES

- Patient record
- DoD Trauma Registry

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed.

The JTS Chief and the JTS PI Branch will perform the systems review and data analysis.

RESPONSIBILITIES

The trauma team leader is responsible for ensuring familiarity, appropriate compliance, and performance improvement monitoring at the local level with this CPG.

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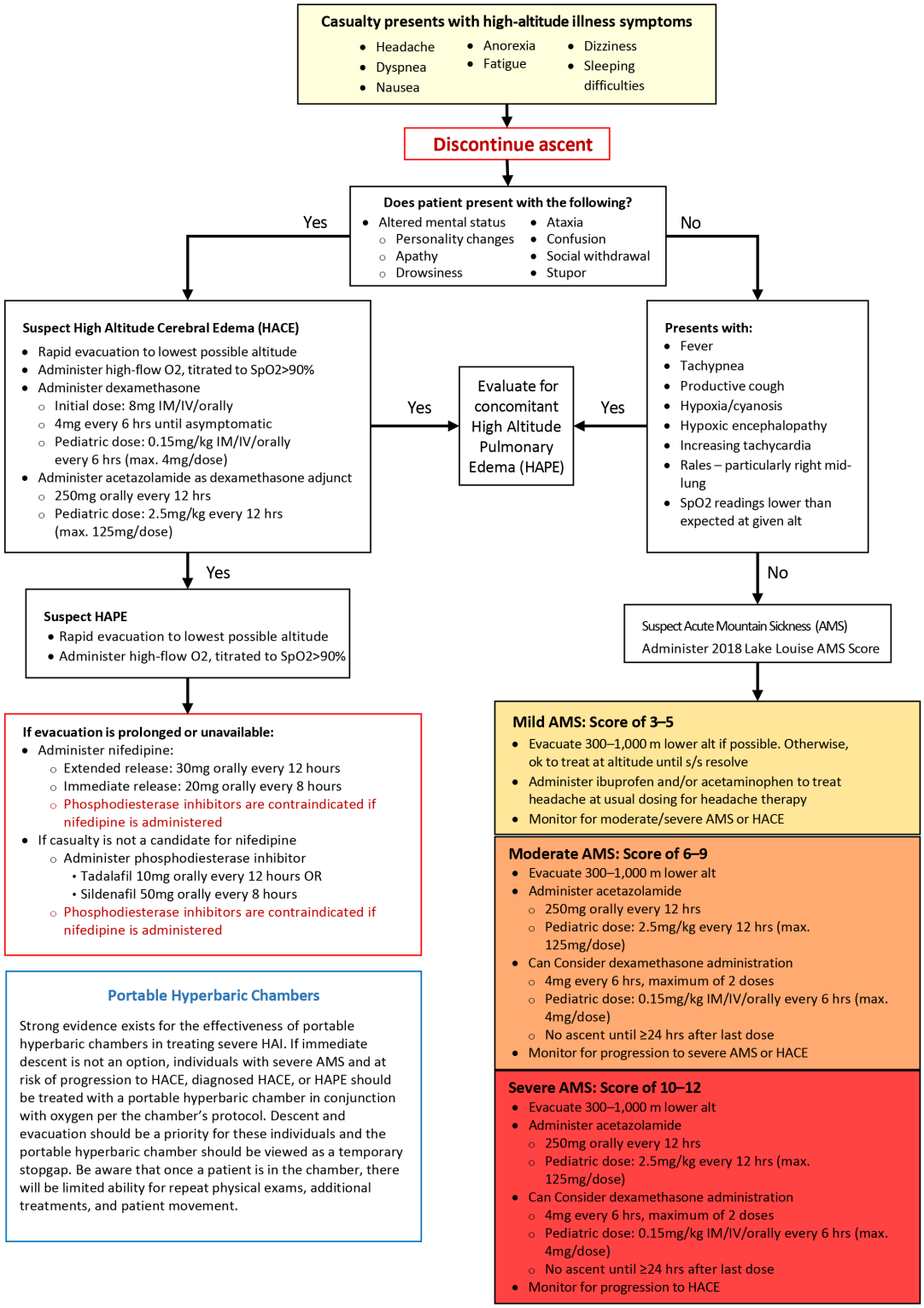
APPENDIX A: ALTITUDE EMERGENCIES INITIAL MANAGEMENT ALGORITHM



APPENDIX B: 2018 LAKE LOUISE ACUTE MOUNTAIN SICKNESS SCORE

2018 LAKE LOUISE ACUTE MOUNTAIN SICKNESS SCORE	
Headache ▪ No headache: **0** ▪ Mild headache: **1** ▪ Moderate headache: **2** ▪ Severe headache/incapacitating: **3**	**Score**
GI Symptoms ▪ Good appetite: **0** ▪ Poor appetite/nausea: **1** ▪ Moderate nausea/vomiting: **2** ▪ Severe nausea/vomiting/incapacitating: **3**	**Score**
Fatigue/weakness ▪ Not tired or weak: **0** ▪ Mild fatigue/weakness: **1** ▪ Moderate fatigue/weakness: **2** ▪ Severe fatigue/weakness/incapacitating: **3**	**Score**
Dizzy/lightheadedness ▪ No dizziness/lightheadedness: **0** ▪ Mild dizziness/lightheadedness: **1** ▪ Moderate dizziness/lightheadedness: **2** ▪ Severe dizziness/lightheadedness/incapacitating: **3**	**Score**
Total score ▪ Mild AMS: score of **3-5** ▪ Moderate AMS: score of **6-9** ▪ Severe AMS: score of **10-12**	**Score**
*Diagnosis requires headache plus 1 or more other listed symptoms *This scoring system was designed for research, not clinical use. It is not a substitute for clinical judgment. (Roach RC, 2018)	

Regarding patients suffering from pre-existing chronic diseases, Figure 1 proposes a non-exhaustive list of important comorbidities needing a particular look before departure.

General recommendations for people with comorbidities are listed in the table on the next page.

Table: Comorbidities and recommendations before altitude expositions.

Disease	Traffic lights	Restrictions	Advice
Mild Asthma (8) (9)		No restriction up to 5000m	• Use a spacer • Take a push of aerosol (Beta2-agonist) before effort • Protect your mouth and nose (with a balaclava), • Carry peak-flow meter and emergency set (oral prednisone)
Moderate Asthma		No restriction up to 3000m	
Severe/uncontrolled Asthma		Avoid altitude	
Chronic Obstructive Pulmonary Disease (COPD)* (9)		Avoid altitude >3000 m Max. altitude allowed depends on the $P_AO_{2,Alt}$: patients with a FEV_1<1.5 L need specialized consultation (hypoxia simulation, assessment for supplemental oxygen)	• Take emergency set (oral steroids, antibiotics, oxygen) • Evaluate pulmonary hypertension prophylaxis
Heart failure (2) (10)		No restriction until 3000-3500 m if: • disease is stable • LVF is preserved • above-normal exercise capacity	
Pulmonary embolism, Deep vein thrombosis, Coagulopathy (9) (11)		Pursue pre-existing therapeutic anticoagulation Stop oral contraceptive in females with coagulopathy	
Pulmonary Hypertension (9)		Avoid altitude >3000 m	Evaluate use of supplemental oxygen and pulmonary vasodilators if stay in altitude unavoidable (from 2000 m)
Obstructive and central sleep apnea (12)		Look for pulmonary arterial hypertension before departure. Travel with CPAP and adjust it before departure, eventually mandibular advancement device. Evaluate acetazolamide for central sleep apnea	

Table 1 : Comorbidities and recommandations before altitude exposition

$P_AO_{2,Alt}$: Alveolar oxygen partial pressure

P_aO_2 : arterial oxgen tension LVF : Left Ventricular Funtion

FEV_1 : Forced Expiratory Volume in 1 second

LVF: left ventricular function

CPAP : Continuous Positive Airway Pressure

* For COPD patient, a P_aO_2 > 50-55 mmHg (6.6 kPa) is needed. PaO2 Altitude = ((0.519 x PaO2 SL) + 11.85 x FEV1) – 1 .76 (13)

REF: David Eidenbenz, 2017. BJSM. Mountain sports: what should a sports doctor check before authorizing patients to go at high altitudes? *https://blogs.bmj.com/bjsm/2017/06/03/mountain-sports-sports-doctor-check-authorizing- patients-go-high-altitudes/*

APPENDIX C: OFF-LABEL USES OF FDA-APPROVED PRODUCTS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e. "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES

Balanced Discussion

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.