Update on High Altitude Medicine

8th World Congress on Mountain and Wilderness Medicine

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Update on High Altitude Medicine

DISCLOSURE STATEMENT

I receive royalty payments for a book on high altitude medicine and physiology for which I am a co-author.

I have no other conflicts of interest to disclose.

Let's See What You Know About The Recent Literature

Statement	True or False
Acetazolamide has been shown to prevent high altitude pulmonary edema in known susceptible individuals	
Exposure to high altitude causes a hypercoagulable state	
Physical activity during ascent does not increase the risk of acute mountain sickness	
Screening lung ultrasound is useful for identifying people at risk for high altitude pulmonary edema	
Patients with moderate COPD or NYHA Class 2-3 pulmonary hypertension can safely travel to 2500 m	

NYHA: New York Heart Association

The Goal For This Session

Review of Recent Literature On High Altitude Medicine

Acetazolamide for Prevention of HAPE

Coagulopathy and exposure to high attitude

Physical activity during ascent

Screening lung ultrasound

Travel to high altitude with known lung disease

A Few Pieces of Recent Literature to Highlight

The WMS Clinical Practice Guidelines Have Been Updated

Disease	Medication	Dose	Recommendation	Evidence
AMS/HACE Prevention	Acetazolamide	125 mg q 12 hr	Strong	High quality
	Dexamethasone	2 mg q 6 hr	Strong	High quality
HAPE Prevention *	Nifedipine SR	30 mg q 12 hr	Strong	Moderate quality
	Tadalafil	10 mg q 12 hr	Strong	Low quality
	Salmeterol	Do not use	Weak	Moderate quality

Overall, few significant changes from the 2019 version

* Reserved for those with a history of HAPE

Luks et al. Wilderness Environ Med 2024. 35 (1 Suppl): 2S

One Significant Update: A New Way To Assess The Risk Of A Planned Ascent

	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 ☐

Luks et al. Wilderness Environ Med 2024. 35 (1 Suppl): 2S

An Important Series Worth Highlighting

Scientific Article—Women at Altitude

High-Altitude Pulmonary Edema in Women: A Scoping Review—UIAA Medical Commission Recommendations

Jacqueline Pichler Hefti [1], Dominique Jean[2,3], Alison J. Rosier [3], Mia Derstine [4], David Hillebrandt[3,5], Lenka Horakova[3,6], Linda E. Keyes[4], Kastė Mateikaitė-Pipirienė [3,7], Peter Paal [3,8], Marija Andjelkovic [3,9], Beth A. Beidlemann[10], and Susi Kriemler [11]

Scientific Article—Women at Altitude

Acute Mountain Sickness and High Altitude Cerebral Edema in Women: A Scoping Review—UIAA Medical Commission Recommendations

Mia Derstine [1], Dominique Jean[2,3], Beth A. Beidleman[4], Jacqueline Pichler Hefti[5], David Hillebrandt[2,6], Lenka Horakova[2,7], Susi Kriemler [8], Kastė Mateikaitė-Pipirienė [2,9], Peter Paal [2,10], Alison J. Rosier [2], Marija Andjelkovic [2,11], and Linda E. Keyes[1]

Scientific Article—Women at Altitude

Frostbite and Mortality in Mountaineering Women: A Scoping Review—UIAA Medical Commission Recommendations

Susi Kriemler [1,*], Kastė Mateikaitė-Pipirienė [2,3,*], Alison Rosier [2], Linda E. Keyes[4], Peter Paal [2,5], Marija Andjelkovic [2,6], Beth A. Beidleman[7], Mia Derstine [4], Jacqueline Pichler Hefti[8], David Hillebrandt[2,9], Lenka Horakova[2,10], and Dominique Jean[2,11]

Special Series - Women at Altitude

Menopause and High Altitude: A Scoping Review—UIAA Medical Commission Recommendations

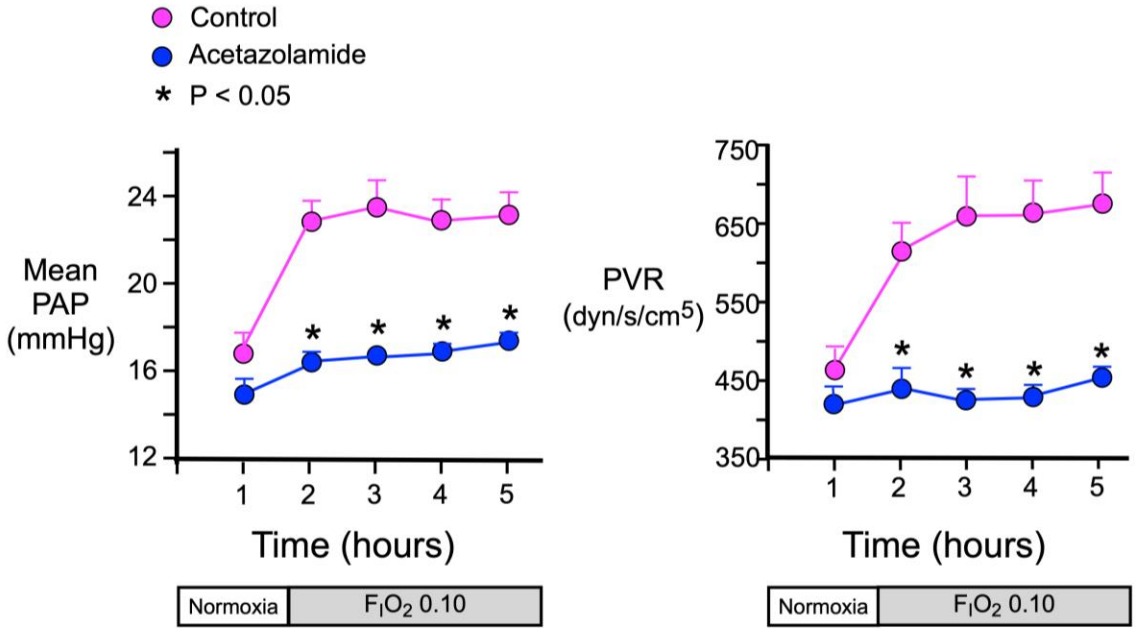
Kastė Mateikaitė-Pipirienė [1,2], Dominique Jean[1,3], Peter Paal [1,4], Lenka Horakova[1,5], Susi Kriemler [6], Alison J. Rosier [1], Marija Andjelkovic [1,7], Beth A. Beidleman[8], Mia Derstine [9], Jacqueline Pichler Hefti[10], David Hillebrandt[1,11], and Linda E. Keyes[9]

Commissioned by the UIAA Medical Commission
Published in High Altitude Medicine and Biology (2023-2024)

Issue 1

Acetazolamide and HAPE Prevention

One Of Several Studies That Got Interest In This Question Going



Höhne et al. J Appl Physiol 2004. 97: 515

PAP: Pulmonary artery pressure
PVR: Pulmonary vascular resistance

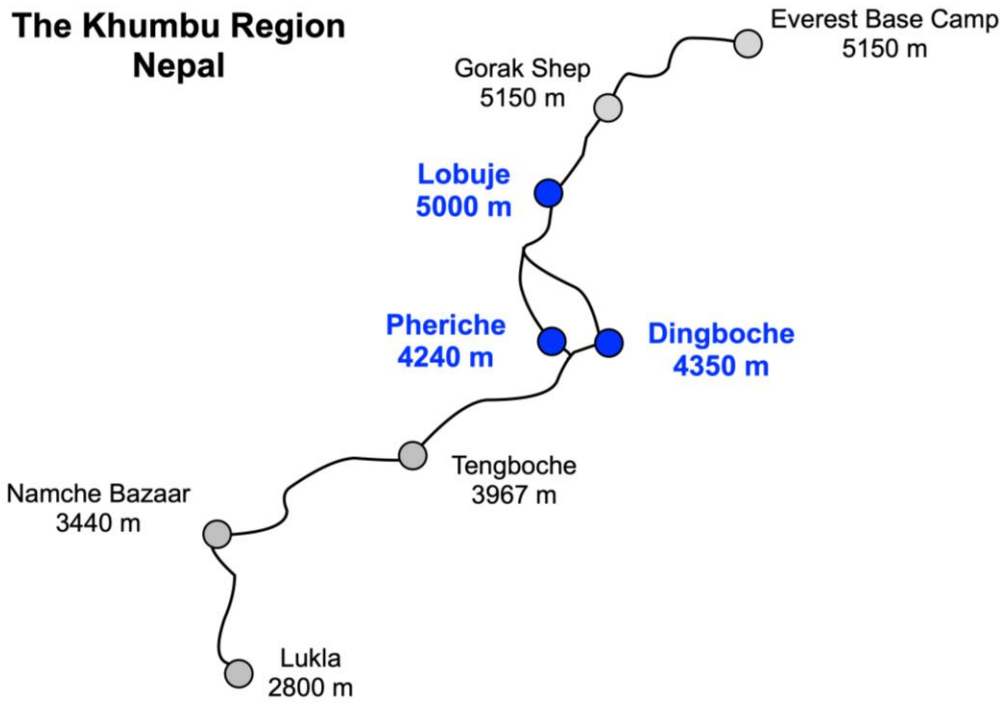
The First Attempt To Study In Humans

Randomized, placebo-controlled trial

Recruited 365 healthy trekkers in Pheriche and Dingboche

Randomized to acetazolamide (250 mg q 12 hr) or placebo

Assessed in Lobuje 36-96 hrs after starting study drug



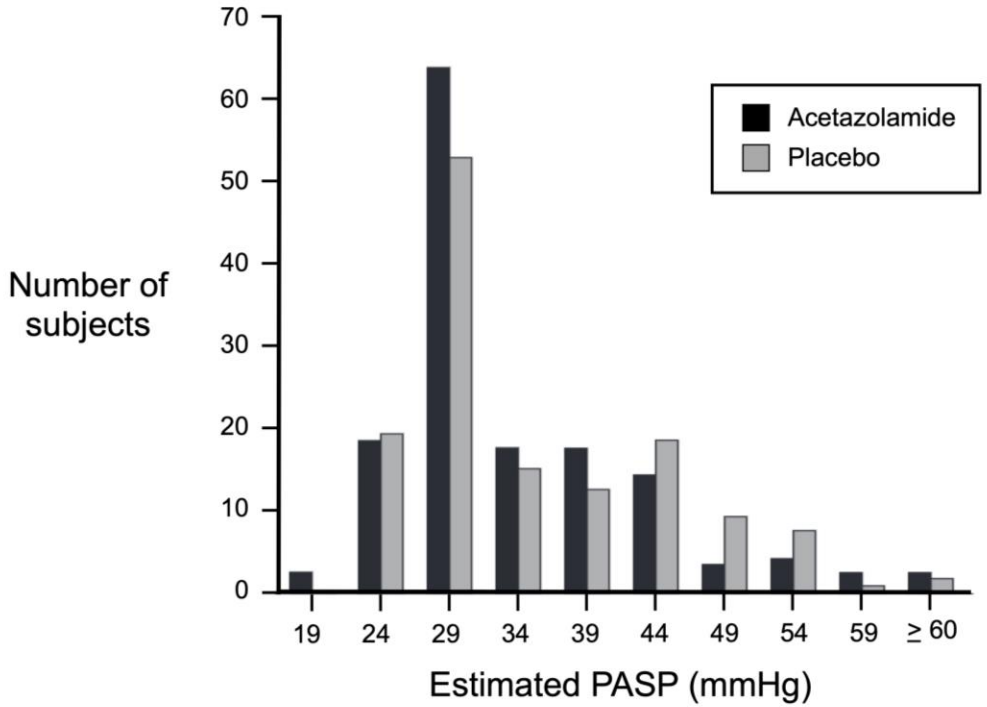
Basnyat et al. High Alt Med Biol 2008. 9: 209

Acetazolamide For HAPE Prevention Among Everest Base Camp Trekkers: Results

No cases of HAPE in either group

No differences in signs and symptoms of HAPE between groups

No difference in mean estimated PASP between groups



PASP: Pulmonary artery systolic pressure

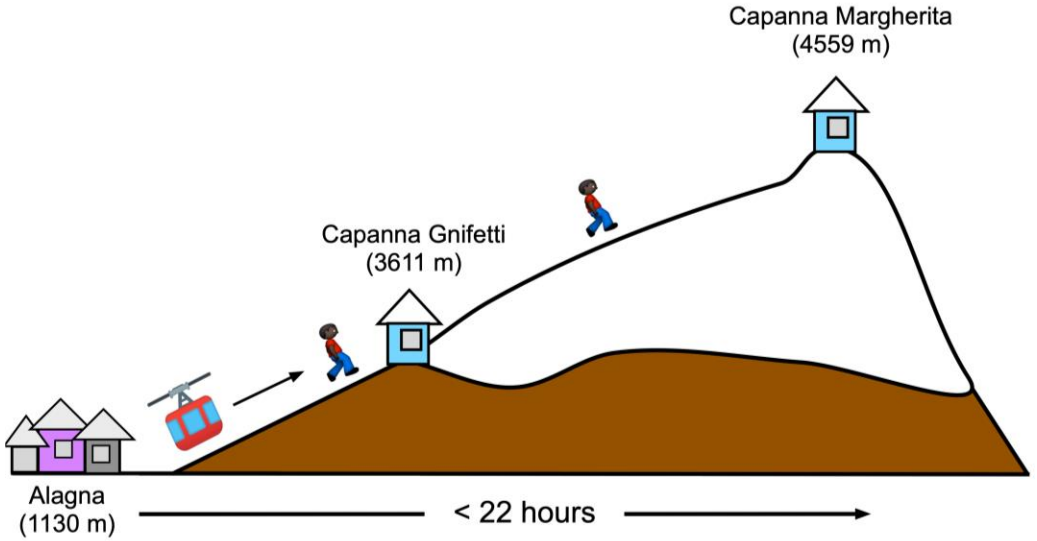
Basnyat et al. High Alt Med Biol 2008. 9: 209

A More Recent (And Effective) Study To Answer The Question

18 healthy lowlanders with history of HAPE *

Randomized to acetazolamide (250 mg q 8 hr) or placebo

Data collection at 5, 19, 29, 43, 53 and 67 hr after arrival at 4559 m



* Radiographically documented

Berger et al. J Appl Physiol 2022. 132: 1361

Acetazolamide For HAPE Prevention

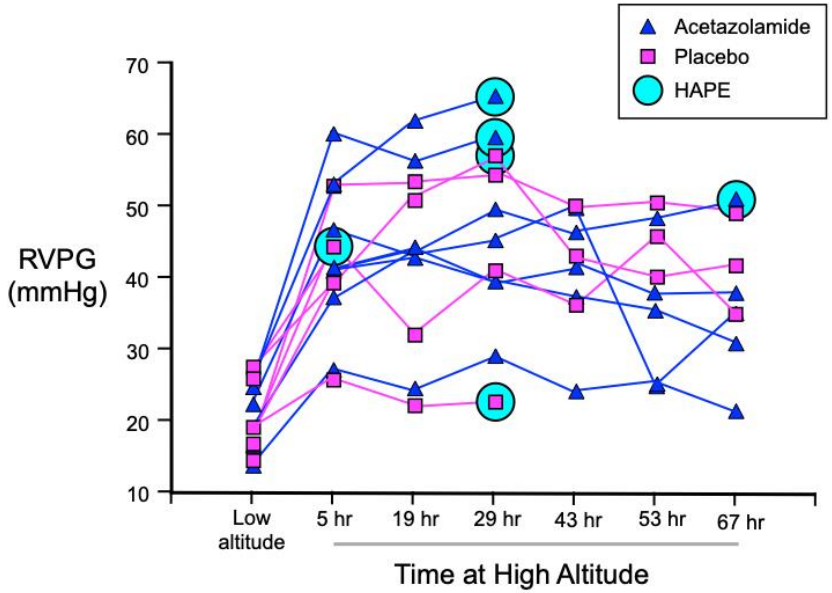
Outcome *	Acetazolamide	Placebo	P-Value
HAPE Incidence (%)	43	67	0.39
AMS Incidence (%)	57	83	0.31
P_aO_2 (mmHg)	45.4 (3.6)	36.9 (4.6)	0.025
(A-a)ΔO_2 (mmHg)	8.7 (3.1)	13.1 (4.1)	0.196

The 43% incidence of HAPE with acetazolamide is far higher than that seen in studies with nifedipine, tadalafil and dexamethasone

* At 4559 m

Berger et al. J Appl Physiol 2022. 132: 1361

No Differences In The Right Ventricular Pressure Gradient (RVPG) With Acetazolamide



RVPG at High Altitude

Acetazolamide: 43 ± 4 mmHg

Placebo: 41 ± 5 mmHg

There were also no difference in chest radiograph scores

Berger et al. J Appl Physiol 2022. 132: 1361

The Bottom Line

For individuals known to be susceptible to HAPE

Do not rely on acetazolamide alone for HAPE prophylaxis

Stick with slow ascent and nifedipine (or tadalafil)

Issue 2

Coagulopathy and High Altitude Travel

There Has Long Been Suspicion Of A Hyper-Coagulable State At High Altitude

High-altitude Pulmonary Edema with Pulmonary Thromboembolism*

Sawako Nakagawa, M.D.; Keishi Kubo, M.D.; Tomonobu Koizumi, M.D.; Toshio Kobayashi, M.D.; and Morie Sekiguchi, M.D.

Chest 1993. 103: 948

Article

November 1981

High-Altitude Pulmonary Infarction

John E. Heffner, MD; Steven A. Sahn, MD

Arch Intern Med 1981. 141: 1721

CASE REPORT

Pulmonary embolism presenting as high-altitude pulmonary edema

DAVID R. SHLIM* and KURT PAPENFUS

Wilderness Environ Med 1995. 6: 220

CASE REPORT

A Case of Cerebral Sinus Thrombosis Developed During a High-Altitude Expedition to Gasherbrum I

Shigeru Saito, MD; So-kichi Tanaka, MD

Wilderness Environ Med 2003. 14: 226

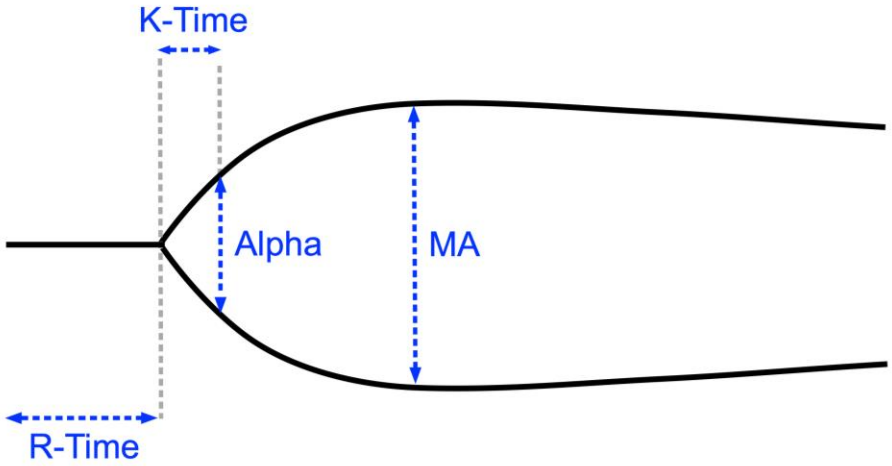
Conflicting Results In Studies Of Isolated Aspects Of The Coagulation System

Study	Result
Sharma et al. 1980	Increased platelet counts above 3,000 m
Chatterji et al. 1982	Decreased platelet counts above 3,000 m
Mannucci et al. 2002	Increased inhibitors of fibrinolytic activity
Bärtsch et al. 1988	Activation of the fibrinolytic system (P_B ~ 250-310 mmHg)
Bendz et al. 2000	Increased thrombin-antithrombin III complexes at 2400 m
Bärtsch et al. 2001	No change in thrombin formation at 4,559 m

Sharma et al. J Appl Physiol 1980. 49: 1047
Chatterji et al. Thromb Res 1982. 26: 177
Mannucci et al. Thromb Haemost 2002. 87: 32
Bärtsch et al. Aviat Space Environ Med 1988. 59: 428
Bendz et al. Lancet 2000. 356: 1657
Bärtsch et al. Lancet 2001. 357: 955

A Better Way To Study This Issue: Look At The Entire Clotting System At Once

Thromboelastography



R (Reaction time)
Time to fibrin formation
Assesses clotting factors and inhibitors

K (Kinetics)
Time to achieve level of clot strength
Assesses fibrin polymerization

Alpha (slope angle)
Speed of fibrin build up / cross-linking
Assesses rate of clot formation

MA (Maximum amplitude)
Assesses clot stability
Assesses fibrin clot and platelets

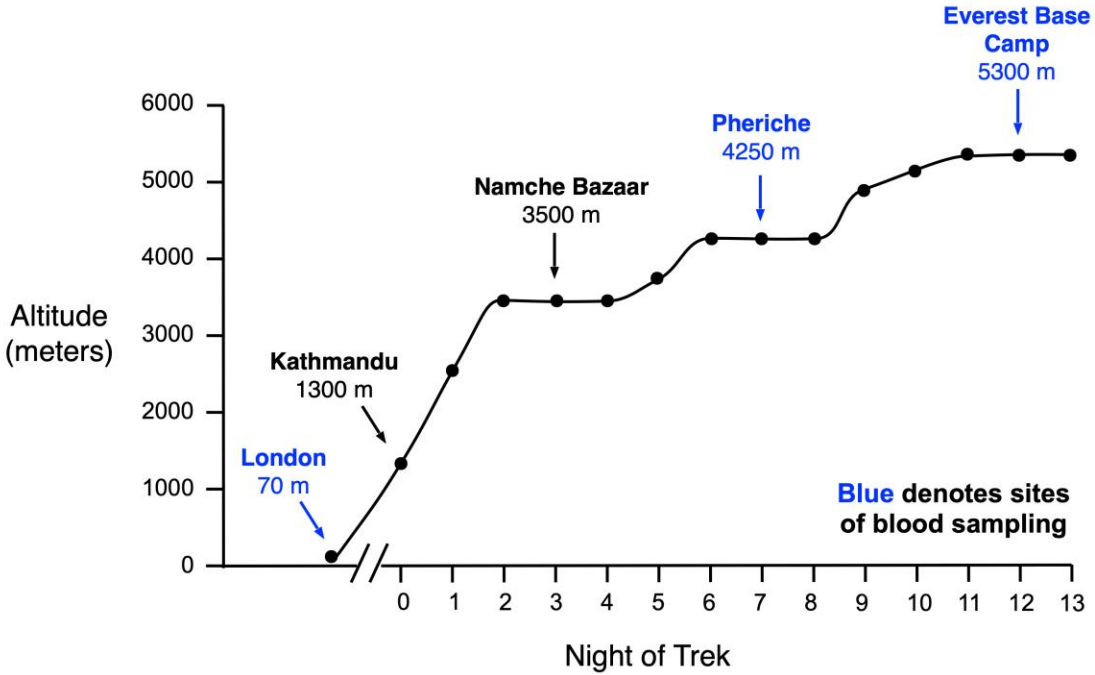
A Field Study Of Coagulation At High Altitude Using Thromboelastography

17 healthy volunteers (12 male, 5 female)

No known coagulopathy

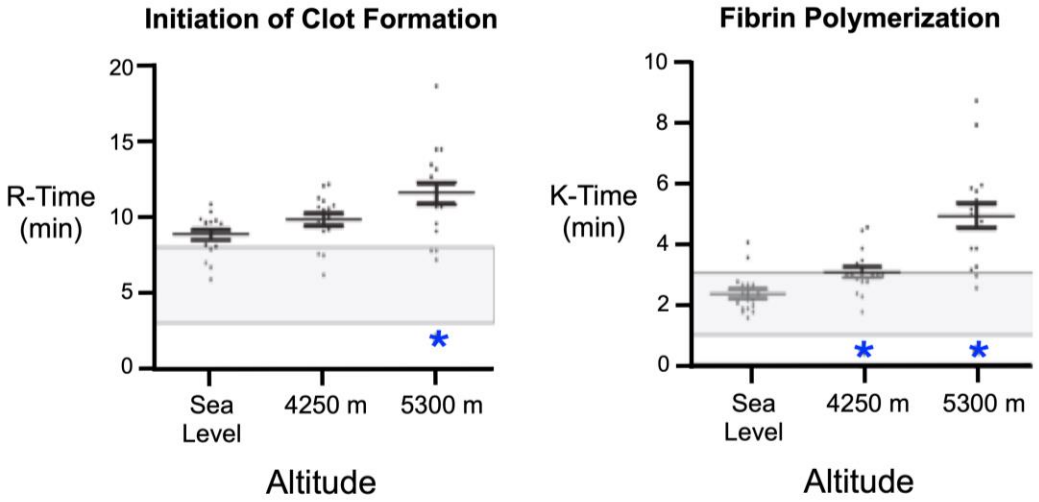
Similar ascent profiles

No altitude illness prophylaxis



Martin et al. Thromb Haemost 2012. 107: 1066

R-Time And K-Time Were Longer At High Altitude



These findings are indicative of slower coagulation

Clot formation was slower while maximum clot strength was unchanged

Martin et al. Thromb Haemost 2012. 107: 1066

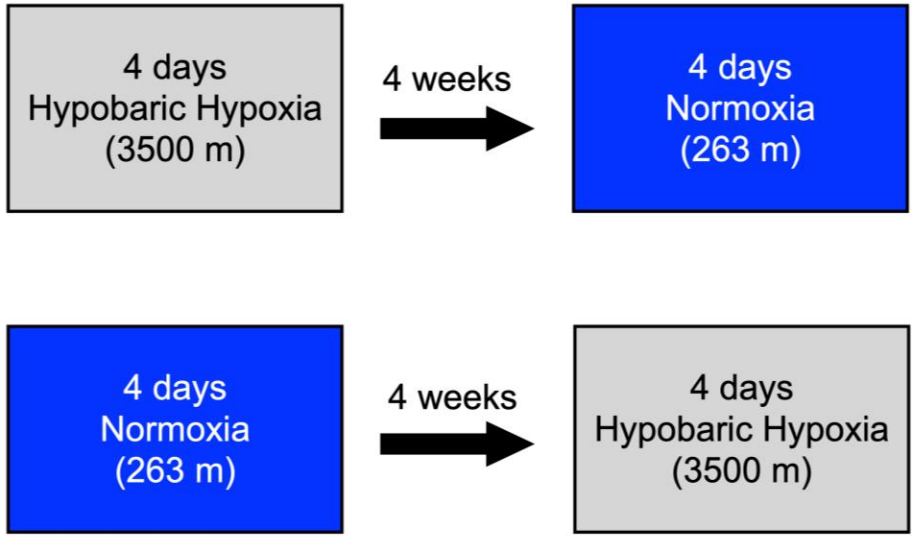
A Chamber Study Of Coagulation In Hypoxia Using Viscoelastometry

12 healthy, sedentary females

24.1 ± 4.4 years,

Controlled for nutrition and fluid intake, menstrual cycle variation

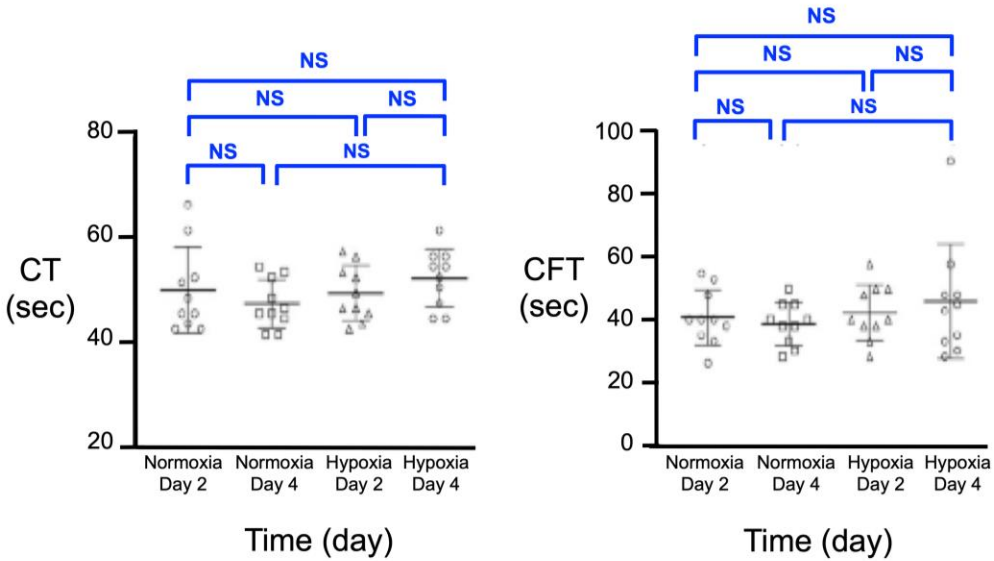
Strict environmental control in Terra X-Cube



Lab draws: days 2 and 4 of each exposure

Kammerer et al. High Alt Med Biol 2023. 24: 94

Clotting Time (CT) And Clot Formation Time (CFT) Were Unchanged In Hypobaric Hypoxia



Also found no changes in prothrombin time, partial thromboplastin time, fibrinogen, von Willebrand factor antigen concentrations

Kammerer et al. High Alt Med Biol 2023. 24: 94

NS: Non-significant

Other Issues To Consider

In many of the reported cases in the literature, the affected individual was known or found to have a genetic defect in coagulation

No clear evidence that the background rate of venous or arterial thromboembolism is higher at high compared to low elevation

The Bottom Line:

It’s time we stop propagating the idea that high altitude predisposes to a hypercoagulable state

Issue 3

Activity During Ascent And Risk of AMS

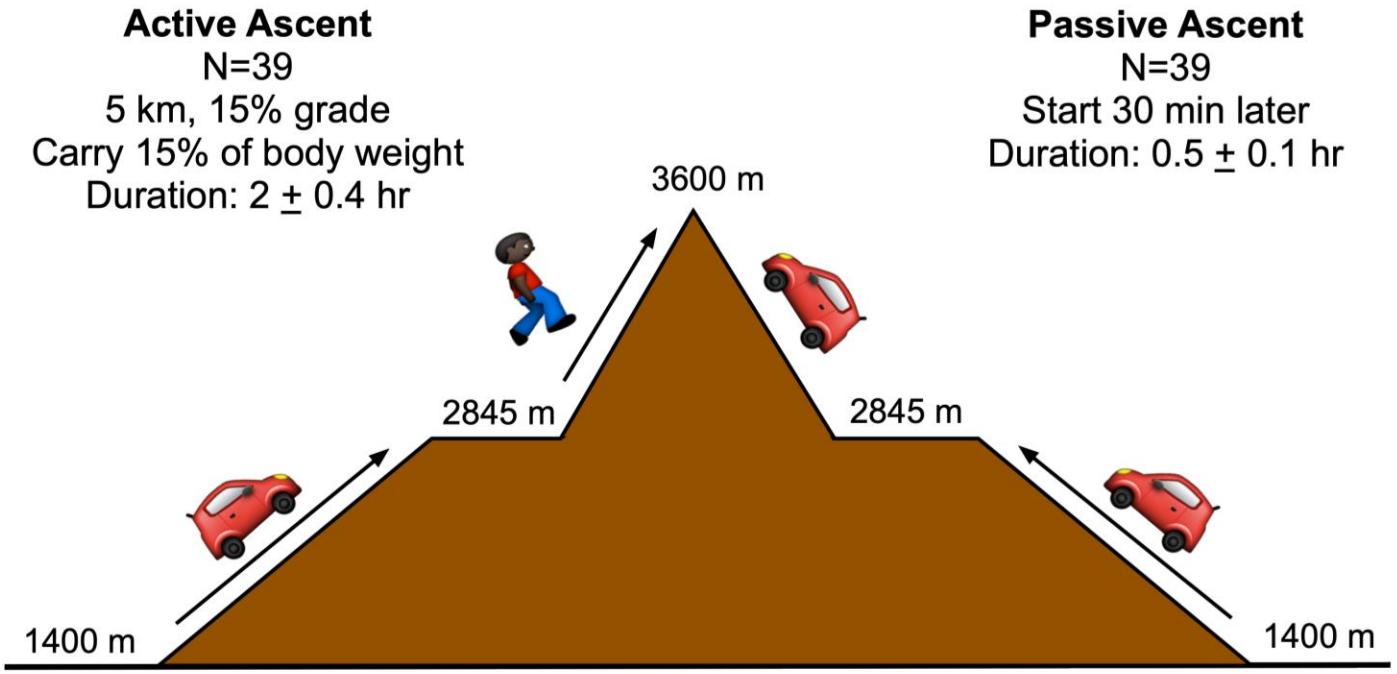
Prior Studies On The Effect Of Activity On The Risk Of AMS

Study	Design	Result
Roach et al. 2000	10 hours hypobaric hypoxia (4800 m); Four 30 min bouts of exercise at 50% of maximum workload vs. remaining sedentary	Higher incidence and severity of AMS with exercise
Schömmer et al. 2012	18 hours normobaric hypoxia (4500 m); Three 45 min bouts of exercise at 50% of maximum workload vs. remaining sedentary	No difference in AMS at 5, 8 or 18 hr of exposure

Limitations: Short duration of hypoxia
Cycle ergometry
Chamber study
Low number of subjects

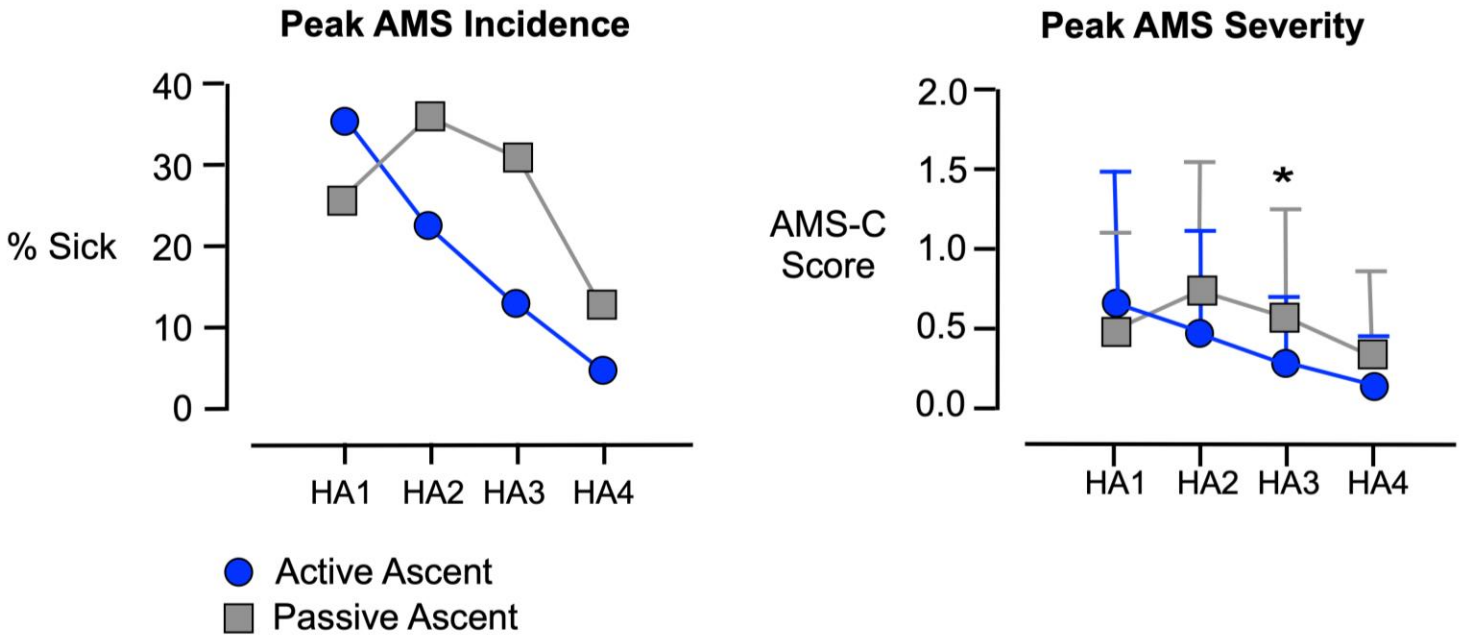
Roach et al. J Appl Physiol 2000. 88: 581
Schommer et al. J Appl Physiol 2012. 113: 1068

A Larger Field Study To Address This Issue



Beidleman et al. J Appl Physiol 2023. 135: 436

No Differences In Overall Incidence And Severity Of Acute Mountain Sickness (AMS)



Beidleman et al. J Appl Physiol 2023. 135: 436

Issues To Consider

Mostly young, male study population

Only did assessments at a single altitude

Did not control diet and water intake

Relatively short period of activity during ascent

The Bottom Line

This study provides no reason to vary from current recommendations regarding activity during or following ascent

Issue 4

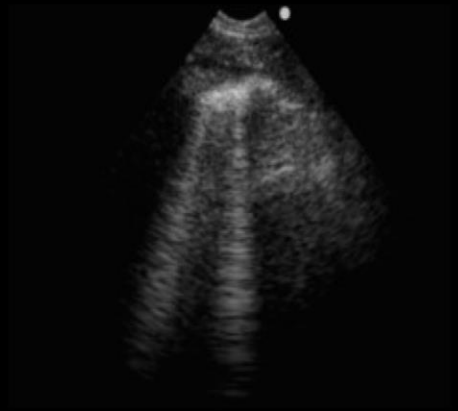
Lung Ultrasound at High Altitude

Comet Tails (B-Lines) Are Increased In People With HAPE

Normal lung in healthy controls

Comet Tail Score: 0.9 ± 0.8
S_pO_2: 87 ± 2.8% (N=7)

Comet tails in patients with HAPE



Comet Tail Score: 31 ± 11
S_pO_2: 61 ± 9.2% (N=11)

No clear cut off in the literature with documented sensitivity and specificity

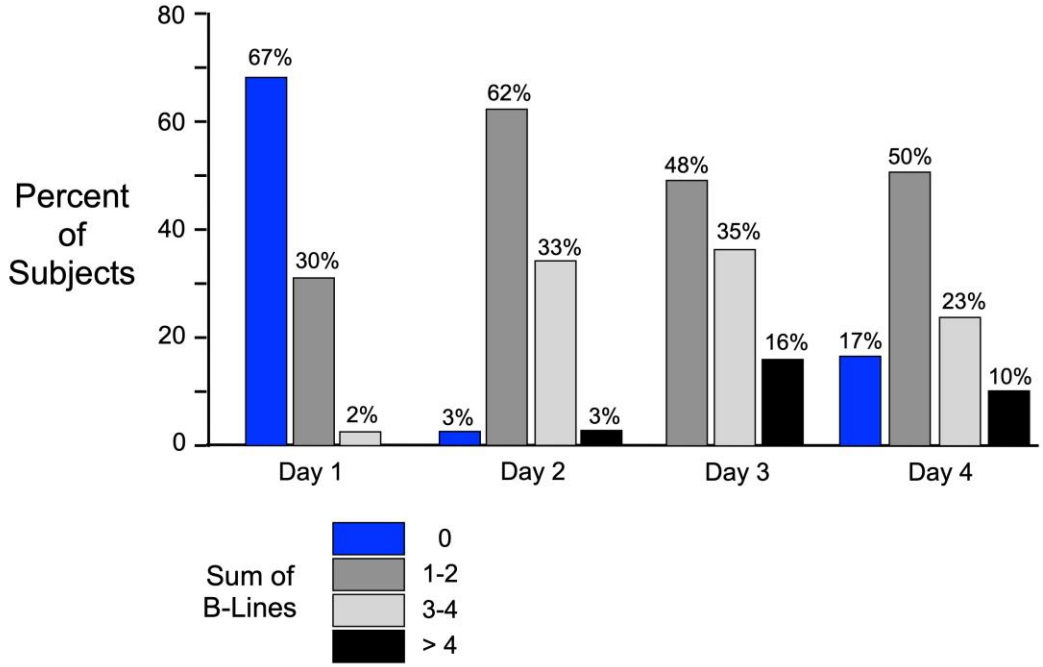
Fagenholz et al. Chest 2007. 131(4): 1013

Small Numbers Of B-Lines Are Common, Even At Moderate Altitudes

N = 42 (21 male, 22 female)

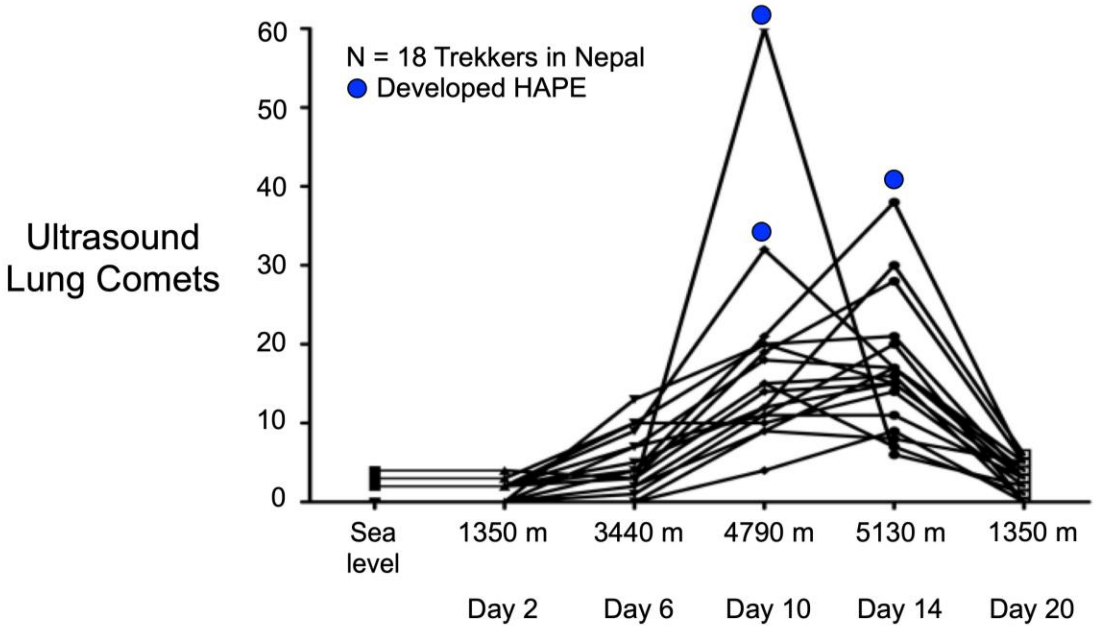
Enrolled on first day after arrival from sea level at a ski resort at 2745 m

Did not control for level of activity each day



Lahham et al. West J Emerg Med 2023. 24(2) 359

Comet Tails Are Also Common At Higher Elevations



Increase in comet tails related to Lake Louise Score and S_pO_2

Very weak relation to changes in pulmonary artery pressure

Pratali et al. Crit Care Med 2010. 39(9): 1818

Is An Increase In Comet Tails Indicative Of Worsening Gas Exchange And HAPE?

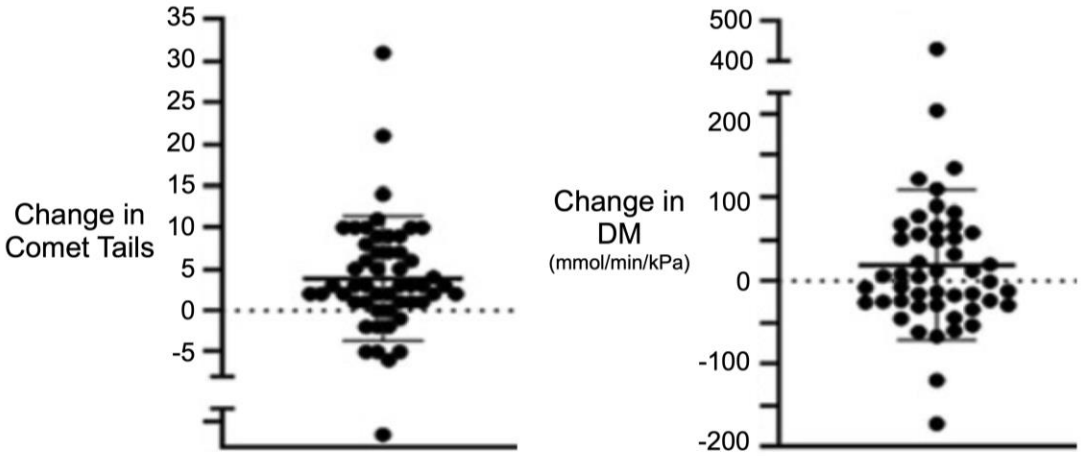
51 healthy ultra-endurance trail runners

Highest elevation: 2,537 m

Lung ultrasound and diffusion capacity measurements before and within 3-5 hours of finishing the race

Parks et al. High Alt Med Biol 2023. 24(3): 230

Comet Tail Scores Increased But Membrane Diffusing Capacity Was Unchanged



42 subjects with increase in comet tails

50% with decreased D_M

50% with increased D_M

This and other data suggest increased comet tails are not necessarily associated with impaired gas exchange

D_M: membrane diffusing capacity

Parks et al. High Alt Med Biol 2023. 24(3): 230

Summarizing What We Know

Comet tail scores increase following ascent in large numbers of people

Many people with increased comet tails are asymptomatic

Increased comet tail scores are not necessarily indicative of impaired gas exchange

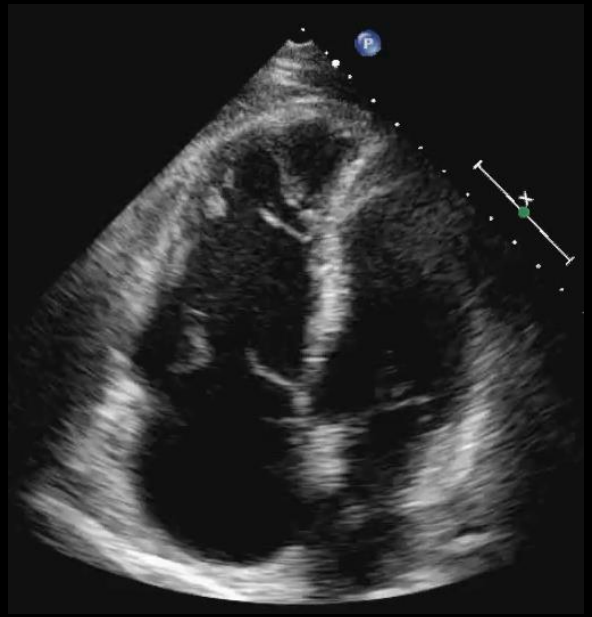
The Bottom Line

As with pulse oximetry, lung ultrasound should not be used for routine monitoring and, instead, should only be used to evaluate people with respiratory symptoms

Issue 5

Travel to High Altitude With Known Lung Disease

Planned Travel To High Altitude With Either Of These Two Conditions Should Provoke Concern



Fortunately, there has been some high quality research in recent years

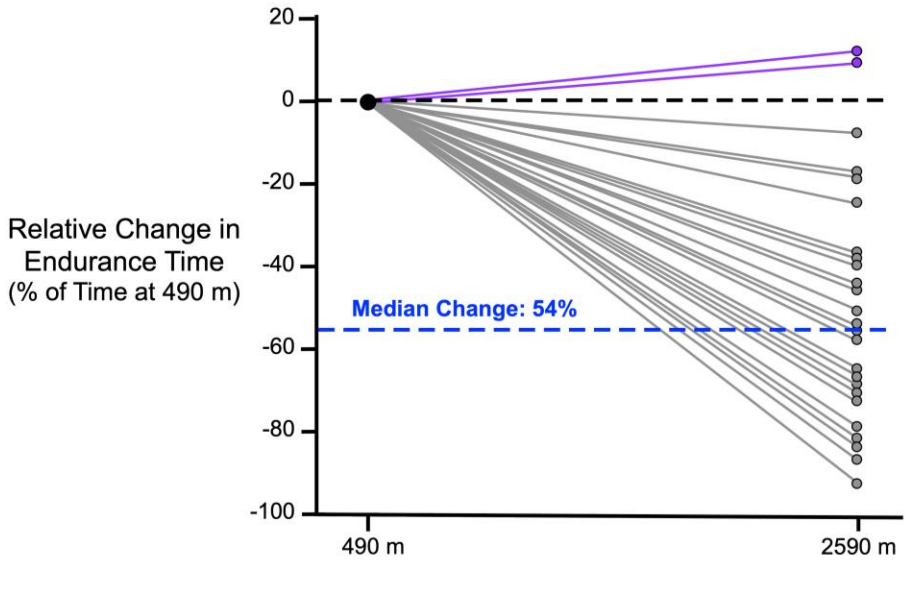
What Have We Learned: COPD

Some patients are prone to exaggerated hypoxemia

No significant change in pulmonary function

Low risk of pneumothorax

Variable changes in exercise capacity



Furian et al. Respiration 2018. 95: 422
Furian et al. Int J Chron Obstruct Pulmon Dis 2018. 13: 3529

The Approach To High Altitude Travel: COPD

Very severe disease, hypercarbia and/or moderate-severe hypoxemia at low elevation

Worsening symptom control leading up to trip

Travel up to 2500-3000 m okay for those with moderate -severe disease, normocapnia and only mild hypoxemia

Monitor symptoms and pulse oximetry
Continue existing medications, consider acetazolamide
Have a plan to access supplemental oxygen or descend

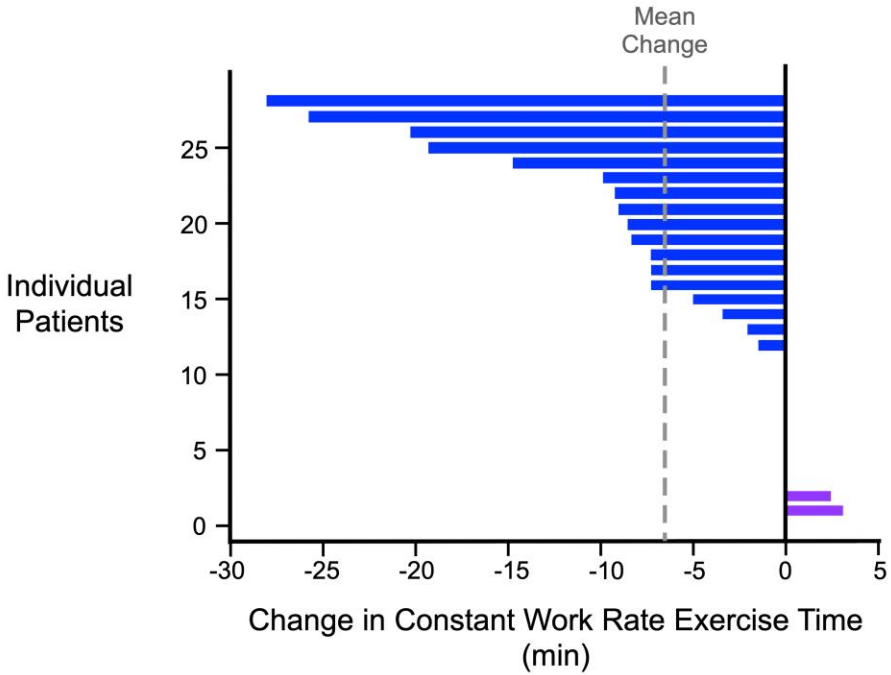
What Have We Learned: Pulmonary Hypertension *

Some patients are prone to exaggerated hypoxemia

Hypoxic pulmonary vasoconstriction is blunted

No deterioration in hemodynamics

Variable changes in exercise capacity



* Due to pulmonary arterial hypertension or chronic thromboemblolic pulmonary hypertension

Schneider et al. ERJ Open Res 2021. 7: 00314
Ulrich et al. High Alt Med Biol 2022. 23: 201

The Approach To High Altitude Travel: Pulmonary Hypertension

NYHA Class 4 disease or hypoxemia

Worsening symptom control leading up to trip

Travel up to 2500 m okay for those with NYHA Class 1-3 disease

Monitor symptoms and pulse oximetry
Continue existing medications
Have a plan to access supplemental oxygen or descend

Summary

Let's See What We've Learned About The Recent Literature

Statement	True or False
Acetazolamide has been shown to prevent high altitude pulmonary edema in known susceptible individuals	
Exposure to high altitude causes a hypercoagulable state	
Physical activity during ascent does not increase the risk of acute mountain sickness	
Screening lung ultrasound is useful for identifying people at risk for high altitude pulmonary edema	
Patients with moderate COPD or NYHA Class 2-3 pulmonary hypertension can safely travel to 2500 m	

NYHA: New York Heart Association

Thanks for Listening!

Questions?

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