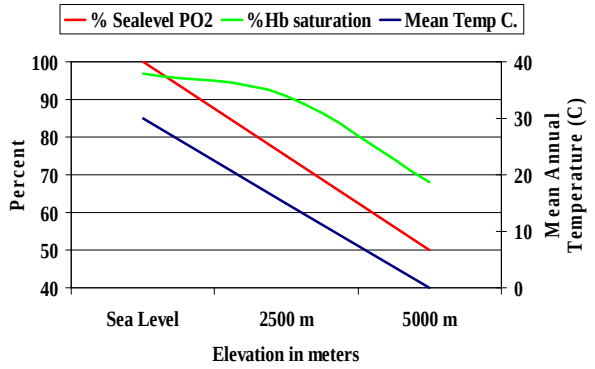
Altitude Adaptation

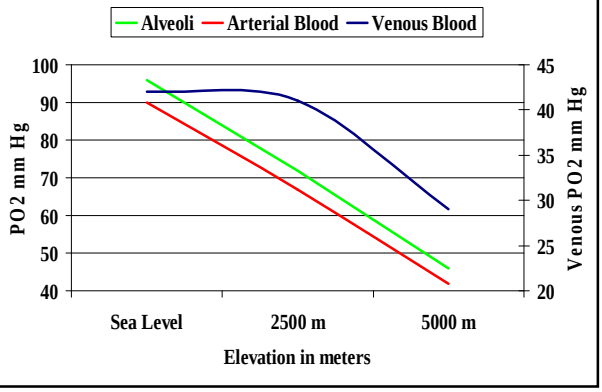
Altitude Stressors

- Radiation: cosmic, ultraviolet
- Energy: limited biota
- Aridity: low water vapor pressure
- Cold: 0 ºC MAT at 5,000 meters elevation on the equator
- Hypoxia: PO_2 at 5,000 meters is 50% that at sea level

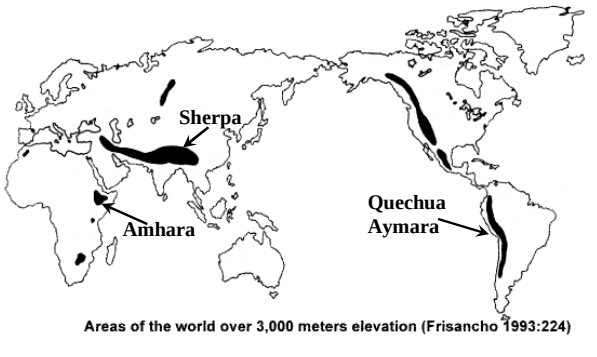
Altitude, Oxygen, Temperature

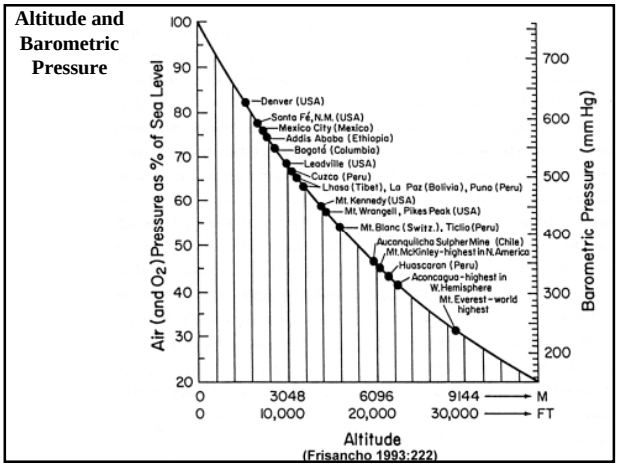


Circulatory PO_2



Altitude Areas





Physiological Changes with Altitude

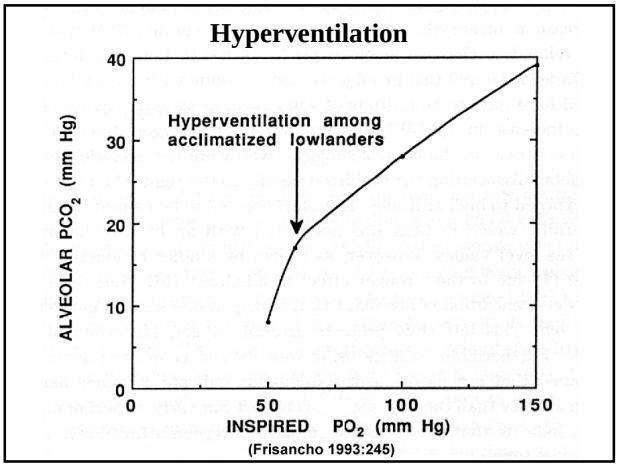
- Resting HR goes from 70 beats/min to about 105 beats/min
  - Maximal HR reduced
- Retinal circulation increases and after 5 - 7 weeks remains elevated
- Light sensitivity decreases within 1 hour and returns to normal after 48 hours

Physiological Changes with Altitude, 2

- Memory and recall are diminished
  - Ability to learn new tasks is most affected
- Food preferences change to emphasize sugars
  - May be due to oxygen efficiency of glucose
  - Decrease desire for fat
- Anorexia and weight loss

Adult Acclimatization

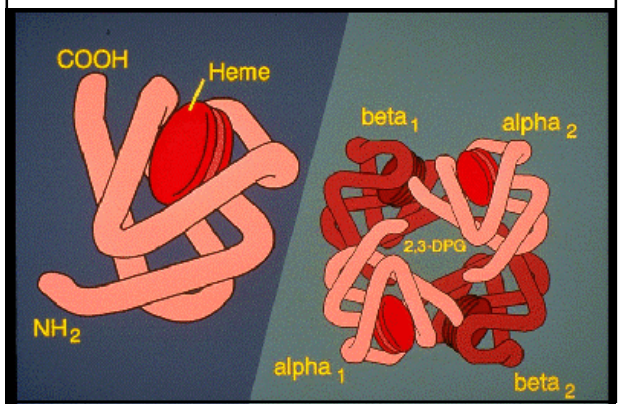
- Increased pulmonary ventilation
  - Up to doubled minute volumes
    - Both at rest and during exercise (activity)
  - Supports increased Alveolar PO_2 and an increased arterial oxygen saturation
  - Hyperventilation reduces alveolar PCO_2
    - Shifts pH to alkaline values (> 7.4)

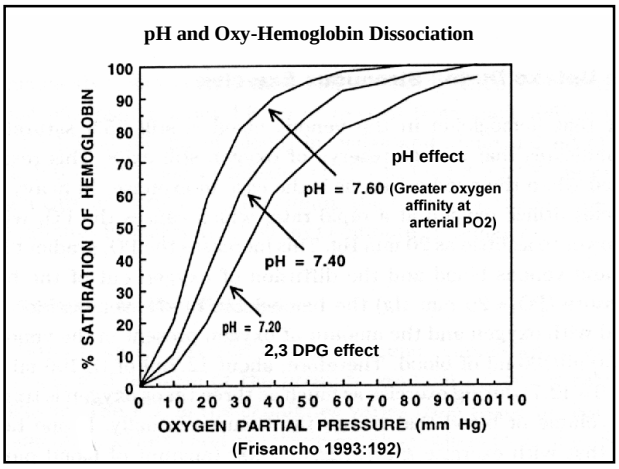


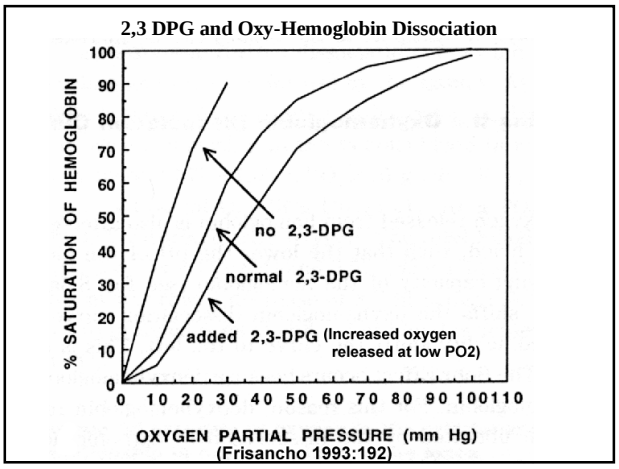
Adult Acclimatization, 2

- Oxygen-Hemoglobin Dissociation Curve
  - Right shift in the curve yields a decreased oxygen affinity at low PO_2
    - Hyperventilation generates lower pH which increases 2,3-diphosphoglycerate (2,3-DPG)
  - Left shift in the curve generates
    - With greater alkalinity, the 2,3-DPG effect is over-ridden and the pH effect takes over

Structure of Hemoglobin







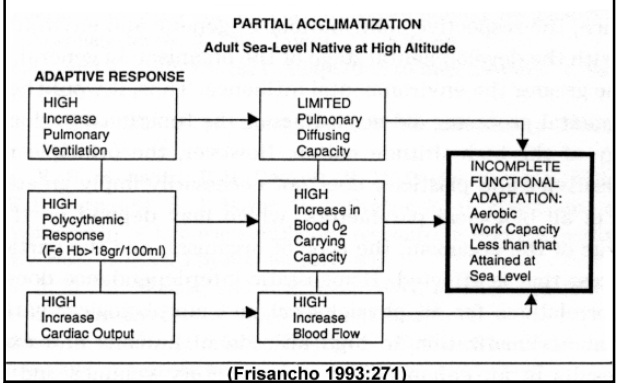
Adult Acclimatization, 3

- Hypoxia causes bone marrow to be stimulated by an erythropoietic factor that increases the production of red blood cells
  - Within 2 hours of exposure, iron turnover increases reflecting the increasing synthesis of hemoglobin
- Erythropoietic stimulation falls over the first few days to a level somewhat above sea level values

Adult Acclimatization, 4

- Work capacity as measured by oxygen consumption is dramatically reduced but increases over a period of 2 - 8 weeks
  - Oxygen consumption is a function of cardiac output (how much blood is pumped) and the difference between arterial and venous PO_2
  - Drops approximately 11% for every 1000 meters above 1500 meters elevation
  - Remains 15 - 25% lower than sea level values

Partial Acclimatization



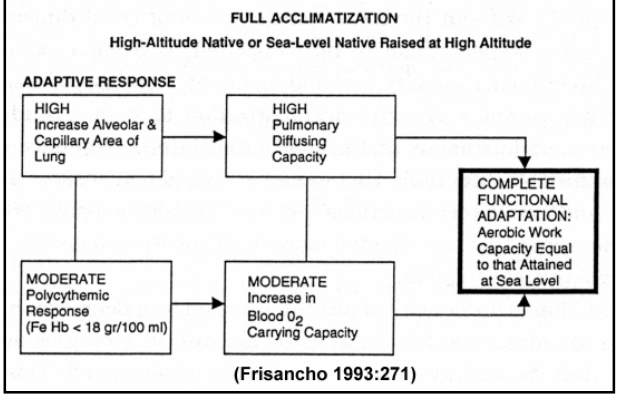
Developmental Acclimatization

- Increased lung volumes occur with development at high altitude
  - True for Andeans, Himalayans, and Ethiopians
- Increased pulmonary diffusing capacity
  - Greater alveolar area and increased capillary volume
  - Higher pulmonary blood pressure
  - Increased pulmonary ventilation

Developmental Acclimatization

- Work capacity of high altitude natives is comparable to that of related populations native to and tested at sea level
  - Results from improved pulmonary diffusing capacity which provides higher arterial PO_2 and a greater arterial versus venous PO_2

Full Acclimatization



High Altitude Resident Populations

- Ethiopian Plateau: population dates back to about 50,000 years ago, resident at 2500 – 3500 m
  - Ambaras
- Himalayas: population dating back about 23,000 years, resident at 3500 – 5000 m
  - Tibetans, Sherpa, Bods
- Andes: population dates to 10,000 years ago, resident at 3500 – 4500 m
  - Aymara and Quechua

Comparison of high altitude adaptations

Population	PO_2 inspired (% of sea level)	Over production of RBC	Arterial hypoxia	Hemoglobin Oxygen saturation
Sea Level	100	—	—	Normal
Ethiopian	64	—	—	Normal
Tibetan	60	—	+	Low/High*
Andean	60	+	+	Low

* High altitude Tibetan populations show a high frequency (0.55 – 0.74) of an allele that increases oxygen saturation of hemoglobin by about 5% at rest

A Genetic Pathway of Adaptation

- HIF-1: Hypoxia Inducible Factor-1 is a transcription factor that alters the transcription activity of more than 40 genes in a downstream position that are related to hypoxia regulation
  - Erythropoietin (EPO): stimulates RBC synthesis
  - Nitric Oxide Synthetase (NOS): Increases Nitric Oxide which causes vasodilation and affects oxygen delivery
    - Especially important in mitochondrial oxidative metabolism
  - Heme Oxgenase-1 (HO-1): an enzyme that helps decompose heme
  - Vascular Endothelial Growth Factor (VEGF): Helps to stimulate growth of blood vessels

Native vs. Newcomer Adaptive Success

- Less intrauterine growth retardation
- Better neonatal oxygenation and fewer complications of fetal cardiopulmonary characteristics
- Enlarged lung volumes and decreased alveolar-arterial oxygen diffusion gradients
- Higher VO_2max
- Better maintained increase in cerebral blood flow during exercise (Tibetans only)
- Lower hemoglobin concentrations (Tibetans only)
- Less susceptibility to chronic mountain sickness (Tibetans only)

Tibetans vs. other High Altitude Natives

- Less intrauterine growth retardation
- Greater reliance on redistribution of blood flow than elevated arterial oxygen content to increase uteroplacental oxygen delivery during pregnancy
- Higher levels of resting ventilation and hypoxic ventilatory responsiveness
- Less hypoxic vasoconstriction and lower pulmonary arterial pressure and resistance
- Lower hemoglobin concentrations
- Lower prevalence of chronic mountain sickness

Sources

- Moore LG, Niermeyer S, and Zamudio S (1998) Adaptation to high altitude: regional and life-cycle perspectives. Yearbook of Physical Anthropology, 41:25-64.