High altitude, hypoxia and the physiology of adaptation

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disclosures

none
objectives

• understand the acute physiological changes that are precipitated by ascent to high altitude

• appreciate the adaptations that occur with acute ascent to altitude

• gain an introduction to altitude related illnesses and their prophylaxis and treatments
“We live submerged at the bottom of an ocean of the element air, which by unquestioned experiments is known to have weight.”

Evangelista Torricelli (1608–1647)
why study high altitude physiology?

• large numbers of people live or recreate at altitude

• many of the adaptive (or maladaptive) mechanisms are applicable to various disease states, especially those that are manifest by hypoxia

• understanding the basic physiology can lead to better understanding and therapies of disorders characterized by hypoxic conditions
physical conditions at altitude

as altitude increases:

• barometric pressure falls
• $P_{AO_2}$ falls with lower $PB$
• partial pressure of water vapor in the lung assumes a greater proportion of alveolar pressure
• temperature falls (~6 - 9°C per 1000m)
• UV exposure increases
• humidity decreases
Pb, PO2, PaO2 and altitude

from West JB. The physiologic basis of high-altitude diseases. Annals of Internal Medicine 2004.
acute adaptive effects of ascent

• increased carotid body discharge accelerates respiratory rate
• most important of the early mechanisms of acclimatization
• also critical for the maintenance of adequate $\text{PaO}_2$ at extreme altitude
• increased $\text{Vm}$
• why does this help?
acute adaptive effects of ascent

- total pressure in the alveolus is the sum of the partial pressures of CO$_2$, O$_2$, N$_2$, and water vapor

\[ P_{aO_2} = P_B - (P_{aCO_2} + P_{N_2} + P_{H_2O}) \]

- Only the $P_{aCO_2}$ can be reduced by altering respiratory rate, therefore (assuming $R=1$):

\[ P_{aO_2} = P_{I O_2} - P_{aCO_2} \]
acute adaptive effects of ascent

from Young AJ, Reeves JT. Human adaptation to high terrestrial altitude. in Medical Aspects of Harsh Environments 2002.
acute effects of ascent to altitude

- heart rate (and cardiac output) increases
- however, maximal heart rate decreases (from increased parasympathetic drive?)
- as high altitude diuresis ensues resulting in hemoconcentration, resting heart rate falls
acute effects of ascent to altitude

- despite a fall in all indices of preload (end-diastolic and end systolic volumes, stroke volume) ejection fraction is preserved
- suggests a small increase in contractility in acclimated subjects

Suarez J, Alexander JK, Houston CS. Enhanced left ventricular systolic performance at high altitude during operation everest II. The American Journal of Cardiology 1987;60:137–42.
circulatory adaptation to altitude

- diuresis begins within 3-6 hours of ascent
- decreased plasma volume with maintained RCM => hemoconcentration
- 2,3 DPG increases (48h-3 weeks after ascent) resulting in increased Hb O₂ affinity
- EPO secretion is increased (but subject to high individual variability)- response takes 3+ weeks
adaptation to altitude: hemoglobin

maladaptation to altitude: high altitude illness
general principals

• although there are those who are genetically more susceptible and those who are genetically resistant to high altitude illness, anyone will get sick if they go high enough fast enough

• the best treatment, when possible, for any high altitude illness is DESCENT
when descent is impossible

- pharmacotherapy (steroids, beta agonists, vasodilators, NO analogs)
- oxygen
- Gamow bag
acute mountain sickness (AMS)

- may affect at least 25% of lowlanders ascending rapidly >2500m
- diagnosed by symptoms (Lake Louise score): headache plus
  - lightheadedness
  - breathlessness
  - fatigue
  - insomnia
  - anorexia
  - nausea
acute mountain sickness (AMS)

• usually self limited (3-4 days)

• etiology may be mild cerebral edema

• hypoxia upregulates the expression of neuropeptide corticotrophin releasing factor, which activates the water channel aquaporin-4 and facilitates water (from CSF) influx into glial cells

• less common > age 50

• those who are more hypoxic at altitude may be more susceptible (Roach RC, et al. Aviat Space Environ Med 1998;69:1182–5.)
acute mountain sickness (AMS)

- Cheyes-Stokes respiration and periodic breathing are common
- unclear mechanism:
  - hypoxia induced instability of central ventilatory drive
  - hypocarbia/ hypercarbia
  - hypoxia-induced arousal
- best treated with acetazolamide, NOT sedatives or sleep agents
acute mountain sickness: prevention & treatment

- slow ascent!
- acetazolamide (Diamox) - 125mg BID
- dexamethasone - 2mg QID
HPV and pulmonary arteriolar hypertension

- HPV response to acute hypoxia varies among individuals
- those with the briskest response, most dramatic elevation in PAP and most heterogeneity are most at risk for acute PAH with ascent
- in severe cases R heart failure can develop

High Altitude Pulmonary Edema (HAPE)

- presents with dyspnea, cough, low grade fever, progressing to frank pulmonary edema
- usually presents within 2-3 days of ascent >2500m
- exacerbated by rapid ascent coupled with exertion
- susceptible individuals have abnormally brisk elevations in PAP in response to hypoxia
- elevated PAP > wall stress in pulmonary capillaries and ultrastructural damage
High Altitude Pulmonary Edema (HAPE)

- central - basilar infiltrates on CXR, usually worse on the left
- caused by HPV that is out of proportion to the hypoxic stimulus & is unevenly distributed
- high pulmonary capillary pressures result in exudate, inflammatory response and lung injury
- treatment with PEEP, vasodilators (nifedipine), steroids, $\beta_2$ agonists (salbutemol), iNO or sildinafil have been effective
High Altitude Cerebral Edema (HACE)
HACE

- inability to compensate for elevation in ICP
- greater compliance-
  - translocation
  - “tight fit”
- vasogenic cerebral edema with breakdown of blood brain barrier, extravasation
- presents with ataxia, confusion, depressed consciousness, papilledema, hemiparesis, coma
- descent, O₂, steroids mandatory
conclusions

• hypoxia from ascent to altitude mandates a multitude of physiologic adaptations that permit humans to survive under conditions that would otherwise be impossible

• maladaptation, whether due to genetics or exceeding the ability of the system to compensate, can lead to serious and life-threatening illness

• successful adaptation requires understanding physiology & the limits of the organism, and occasional intervention with pharmacotherapy


selected references: acute mountain sickness and high altitude illnesses


selected references: altitude physiology

West JB. The physiologic basis of high-altitude diseases. Annals of Internal Medicine 2004;141:789-800.


