



High-Altitude Illness

AMS · HACE · HAPE · Wilderness Medical Society 2024 Update

Descent is the only cure
every drug here only buys time

⚠ THE THREE THAT CARRY THE PAGE

⚠ GO DOWN. NOTHING ELSE IS DEFINITIVE

Descend 300-1000 m for moderate AMS, ≥ 1000 m for HACE or HAPE, until symptoms resolve. Oxygen ($\text{SpO}_2 > 90\%$) and a hyperbaric chamber (2 psi $\approx$ 1000-3000 m of simulated descent) are bridges only: altitude keeps supplying the cause. ⚠ Three rules: never ascend with symptoms · if worse, go down NOW · never leave an ill person alone -HACE removes the ability to self-rescue within hours.

⚠ ATAXIA IS THE HACE ALARM

Mechanism: hypoxia dilates cerebral vessels (flow up $\sim 24\%$ in hours) and VEGF, NO and free radicals make the blood-brain barrier leaky, giving vasogenic white-matter edema (classically the splenium) a tight skull cannot buffer. Vasogenic means steroid-responsive: hence dexamethasone. Test tandem gait on anyone whose AMS is worsening: ataxia is the earliest, most reliable sign and precedes any mental status change. "Looks drunk at altitude" is HACE until proven otherwise. Give dexamethasone 8 mg then 4 mg q6h, plus oxygen and immediate descent; untreated HACE reaches coma within 24 h. ⚠ Acetazolamide is the WRONG drug here -it works over hours to days, the wrong timescale for someone becoming obtunded. ⚠ Focal deficits argue AGAINST HACE (global encephalopathy) -think stroke.

⚠ HAPE IS NOT HEART FAILURE. DO NOT DIURESE

Uneven, exaggerated hypoxic pulmonary vasoconstriction overperfuses unprotected capillary beds $\rightarrow$ stress failure $\rightarrow$ a high-protein PERMEABILITY leak. LV function and wedge pressure are normal and these patients are intravascularly depleted, so furosemide causes hypotension and syncope without touching the edema. Hence patchy ASYMMETRIC infiltrates with a normal cardiac silhouette. Mortality up to 50% untreated -the commonest cause of death from altitude illness.

RECOGNITION AMS and HACE are one continuum; HAPE is a separate pulmonary vascular process, and half of HAPE has no AMS

Point	Detail
⚠ 2018 Lake Louise AMS Score	Four domains scored 0-3: headache, GI symptoms, fatigue/weakness, dizziness. Diagnosis needs a total ≥ 3 AND ≥ 1 point from HEADACHE after a recent gain in altitude. Mild 3-5 · moderate 6-9 · severe 10-12. ⚠ The 2018 revision DELETED the sleep item, since periodic breathing disrupts sleep in almost everyone at altitude, so it diagnosed AMS in well people. Mental status stays NORMAL in AMS; once it does not, treat as HACE. Acetaminophen 1 g or ibuprofen 600 mg for headache, ondansetron 4 mg ODT for nausea, but ⚠ relieving the headache does NOT treat the AMS -a comfortable patient still must not ascend
Onset windows	AMS: headache 6-12 h after arrival (range 2-24 h). HACE: usually > 24 h, most often day 2-4, almost always preceded by AMS. HAPE: day 2-4, rarely within 24 h. ⚠ Timing discriminates: dyspnea at hour 3 is unlikely to be HAPE. Recurrence after prior HAPE exceeds 60% -the basis for prophylaxis
⚠ Spotting HAPE early	The earliest sign is falling behind the group with a dry cough, long before dyspnea at rest -that is where lives are saved. The best bedside test is an SpO_2 compared with COMPANIONS at the same altitude (~ 10 points lower; 50-70% advanced), absolute values meaning little when all are desaturated. ⚠ Fever to 38.5°C , leukocytosis and an infiltrate are TYPICAL of HAPE, not evidence for pneumonia -antibiotics alone at altitude is how HAPE kills. Oxygen first, then descend, minimizing exertion (carry them; exertion and cold both raise PA pressure)

DRUGS · DOSE AND WHY

Drug	Dose, mechanism and cautions
⚠ Acetazolamide the two doses get transposed	PREVENTION 125 mg q12h. TREATMENT 250 mg q12h. (250 mg q12h to prevent if > 100 kg; children 2.5 mg/kg q12h.) Start the day before ascent, continue 2-4 days after arrival; it still works started on the day. Mechanism, not just renal: (1) proximal-tubule CA inhibition wastes bicarbonate, the acidosis cancelling the hypocapnic alkalosis that brakes the hypoxic ventilatory response; (2) tissue and red-cell CA inhibition raises tissue PCO_2 , a second stimulus working from day one; (3) carotid body effects blunt the PCO_2 swings driving periodic breathing; (4) mild diuresis. It truly accelerates acclimatization ⚠ Higher is not better: 250, 500 and 750 mg/day all worked, NNT 3-8 (Low, BMJ 2012), and 250 mg/day IS the 125 mg BID regimen. Paresthesias are near-universal, not an allergy. Avoid in severe hepatic or renal disease
Dexamethasone	AMS 4 mg q6h · HACE 8 mg then 4 mg q6h · prevention 2 mg q6h or 4 mg q12h (children 0.15 mg/kg q6h to treat; not for prophylaxis in children). Reduces vasogenic cerebral edema within 1-2 h. ⚠ It does NOT aid acclimatization, so it suppresses the illness while the maladaptation persists. Taper if used beyond 10 days
⚠ Nifedipine ER and the PDE5 inhibitors HAPE only	Prevention (prior HAPE only): 30 mg ER q12h, day before ascent to 4-7 days after arrival. Treatment: 30 mg ER q12h or 20 mg ER q8h, ONLY when descent is impossible AND oxygen unavailable (narrowed 2024). Pulmonary vasodilation lowers the PA pressure driving the leak: HAPE in 1/10 vs 7/11 placebo at 4559 m (Bärtsch, NEJM 1991). Alternatives: tadalafil 10 mg q12h or sildenafil 50 mg q8h -HAPE in 7/9 placebo, 1/8 tadalafil, 0/10 dexamethasone 8 mg BID (Maggiolini, Ann Intern Med 2006); their headache mimics an AMS headache. ⚠ Extended-release ONLY, and ⚠ NEVER combine nifedipine with a PDE5 inhibitor -additive hypotension in a volume-depleted patient

PREVENTION · AND WHAT 2024 TOOK AWAY

GRADUAL ASCENT BEATS EVERY PILL

Above 3000 m, gain no more than 500 m of SLEEPING altitude per night, with an extra acclimatization night per 1000 m gained. Framed around sleep because ventilation falls and periodic breathing develops overnight, the deepest desaturations of the day: hence "climb high, sleep low". Staged ascent (6-7 days at 2200-3000 m first) is the best non-drug strategy. By tier: low = ascent profile only; moderate and high = acetazolamide (dexamethasone if unusable); prior HAPE also needs nifedipine. ⚠ Fitness, age and sex do NOT predict risk -prior history, ascent rate and sleeping altitude do; fit people often fare worse because fitness lets them ascend faster

⚠ STOP DOING THESE

Forced overhydration is HARMFUL -it does not prevent AMS and causes exercise-associated hyponatremia that then mimics AMS. Drink to thirst. Salmeterol was REMOVED for HAPE prevention. Inhaled budesonide, acetaminophen for prevention and hypoxic tents are recommended AGAINST (the data did not replicate). ⚠ Acetazolamide is now advised against for HAPE TREATMENT; diuretics have no role. Ginkgo, coca, spironolactone, antioxidants, iron: not recommended. Brief oxygen before ascent buys nothing -acclimatization needs sustained hypoxia, not a reserve. NEW 2024: evaluate before altitude travel after COVID-19 if symptoms persist ≥ 2 weeks after a positive test or discharge, or after ICU care

⚠ MIMICS THAT KILL IF YOU ANCHOR ON ALTITUDE

⚠ Carbon monoxide	Stoves and lanterns inside tents; symptoms are indistinguishable from AMS and HACE. The tell is TENTMATES ill at the same time, improving outdoors not on descent. ⚠ Pulse oximetry reads FALSELY NORMAL -it cannot see carboxyhemoglobin
Hyponatremia · hypoglycemia	Both reproduce AMS and early HACE, and both are reversible. ⚠ Check a glucose before calling any confusion HACE; suspect hyponatremia in anyone told to "drink lots of water". Hypothermia and exhaustion mimic HACE too. ⚠ Suspect PE when a "HAPE" fails to improve on oxygen and descent. When unsure, treat as AMS

References: Luks AM et al, WMS Clinical Practice Guidelines for the Prevention, Diagnosis and Treatment of Acute Altitude Illness: 2024 Update, Wilderness Environ Med · Roach RC et al, The 2018 Lake Louise Acute Mountain Sickness Score, High Alt Med Biol 2018;19:4 · Bärtsch P et al, N Engl J Med 1991;325:1284 · Maggiolini M et al, Ann Intern Med 2006;145:497 · Low EV et al, BMJ 2012;345:e6779 · CDC Yellow Book, High-Altitude Travel and Altitude Illness.

Educational aid; verify against current guidance, local formulary and patient factors.

