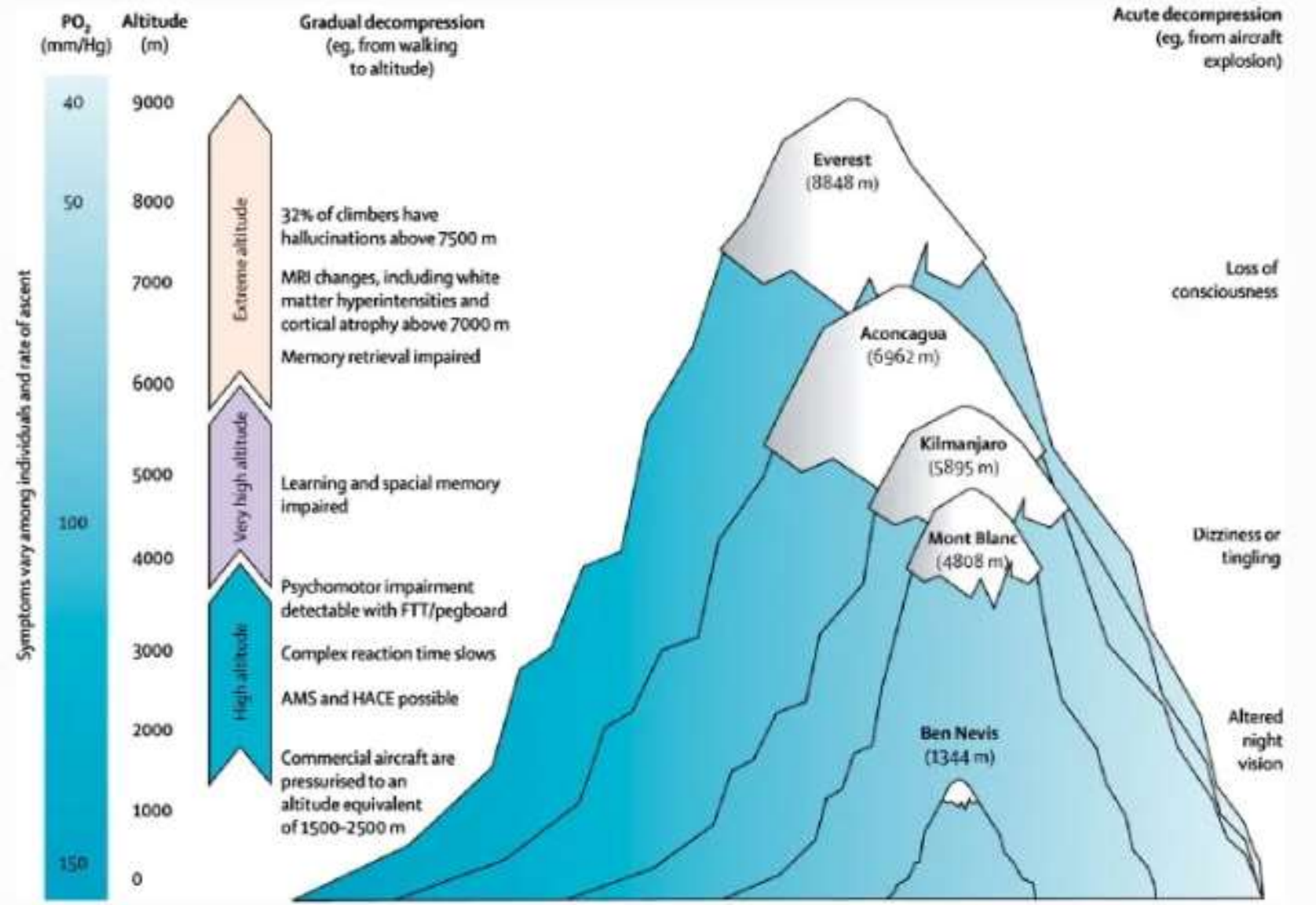
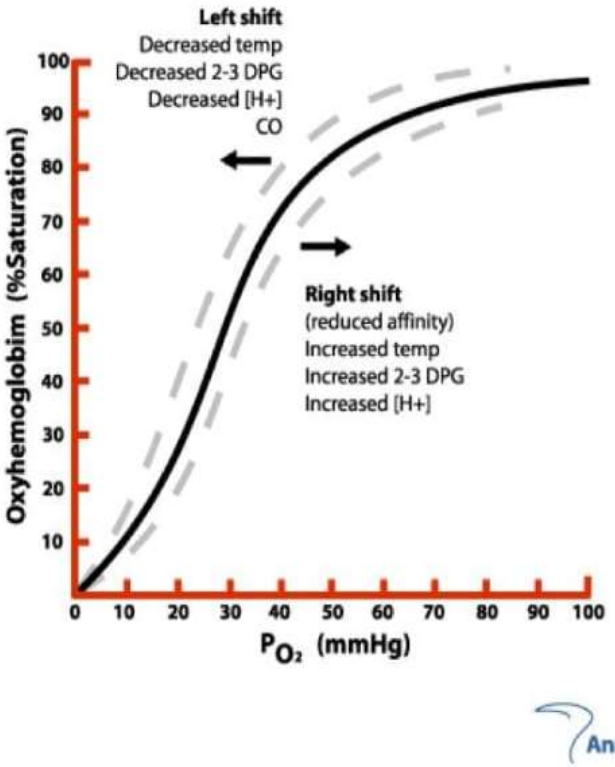
High altitude and its effects on lungs

Dr. Vaibhav Kajaria


PO2 (mm/Hg)
Altitude (m)
Gradual decompression (eg, from walking to altitude)
Acute decompression (eg, from aircraft explosion)
Symptoms vary among individuals and rate of ascent
40
50
100
150
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Extreme altitude
Very high altitude
High altitude
32% of climbers have hallucinations above 7500 m
MRI changes, including white matter hyperintensities and cortical atrophy above 7000 m
Memory retrieval impaired
Learning and spacial memory impaired
Psychomotor impairment detectable with FTT/pegboard
Complex reaction time slows
AMS and HACE possible
Commercial aircraft are pressurised to an altitude equivalent of 1500–2500 m
Everest (8848 m)
Aconcagua (6962 m)
Kilmanjaro (5895 m)
Mont Blanc (4808 m)
Ben Nevis (1344 m)
Loss of consciousness
Dizziness or tingling
Altered night vision

Altitude (meters)	Altitude (feet)	P_B (mm Hg)	PaO_2 (mm Hg)	SaO_2 (%)	$PaCO_2$ (mm Hg)
1646	5400	630	73 (65-83)	95.1 (93-97)	35.6 (30.7-41.8)
2810	9219	543	60 (47.4-73.6)	91 (86.6-95.2)	33.9 (31.3-36.5)
3660	12,008	489	47.6 (42.2-53)	84.5 (80.5-89)	29.5 (23.5-34.3)
4700	15,420	429	44.6 (36.5-47.5)	78 (70.8-85)	27.1 (22.9-34)
5340	17,520	401	43.1 (37.6-50.4)	76.2 (65.4-81.6)	25.7 (21.7-29.7)
6140	20,144	356	35 (26.9-40.1)	65.6 (55.5-73)	22 (19.2-24.8)
6500	21,325	346	41.1 ± 3.3	75.2 ± 6	20 ± 2.8
7000	22,966	324	-	-	-
8000	26,247	284	36.6 ± 2.2	67.8 ± 5	12.5 ± 1.1
8400	27,559	272	24.6 ± 5.3	54	13.3
8848	29,029	253	30.3 ± 2.1	58 ± 4.5	11.2 ± 1.7
8848	29,029	253	30.6 ± 1.4	-	11.9 ± 1.4



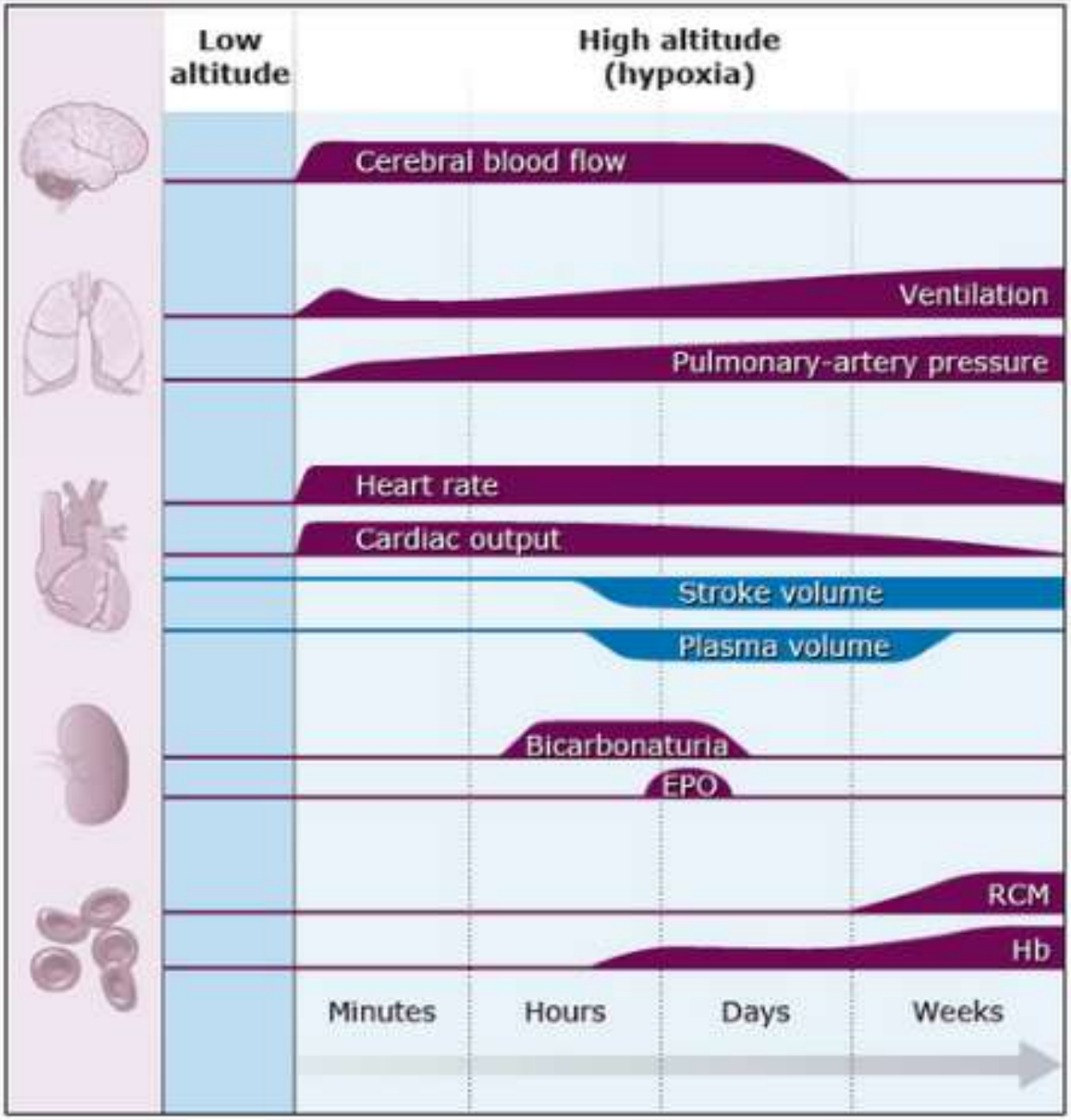
- The percentage of oxygen in inhaled air remains the same - 0.21 (21%) - but as atmospheric pressure decreases, the partial pressure of oxygen also decreases. **PAO2 = (Patm – PH2O) FiO2 – PaCO2/RQ**

Acclimatization

- Exposure to hypobaric hypoxia → ventilation increases
- This is called as *hypoxic ventilatory response* which is mediated by the carotid body chemoreceptors which respond to the decreased pO2 levels in blood
- There is hyperventilation which decreases the pCO2 level -> medullary chemoreceptors partially depress the ventilatory response
- Renal compensation : loss of bicarbonate in urine which causes metabolic response to respiratory alkalosis -> pH towards normal
- But hypocapneic alkalosis persists and hyperventilation continues over days to weeks even after decent

- HVR is associated with increased cardiac output and pulmonary perfusion
- There is hypoxic pulmonary vasoconstriction and increased PVR
- Pulmonary redistribution to areas which are usually less perfused at rest
- There is vascular remodelling (? Chronic) which includes smooth muscle hypertrophy and collagen hyper proliferation and is also in response to increased polycythemia induced hyperviscosity in chronic cases
- Hb starts to rise in days and continues to rise over weeks -> EPO rise
- In tibetan and himalayan people - > low EPO response seen due to mutation of hypoxia inducible factor -2 alpha gene
- Oxygen dissociation curve first shifts left due to alkalosis but with subsequent increase in 2-3 DPG the curve shifts right

- Since the O2 levels are always in the steep portion of the ODC there is rapid fall in SPO2 on minimal activity which decreases exercise capacity
- Sleep is disturbed due to peroidic apneic breathing as CO2 tends to go below the apneic threshold with hyperventilation


Low altitude
High altitude (hypoxia)
Cerebral blood flow
Ventilation
Pulmonary-artery pressure
Heart rate
Cardiac output
Stroke volume
Plasma volume
Bicarbonaturia
EPO
RCM
Hb
Minutes
Hours
Days
Weeks

Physiologic effects of high altitude

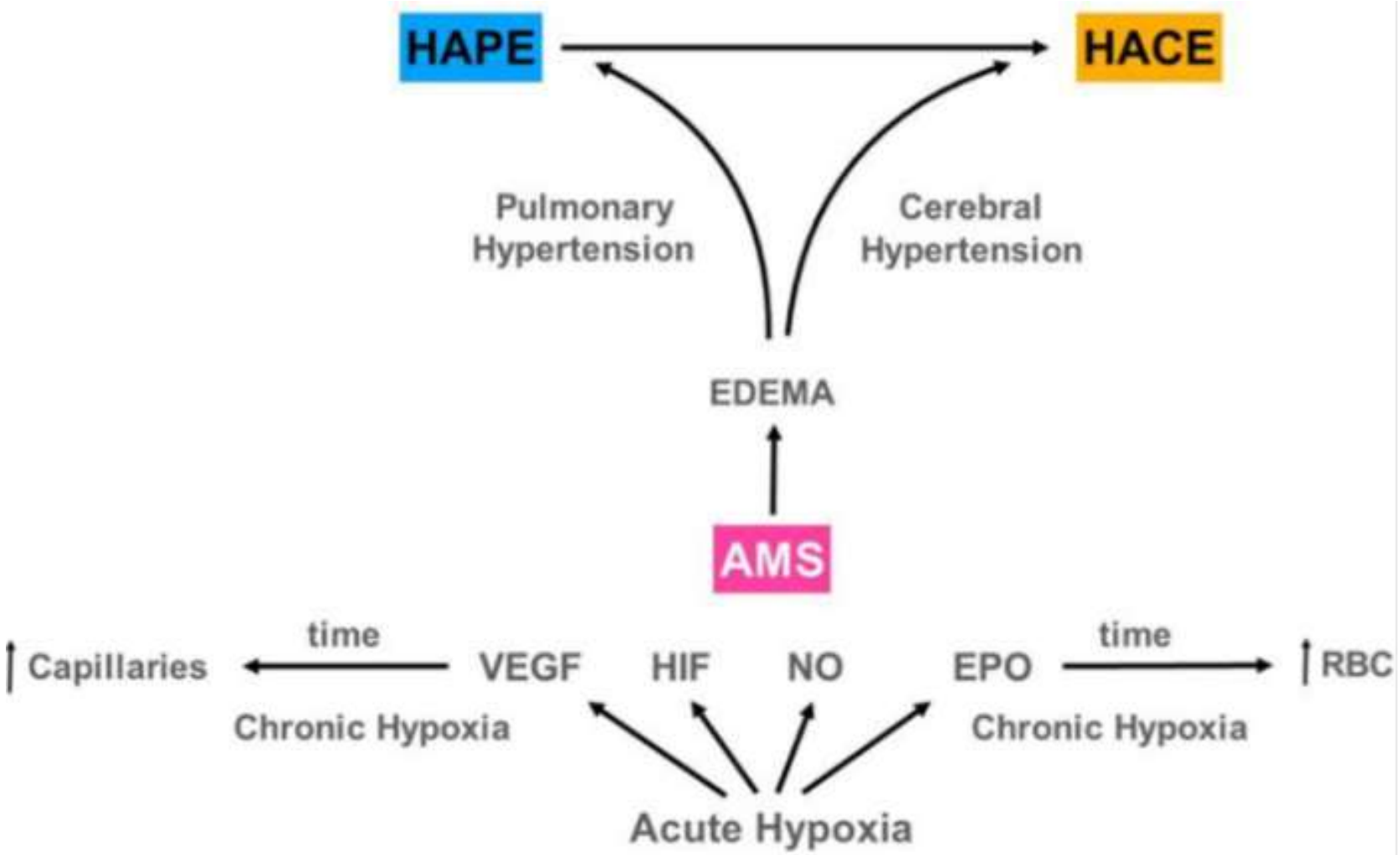
High altitude: 1500 to 3500 m (4921-11,483 ft)
High-altitude illness common with abrupt ascent to above 2500 m (8202 ft)
Decreased exercise performance and increased ventilation
Minor impairment in SpO_2, usually at least 90 percent; PaO_2 significantly diminished 55 to 75 mmHg
Very high altitude: 3500 to 5500 m (11,483-18,045 ft)
Most common range for severe high-altitude illness
Abrupt ascent may be dangerous; requires a period of acclimatization
SpO_2 75 to 85 percent; PaO_2 40 to 60 mmHg
Extreme hypoxia may occur during sleep, exercise and high-altitude illness
Extreme altitude: 5500 to 8850 m (18,045-29,035 ft)
Progressive deterioration of physiologic function eventually outstrips acclimatization
Above the highest permanent human habitation
Abrupt ascent almost always precipitates severe high-altitude illness
A period of acclimatization necessary to ascend to extreme altitude
Severe hypoxia and hypocapnia; SpO_2 58 to 75 percent, PaO_2 28 to 40 mmHg

Pathophysiology

- There is reduced partial pressure of oxygen at altitude > 2500/mtr primarily due to reduced atmospheric pressure with rising altitude
- Principal response to hypoxia is hypoxic pulmonary vasoconstriction (HPV)
- HIF is key transcription factor – α & β subunits
- When normoxia : HIF is hydroxylated by prolyl hydroxylase,
- Hypoxic condition: hydroxylation is inhibited and HIF-1 α becomes stable.
- Hypoxia can cause inflammation by stimulating NF-κB gene transcription and the production of pro-inflammatory cytokines
- IL-1β, NF-κB and TNF-α also stabilise HIF-1 α
- Hypoxia also increases the production of ROS and thus oxidative stress

Inflammation in Pulmonary Hypertension and Edema Induced by Hypobaric Hypoxia Exposure. Int J Mol Sci. 2022 Oct 21. doi: 10.3390/ijms232012656

- Hypoxia induced endothelial damage, oxidative free radical injury , dysregulated microcirculatory flow , increased vessel permeability , hypoxic stress during sleep all in combination lead to symptoms of high altitude headache , acute mountain sickness , high altitude pulmonary hypertension & high altitude cerebral edema and pulmonary edema


HAPE
HACE
Pulmonary Hypertension
Cerebral Hypertension
EDEMA
AMS
time
Capillaries
VEGF
HIF
NO
EPO
time
RBC
Chronic Hypoxia
Chronic Hypoxia
Acute Hypoxia

Acute mountain sickness

- Develops in hours after ascend, and progress with increased duration of exposure + overnight stay
- Headache is commonest symptom, nausea, appetite loss, fatigue , dizziness and disturbed sleep
- Diagnosed with the lake louise symptom score >3 (headache + one other symptom)

Lake Louise Acute Mountain Sickness Scoring System **(please circle appropriate)**

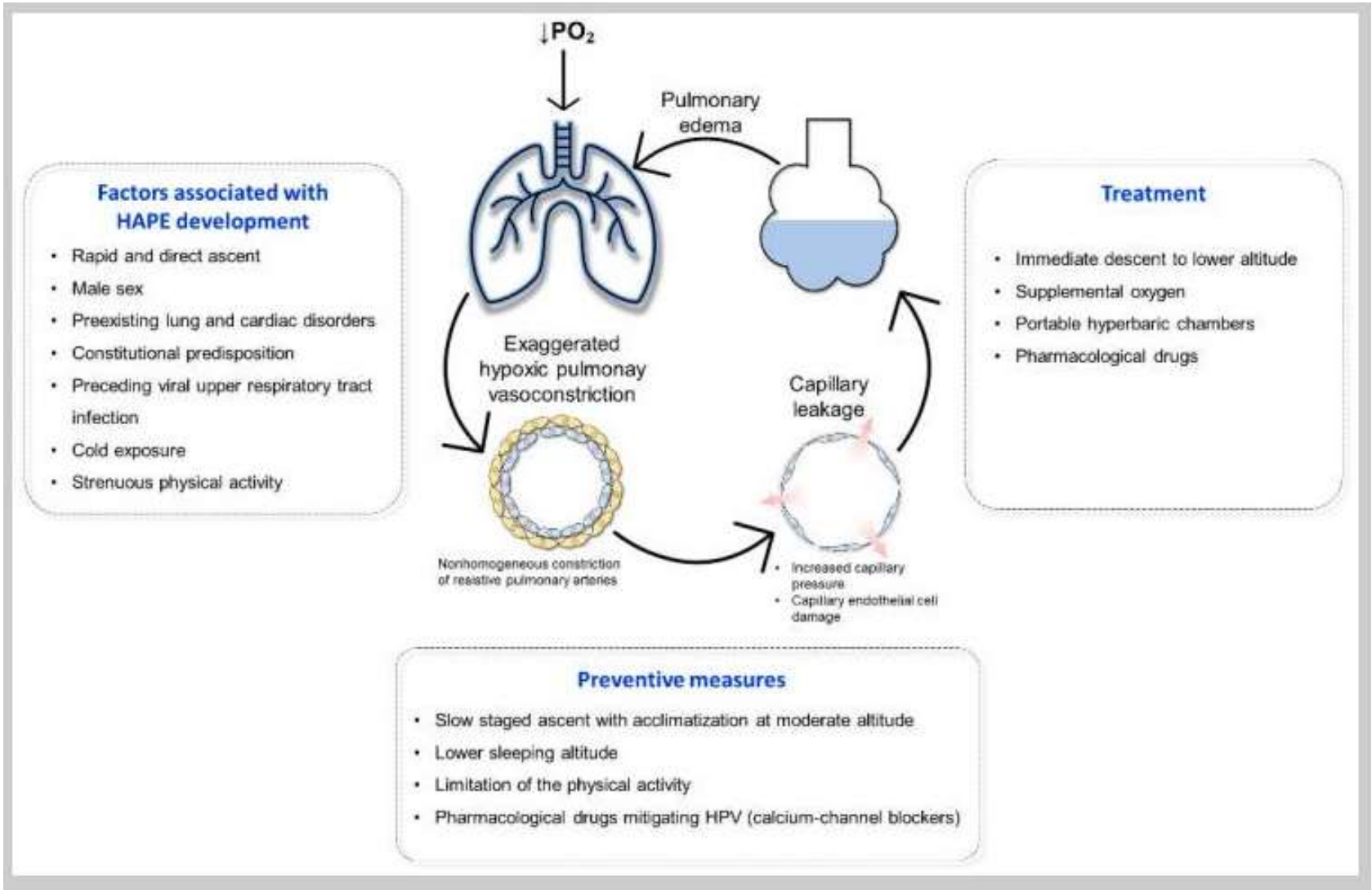
1) Headache	0	No headache
	1	Mild headache
	2	Moderate headache
	3	Severe headache, incapacitating
2) Gastrointestinal symptoms	0	No gastrointestinal symptoms
	1	Poor appetite or nausea
	2	Moderate nausea or vomiting
	3	Severe nausea & vomiting, incapacitating
3) Fatigue and/or weakness	0	Not tired or weak
	I	Mild fatigue/weakness
	2	Moderate fatigue/weakness
	3	Severe fatigue/weakness, incapacitating
4) Dizziness/lightheadedness	0	Not dizzy
	1	Mild dizziness
	2	Moderate dizziness
	3	Severe dizziness, incapacitatin
5) Difficulty sleeping	0	Slept as well as usual
	1	Did not sleep as well as usual
	2	Woke many times, poor night's sleep
	3	Could not sleep at all

- Prevention & Treatment – generally self limiting
- Adequate hydration is important
- Slow staged ascent with rest days
- If only headache then Ibuprofen may be helpful
- Acetazolamide , dexamethasone or combination if symptoms severe
- If AMS develops then one should not ascend ,
- If symptoms not improving then descend is most important

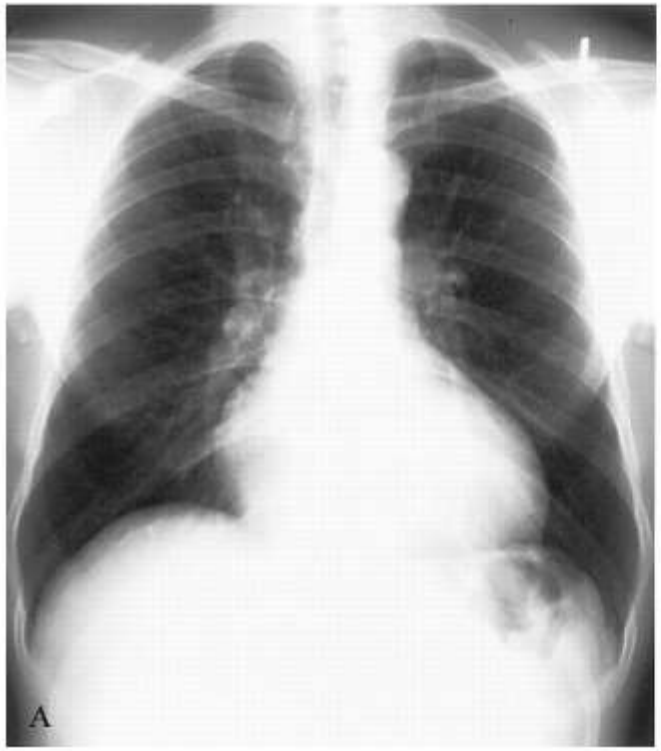
High altitude pulmonary edema

- Non cardiogenic pulmonary edema, elevated PA pressure
- Uneven hypoxic vasoconstriction, over perfusion in certain areas cause capillary leak due to high pressures and shear stress. There is high permeability leak of fluid and RBCs from capillary to alveoli.
- Increased inflammatory premediators may be contributory
- ↑endothelin & ↓ endothelium nitric oxide
- Viral infections may trigger responses & cause HAPE at lower altitude
- Acute ascent or Re-entry from high → low → high altitude

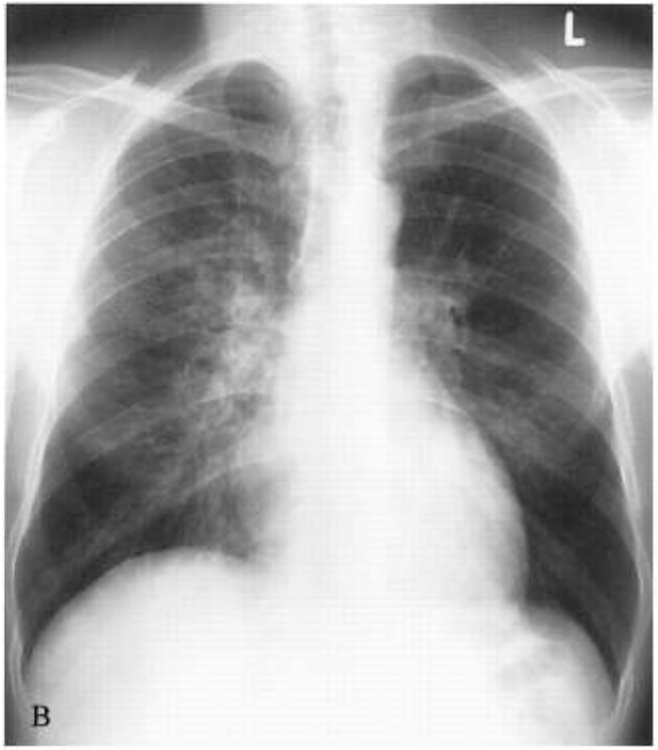
- Manifests in 2-4 days of ascent , decreased exercise performance, dyspnea hypoxemia, fatigue , dry cough, AMS symptoms, pink frothy sputum (severe cases). Can occur without symptoms of cerebral edema
- Fever, tachycardia , tachypnea, low SPO2 (50-75%) , crackles , cyanosis , rapid reversal on O2 supplementation / descent
- CXR – unilateral or bilateral opacities (commonly starts from right midzone)
- Prevention : staged and slow ascent
- Treatment : early descent , oxygen supplementation, hyperbaric chambers , pulmonary vasodilators such as nifedipine , tadalafil


↓PO2
Pulmonary edema
Exaggerated hypoxic pulmonay vasoconstriction
Capillary leakage
Nonhomogeneous constriction of resistive pulmonary arteries
Increased capillary pressure
Capillary endothelial cell damage
Factors associated with HAPE development
Rapid and direct ascent
Male sex
Preexisting lung and cardiac disorders
Constitutional predisposition
Preceding viral upper respiratory tract infection
Cold exposure
Strenuous physical activity
Treatment
Immediate descent to lower altitude
Supplemental oxygen
Portable hyperbaric chambers
Pharmacological drugs
Preventive measures
Slow staged ascent with acclimatization at moderate altitude
Lower sleeping altitude
Limitation of the physical activity
Pharmacological drugs mitigating HPV (calcium-channel blockers)

LOW ALTITUDE



HIGH ALTITUDE



https://doi.org/10.1161/01.CIR.103.16.2078

Chronic mountain sickness

- Found in people staying at high altitude and also in lowlanders who shift to higher altitude and stay there
- Found less in tibetan high landers
- Chronic hypobaric hypoxia & decreased HVR increases PVR due to vasoconstriction and increased EPO secretion causes raised Hb
- Chronic lung diseases like COPD, bronchiectasis and cystic fibrosis can cause secondary CMS
- Headache, dizziness cyanosis of lips , mouth & throat, clubbing, plethora
- High hematocrit (60-70%) (rule out other causes of polycythemia)

- CXR - RA/RV enlargement, cardiomegaly and prominent PA
- ECG – P pulmonale and Right axis deviation
- Treatment is to reduce hypoxic stimulus which can be done by relocating to a lower altitude
- Phlebotomy can reduce symptoms / isovolemic hemodilution
- Acetazolamide (250 mg/day) decreases hematocrit, serum Epo, and serum transferrin; and it increased PaO_2 and serum ferritin.
- Acetazolamide increases nocturnal SpO_2 and reduced the number of apnea–hypopnea episodes and PVR

Acetazolamide: a treatment for chronic mountain sickness. Am J Respir Crit Care Med. 2005 Dec 1;172(11):1427-33. doi: 10.1164/rccm.200505-807OC. Epub 2005 Aug 26.

Signs or symptoms	*Score*
Breathlessness and/or palpitations	0 No breathlessness/palpitations
	1 Mild breathlessness/palpitations
	2 Moderate breathlessness/palpitations
	3 Severe breathlessness/palpitations
Sleep disturbance	0 Slept as well as usual
	1 Did not sleep as well as usual
	2 Woke up many times, poor night's sleep
	3 Could not sleep at all
Cyanosis	0 No cyanosis
	1 Mild cyanosis
	2 Moderate cyanosis
	3 Severe cyanosis
Dilatation of veins	0 No dilatation of veins
	1 Mild dilatation of veins
	2 Moderate dilatation of veins
	3 Severe dilatation of veins
Paresthesia	0 No paresthesia
	1 Mild paresthesia
	2 Moderate paresthesia
	3 Severe paresthesia
Headache	0 No headache
	1 Mild headache symptoms
	2 Moderate headache
	3 Severe headache, incapacitating
Tinnitus	0 No tinnitus
	1 Mild tinnitus
	2 Moderate tinnitus
	3 Severe tinnitus
Hemoglobin concentration	Men:
	<21 g/dL; score = 0
	≥21 g/dL; score = 3
	Women:
	<19 g/dL; score = 0
	≥19 g/dL; score = 3

Total score	*CMS*
0–5	Absent
6–10	Mild
11–14	Moderate
>15	Severe

THE QINGHAI SCORE FOR CMS

High altitude pulmonary hypertension

- Pulmonary hypertension at high altitude without excessive erythrocytosis
- May be a *prequel* to chronic mountain sickness
- Can occur in lowlanders after weeks and months of living in high altitude
- Raised PA pressures (mPAP>30, sPAP>50) / RVH / right heart failure
- Symptoms are dry cough, dyspnea, cyanosis, peripheral edema
- CXR and ECG findings are similar to Chronic mountain sickness
- Moving to a lower altitude is treatment of choice
- Definite anti PH therapy is not yet recommended

Brisket disease in a cow due to
heart failure secondary to
pulmonary hypertension

HACE

- Rapid ascent to high altitude (generally > 3000mtr) , signs of encephalopathy , ataxia along with symptoms of acute mountain sickness
- Signs and symptoms may be confused because of similarity to symptoms due to cerebral hypoxia which may be due to pulmonary edema
- Apathy , irritability, confusion, somnolescence, global neurological symptoms , dizziness , severe headache , vomiting, coma (severe cases)
- *Sudden onset signs, high fever , focal deficits , neck stiffness – inconsistent*

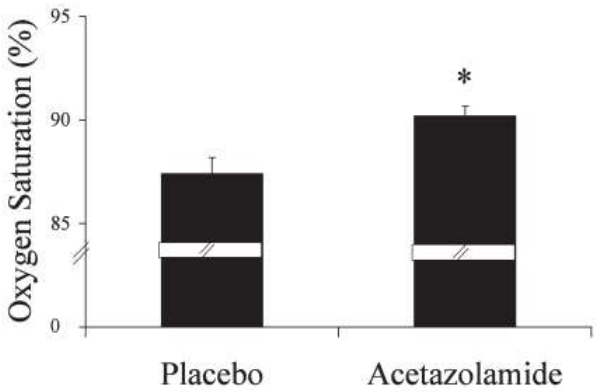
- *Heel to toe walking is a good immediate test for ataxia*
- Positive romberg sign , papilledema
- Alteration of pupillary reflex , stupor – fatal signs
- Imaging : CT – cerebral edema , MRI – reversible increased T2 weighted signal in the splenium and genu of the corpus callosum + micro Hhg
- Microhemorhages stay for months – can help diagnose retrospectively
- Rapid descent , oxygen , portable hyperbaric oxygen chamber
- Dexamethasone is the treatment of choice – 4 to 8mg im 6 to 8 hrly

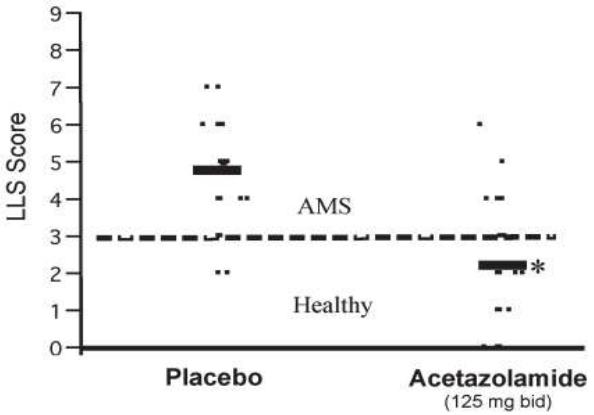
Drugs

- Acetazolamide : renal carbonic anhydrase inhibition which causes met acidosis and bicarbonate diuresis. It causes hyperventilation, increases alveolar O2 & increased O2 delivery to the tissue.
- Dexamethasone : Stimulating surfactant secretion, preventing pulmonary transvascular protein exudation and enhancing the integrity of airway epithelia barrier. It has anti-inflammatory effects and prevent dysfunctional tissue edema that occurs from a lack of oxygen
- Sildenafil/tadalafil – pulmonary vasoldilators by inhibiting PDE 5 and consequent increase in nitric oxide levels
- Nifedipine – CCB

Prophylactic low-dose acetazolamide reduces the incidence and severity of acute mountain sickness

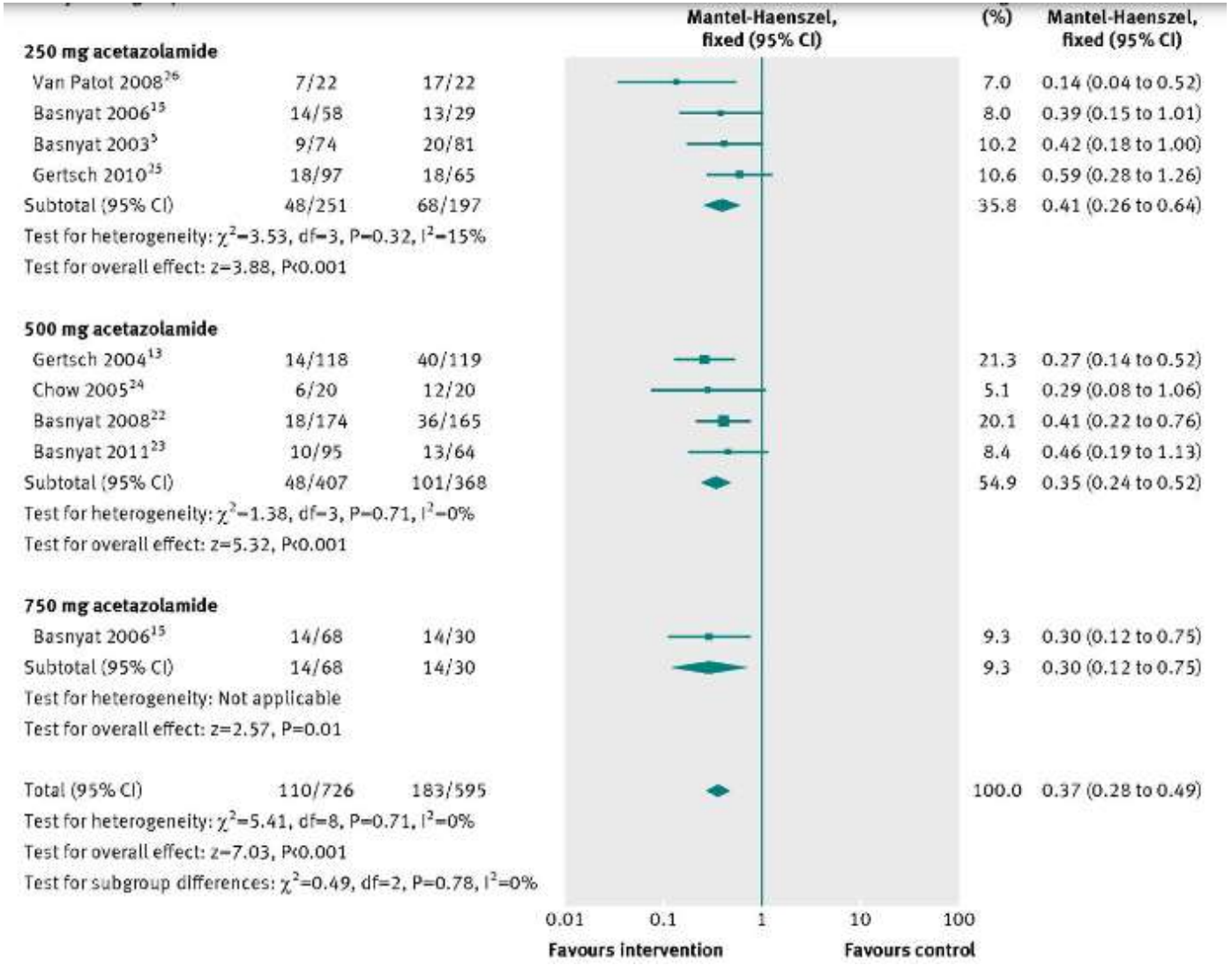
- Acetazolamide vs placebo to prevent AMS in rapid ascent from 1600mtr to 4300mtr (within 2 hrs)
- Double blind RCT (22 in each arm) , 125 mg BD dose for 3 days prior to ascent and one day at the altitude
- Acetazolamide reduced the incidence of AMS compared to placebo-treated subjects (14% vs. 45%, respectively, p=0.02), NNT - > 3
- Less severe AMS reported in acetazolamide treated patients





Prophylactic low-dose acetazolamide reduces the incidence and severity of acute mountain sickness. High Alt Med Biol. 2008 Winter;9(4):289-93. doi: 10.1089/ham.2008.1029. PMID: 19115912.

Identifying the lowest effective dose of acetazolamide for the prophylaxis of acute mountain sickness: systematic review and meta-analysis



BMJ 2012;345:e6779 doi: https://doi.org/10.1136/bmj.e6779

Annals of Internal Medicine

Acetazolamide in the Treatment of Acute Mountain Sickness: Clinical Efficacy and Effect on Gas Exchange

- Small trial , high-altitude research station (4200 m) on Mt. McKinley, Alaska
- Double blind RCT , 12 climbers with AMS , acetazolamide 250 mg vs placebo at 0 hour and 8 hours
- After 24 hrs: Acetazolamide group, 5 out of 6 recovered vs 0 out of 6 (p=0.015)
- PAO2-PaO2 difference- decreased in acetazolamide group vs increased in placebo group (-0.8 +/- 1.2 mm Hg vs +3.3 +/- 2.3 mm Hg, P = 0.024)
- Acetazolamide improved PaO2 over 24 hours (+2.9 +/- 0.8 mm Hg) when compared with placebo (-1.3 +/- 2.8 mm Hg) (P = 0.045)

https://doi.org/10.7326/0003-4819-116-6-461

International Journal of Cardiology

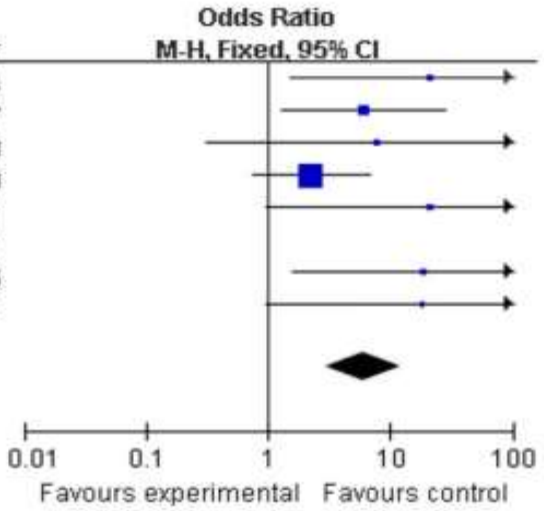
Dexamethasone for the prevention of acute mountain sickness: Systematic review and meta-analysis

- 8 trials with 6 field trials (n-116 dexa vs n-100 placebo) 8,12,16mg/day
- Dexamethasone could reduce the incidence of AMS with an odds ratio of 6.03 (95% CI, 2.23 to 21.00) for dexamethasone compared with placebo; the p value for overall effect was less than 0.00001

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Johnson	7	8	2	8	3.5%	21.00 [1.50, 293.25]	1984
ALLAN J	12	17	4	14	18.3%	6.00 [1.26, 28.55]	1987
Hackett	2	7	0	8	4.6%	7.73 [0.31, 193.44]	1988
Montgomery	12	38	6	35	60.6%	2.23 [0.73, 6.79]	1989
ELLSWORTH	10	10	5	10	3.5%	21.00 [0.97, 453.91]	1991
Hussain	0	6	0	6		Not estimable	2001
Maggiorini	7	10	1	9	4.5%	18.67 [1.56, 222.93]	2006
Subudhi AW	20	20	14	20	4.9%	18.38 [0.96, 352.57]	2011
Total (95% CI)		**116**		**110**	**100.0%**	**6.03 [2.99, 12.18]**	
Total events	70		32				

Heterogeneity: $Chi^2 = 5.92$, $df = 6$ ($P = 0.43$); $I^2 = 0\%$

Test for overall effect: $Z = 5.01$ ($P < 0.00001$)



http://dx.doi.org/10.1016/j.ijcard.2014.03.019

Budesonide Versus Acetazolamide for Prevention of Acute Mountain Sickness

- Double-blind, RCT inhaled budesonide vs oral acetazolamide vs placebo
- Drugs started on the morning of ascent
- 1240 m (4100 ft) to 3810 m (12,570 ft) over 4 hours
- 33 (32%) budesonide,35 (34%) acetazolamide, & 35 (34%) placebo
- AMS : Acetazolamide compared with budesonide (odds ratio [OR] 3.5, 95% [CI] 1.3-10.1) and placebo (OR 0.5, 95% CI 0.2-1.2).

	Budesonide 180 bd	Acetazolamide 250/d	Placebo
Incidence of AMS	(n = 24, 73%)	(n = 15, 43%)	(n = 22, 63%)
Severe AMS (LLS >5)	(n = 18, 55%)	(n = 11, 31%)	(n = 19, 54%)

Ajm2018 https://doi.org/10.1016/j.amjmed.2017.05.034

Altitude Sickness Prevention with Ibuprofen Relative to Acetazolamide

- Ibuprofen 600 mg TID 4 hours before ascent or acetazolamide 125 mg, BD started the night before ascent to 3810m in California from 1240mtr
- Predetermined 26% noninferiority margin
- N=45 (49%) ibuprofen and 47 (51%) acetazolamide
- Incidence of AMS : 62.2% vs 51.1%; 95% [CI], -11.1 to 33.5
- No difference in LLQ score / sleep score
- Acetazolamide group had higher peripheral capillary oxygen saturation than the ibuprofen group (88.5% vs 85.6%; P = .001)
- Ibuprofen should not be preferred over acetazolamide

Burns Petal., Altitude Sickness Prevention with Ibuprofen Relative to Acetazolamide. Am J Med. 2019 Feb;132

Headache Evaluation at Altitude Trial (HEAT)

- 343 trekkers recruited at altitudes of 4280 m and 4358 m and assigned to receive ibuprofen 600 mg, acetazolamide 85 mg, or placebo TID before continued ascent to 4928 m
- Double blind RCT , 265 out of 343 completed the trial
- HAH incidence : acetazolamide (27.1%) or ibuprofen (27.5%; P = .95) vs placebo (45.3%; P = .01)
- AMS incidence: acetazolamide (18.8%) or ibuprofen (13.7%; P = .34) vs placebo (28.6%; P = .03)
- Moderate to severe headache : acetazolamide (3.8%) or ibuprofen (4.7%; P = .79) vs placebo (13.5%; P = .03)

https://doi.org/10.1016/j.wem.2010.06.009

Annals of Internal Medicine®

Both Tadalafil and Dexamethasone May Reduce the Incidence of High-Altitude Pulmonary Edema: A Randomized Trial

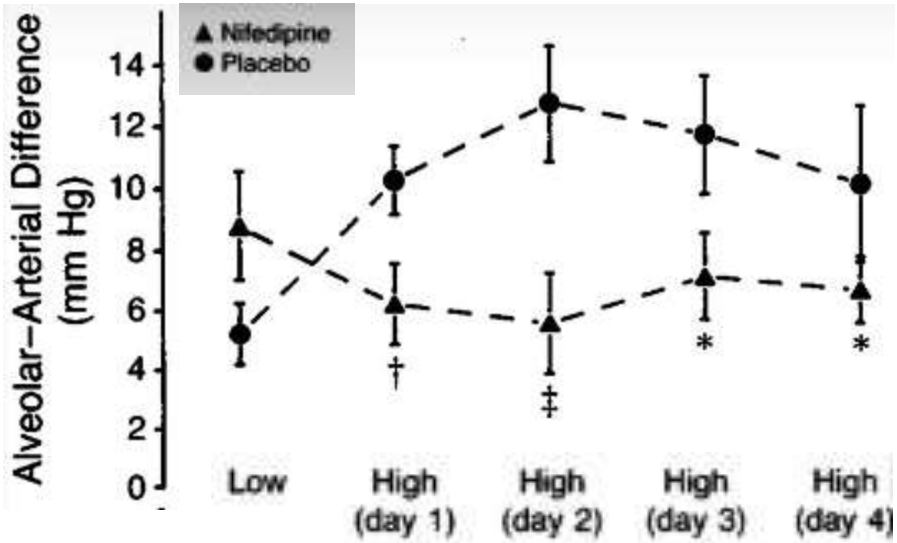
- 29 adults with previous HAPE.
- Ascent from 490 m within 24 hours and stay for 2 nights at 4559 m.
- Prophylactic tadalafil (10 mg), dexamethasone (8 mg), or placebo twice daily during ascent and stay at 4559 mtr
- AMS in 2 patients on tadalafil – opted out of study
- HAPE in 7 out of 9 on placebo vs 1 out of 8 participants on tadalafil vs none in 10 on dexamethasone ($P = 0.007$ for tadalafil vs. placebo; $P < 0.001$ for dexamethasone vs. placebo)
- Rise in SPAP : dexa 16mm vs tada 13mm vs 28mmHG placebo

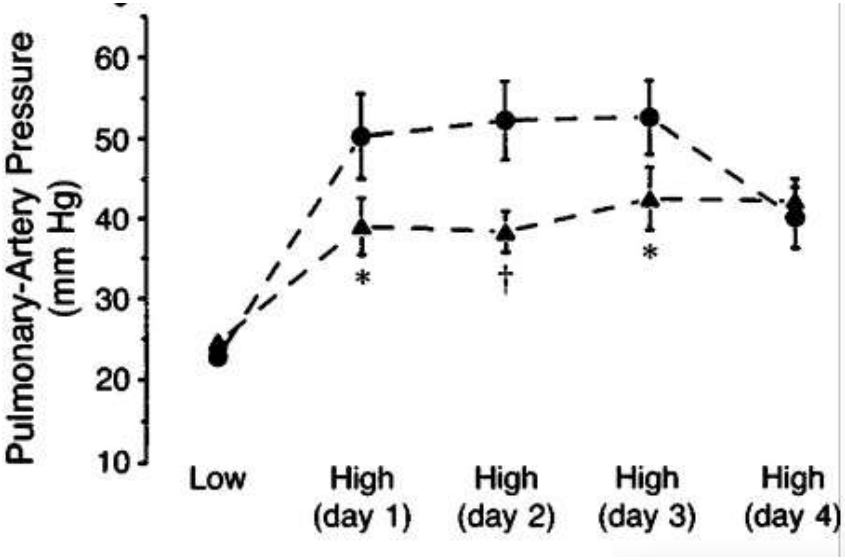
  ($P = 0.005$ for tadalafil vs. placebo; $P = 0.012$ for dexamethasone vs. placebo)

DOI : https://doi.org/10.7326/0003-4819-145-7-200610030-00007

Prevention of high-altitude pulmonary edema by nifedipine

- N= 21 , 20 men & 1 woman with previous history of HAPE
- Nifedipine SR 20mg vs placebo TID
- 1130 m to 4559 m within 22 hours, staying overnight at 3611 m
- Clinical examination + CXR + ECHO + ABG + end expiratory gas analysis
- Study terminated early in placebo group as early HAPE
- 7 of 11 in placebo vs 1 of 10 in nifedipine had radiographic evidence of pulmonary edema ($P = 0.01$)
- Mean AMS score : 2.0 ± 0.7 in the nifedipine group and 3.9 ± 1.9 in the placebo group ($P<0.01$)





Characteristic	490 m	3611 m	4559 m			
			Day 1	Day 2	Day 3	Day 4
No. of subjects						
Nifedipine	10	10	10	10	10	10
Placebo	11	11	11	10	9	5
Mean blood pressure (mm Hg)†						
Nifedipine	94±3	96±3	90±2	94±3	94±3	98±3
Placebo	95±3	97±3	95±3	97±3	101±4	95±4
PaO_2 (mm Hg)						
Nifedipine	91.1±2.8	—	41.7±1.5	44.0±1.9	42.5±2.0	43.0±1.4
Placebo	96.5±1.6	—	37.1±1.7‡	36.9±2.4‡	40.1±3.1§	42.6±3.8
$PaCO_2$ (mm Hg)						
Nifedipine	39.2±1.1	—	31.0±1.3	29.7±0.7	28.8±0.9	29.0±1.0
Placebo	41.6±0.9	—	30.5±0.7	29.2±1.5	27.6±1.3	27.6±1.7
SaO_2 (%)						
Nifedipine	95.2±0.3	83.7±1.8	68.4±3.3	72.7±3.5	73.0±2.6	74.0±2.6
Placebo	95.6±0.3	82.2±1.4	61.4±5.1	65.6±5.2	66.2±6.5	69.8±5.3
AT/RVET						
Nifedipine	0.32±0.03	0.30±0.01	0.28±0.01	0.26±0.01	0.26±0.01	0.28±0.02
Placebo	0.31±0.02	0.24±0.01	0.24±0.02	0.25±0.02	0.24±0.02	0.24±0.02

*Plus–minus values are means ±SE.

†The mean blood pressure was defined as one third of the systolic blood pressure plus two thirds of the diastolic blood pressure.

‡$P<0.01$ for the comparison of changes from base line between the study groups.

§$P<0.05$ for the comparison of changes from base line between the study groups.

NIFEDIPINE FOR HIGH ALTITUDE PULMONARY OEDEMA

- 6 patients from another study who developed HAPE on rapid ascent to 4559 mtr were administered nifedipine 10mg stat f/b 20mg SR Q6hrly
- Clinical Exn + CXR + echocardiography + Alveolar arterial O2 gradient

—	Controls	HAPO				
		Pre-treatment	Nifedipine treatment			p*
			1 h	14·6 h	34·7 h	
AMS score	3·4 (1·7)[a]	9 2 (1·6)	5·7 (1·8)	2·5 (0·8)	3·0 (1·5)	<0·001
PaO_2, torr	41·3 (4·5)[b]	30·8 (5·4)	35·3 (6 8)	32·8 (5·2)	32·8 (4·3)	<0·10
SaO_2%	80·7 (5·3)[c]	65·5 (11·0)	73·4 (11·3)	68 9 (8·1)	68·9 (7·5)	<0·10
$AaDO_2$, torr	1·9 (3·7)[a]	13·0 (2·9)	9·0 (2·8)	6 3 (2 5)	6 6 (3·6)	<0 001
$PaCO_2$, torr	29·0 (3·0)[d]	26 6 (3 0)	25·9 (4·7)	28·9 (3·8)	30·1 (2 0)	<0·005
Radiographic score	0·5[a]	7·7 (4·3)		4 8 (5·2)	4 0 (3·6)	<0·05

—	Controls	HAPO				
		Pretreatment	Nifedipine treatment			p*
			1 h	14·6 h	34·7 h	
PAP, mm Hg	63·5 (14·9)[a]	133·7 (19·8)	73·7 (13·8)	58·2 (5·0)	65·5 (11·7)	<0·001
AT/RVET	0·24 (0·06)[c]	0·21 (0·04)	0·32 (0·09)	0·30 (0·05)	0 29 (0·04)	<0·01
RA cm	4·8 (0·5)[c]	4·7 (0·3)	4·1 (0·4)	4·3 (0·3)	4·4 (0·5)	<0·05
RV cm	4·5 (0·4)[c]	4·6 (0·3)	4·2 (0·4)	4·2 (0·3)	4·3 (0·4)	<0·05
HR/min	77 (17)[b]	100 (9)	103 (12)	101 (9)	94 (6)	>0·05
BP mm Hg	135/81[c]	131/78	119/73	123/72	128/70	>0·05

Wilderness Medical Society Clinical Practice Guidelines for the Prevention, Diagnosis, and Treatment of Acute Altitude Illness: 2024 Update

- Unacclimatized individuals are at risk of high altitude illness when ascending to altitudes above 2500 m
- ‘Staged ascent’ with 2 night stay at 3000 mtr helps in acclimatization
- *Hypoxic tents :* do not facilitate acclimatization
- On ascending > 3000mtr , do not ascend more than 500mtr/day and have a rest day every 3-4 days
- Maintenance of adequate hydration is important

	Risk Category		
Variable	**Low**	**Moderate**	**High**
History of acute altitude illness	None or mild AMS ☐	Moderate-Severe AMS ☐	HAPE or HACE ☐
Sleeping elevation on Day 1 (meters)	< 2800 ☐	2800-3500 ☐	> 3500 ☐
Ascent rate (meters/day)	≤ 500 m/d above 3000 m with extra days for acclimatization every 1000 m ☐	≥ 500 m/d above 3000 m with extra days for acclimatization every 1000 m ☐	≥ 500 m/d above 3000 m without extra days for acclimatization every 1000 m ☐

Medication	Indication	Route	Dosage
Acetazolamide	AMS, HACE prevention	Oral	125 mg every 12 h[a,b] Pediatrics: 1.25 mg·kg^{-1} every 12 h (maximum 125 mg per dose)
	AMS treatment[c]	Oral	250 mg every 12 h Pediatrics: 2.5 mg·kg^{-1} every 12 h (maximum: 250 mg per dose)
Dexamethasone	AMS, HACE prevention	Oral	2 mg every 6 h or 4 mg every 12 h[a] Pediatrics: should not be used for prophylaxis
	AMS, HACE treatment	Oral, IV, IM	AMS: 4 mg every 6 h HACE: 8 mg once then 4 mg every 6 h Pediatrics: 0.15 mg·kg^{-1}·dose^{-1} every 6 h (maximum: 4 mg per dose)
Ibuprofen	HAH treatment	Oral	600 mg every 8 h
Nifedipine	HAPE prevention	Oral	30 mg ER version every 12 h or 20 mg ER version every 8 h[d]
	HAPE treatment	Oral	30 mg ER version every 12 h or 20 mg ER version every 8 h
Tadalafil	HAPE prevention	Oral	10 mg every 12 h[d]
Sildenafil	HAPE prevention	Oral	50 mg every 8 h[d]

Treatment of AMS and HACE

- Descent remains the single best treatment for AMS and HACE
- Individuals should descend until symptoms resolve
- Symptoms typically resolve following descent of 300 to 1000 m
- Oxygen supplementation to keep SPO2 – 90% while awaiting descent
- Portable hyperbaric chambers
- AMS : Acetazolamide 250mg twice daily dose for treatment
- HACE : Dexamethasone 8mg stat → 6mg QID
- PCM / Ibuprofen – headache treatment
- *Use of CPAP – no recommendation*

Category	Mild AMS	Moderate-severe AMS	High altitude cerebral edema
Symptoms	Headache plus 1 or more other symptoms (nausea/vomiting, fatigue, lassitude, dizziness) All symptoms of mild intensity	Headache plus 1 or more other symptoms (nausea/vomiting, fatigue, lassitude, dizziness) All symptoms of moderate-severe intensity	Worsening of symptoms seen in moderate to severe AMS
Signs	None	None	Ataxia, severe lassitude, altered mental status, encephalopathy
Lake Louise AMS Score[a]	3–5	6–12	Not applicable

- Acetazolamide and dexamethasone are generally not necessary for treatment of mild AMS but may be useful in moderate-severe cases
- Prefer dexamethasone to treat mod / severe cases along with descent
- If AMS resolves re-ascent may be tried but with acetazolamide prophylaxis
- In HACE – re-ascent not recommended

Prevention of HAPE

- Same as AMS and HACE
- Nifedipine prophylaxis only for patients with past history of HAPE
- It should be started the day prior to ascent and continued either until descent is initiated or the individual has spent 4 d at the highest elevation.
- For 7 days if fast ascent to higher altitude
- Acetazolamide not helpful in such patients

Treatment of HAPE

- Descend atleast 1000mtr or until the symptoms resolve
- Oxygen supplementation to keep SPO2 – 90% while awaiting descent
- Portable hyperbaric chambers
- Nifedipine SR to be used only when descend is not feasible
- Sildenafil/ tadalafil – only when descend is not feasible
- Beta agonist/dexamethasone – no recommendation
- CPAP along with oxygen may be helpful (weak recommendation)
- Diuretics/acetazolamide shouldn’t be used
- Re-ascent may be allowed if symptoms resolve & SPO2 maintained on RA

HAPE + HACE

- Difficult to diagnose presence of HACE in HAPE patients with profound hypoxia as symptoms often overlap in field settings
- Descent
- Oxygen +/- hyperbaric chamber
- Dexamethasone
- Avoid nifedipine to avoid systemic hypotension to further reduce cerebral perfusion
- Tadalafil and sildenafil can be tried

Thank you