



Lung Disease
KSSG 2017

UniversitätsKlinikum Heidelberg

Travel to Altitude Part 1: Mechanisms of Acclimatization

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Responses to Hypoxia

Acute Adjustment (immediate response)

- Increase of ventilation
- Increased cardiac output, mostly by increasing heart rate
- Systemic circulation: vasodilation
- Pulmonary circulation: vasoconstriction

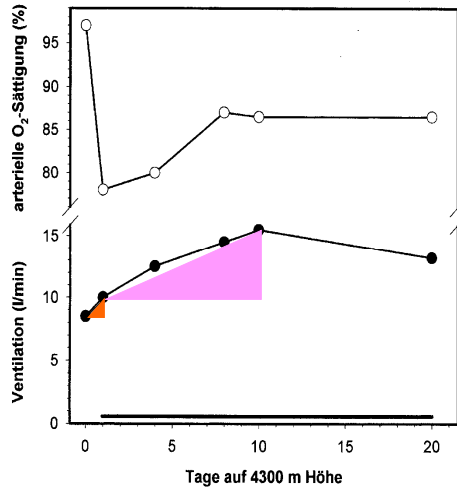
Acclimatization (within days to weeks)

- Ventilatory acclimatization
- Increasing oxygen carrying capacity of blood
- Metabolism: Reduction of ROS Production



1. Ventilatory Acclimatization

Ventilation at 4300 m



SaO₂: 78 → 87 %

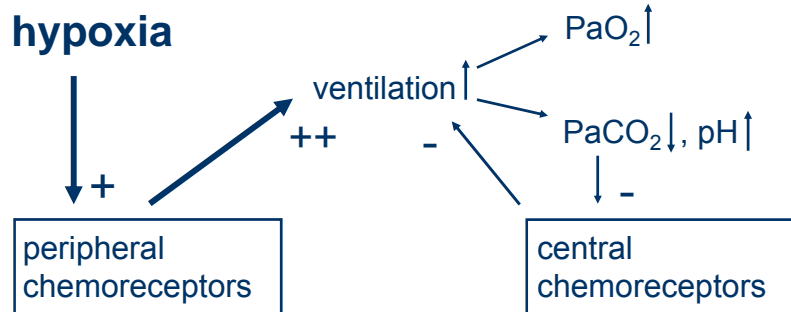
Increase of ventilation :

- day 1: 8.5 → 10 l (18%)
- day 1-10: 10 → 15 l (50 %)

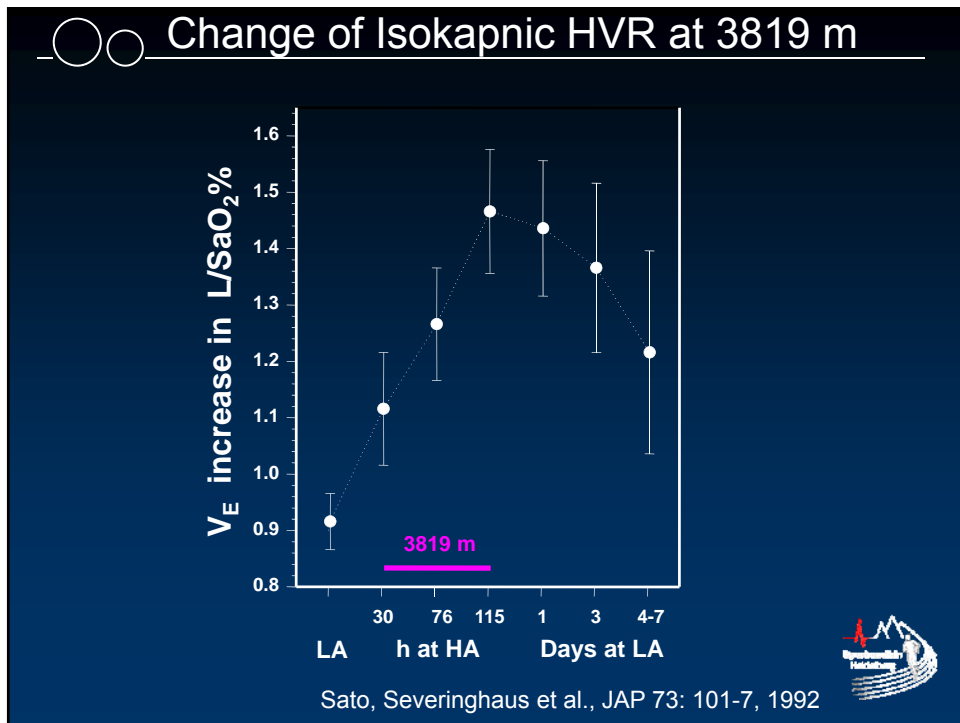
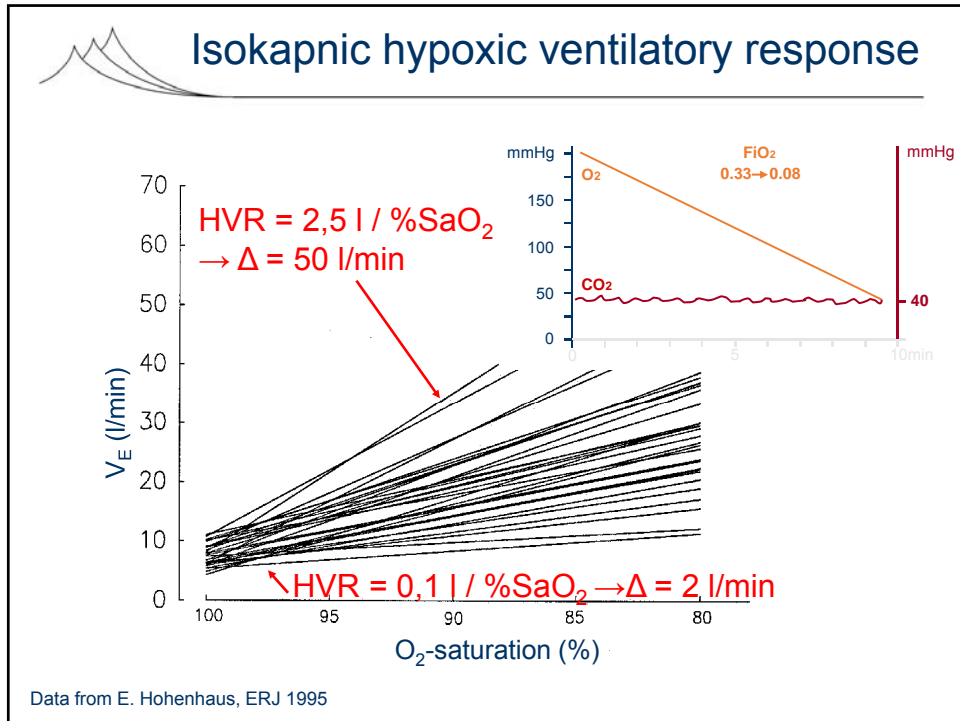
Bender PR, JAP 1989;66:2733

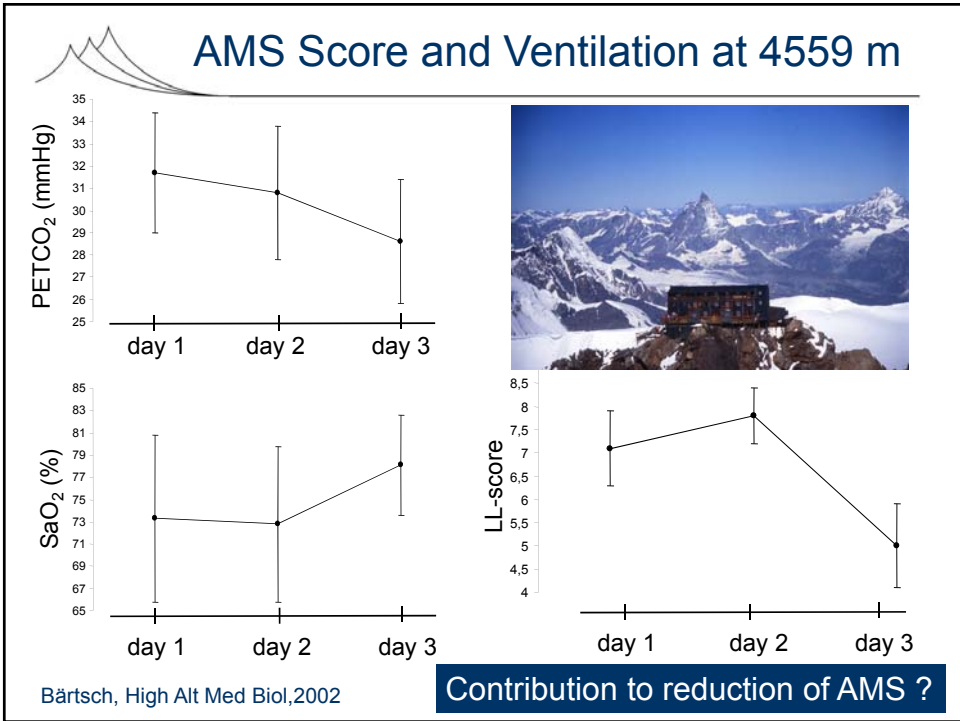
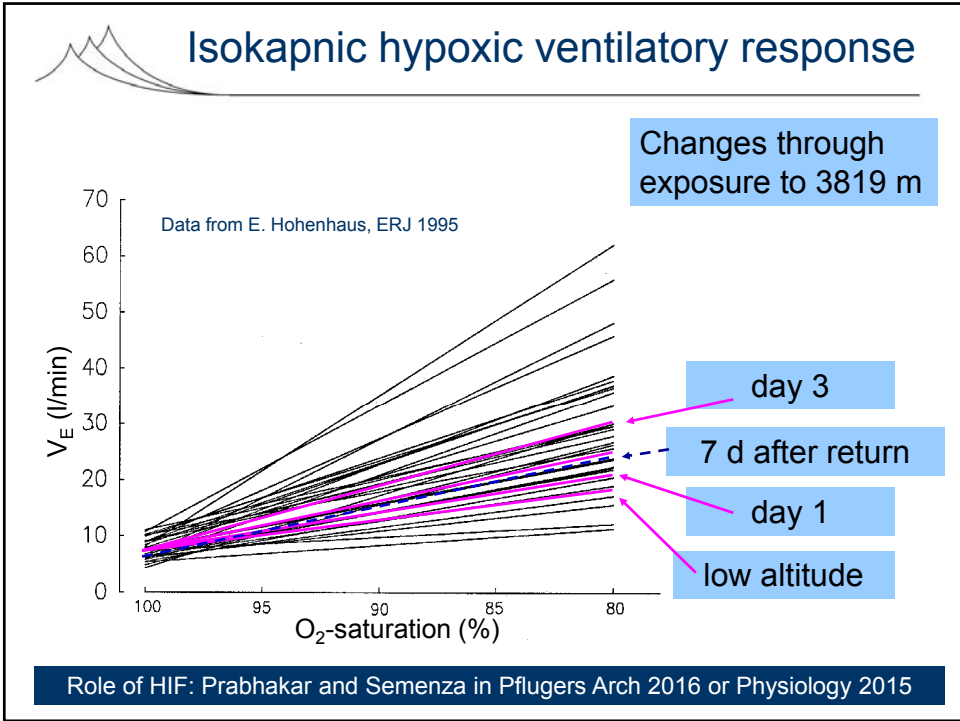


Regulation of Ventilation in Hypoxia



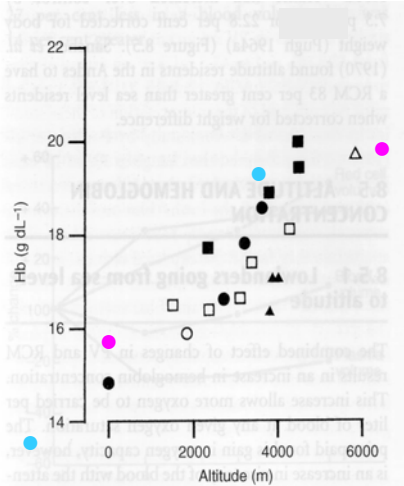
~~Hypothesis
Ventilatory acclimatization through renal compensation of the respiratory alkalosis~~







2. Increase of O₂- Carrying Capacity



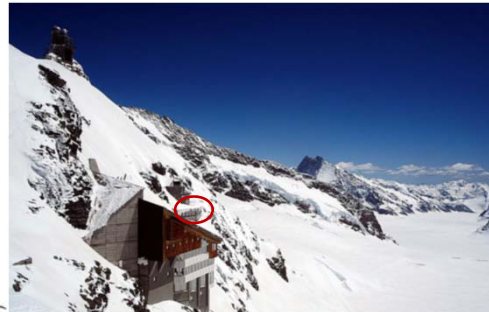
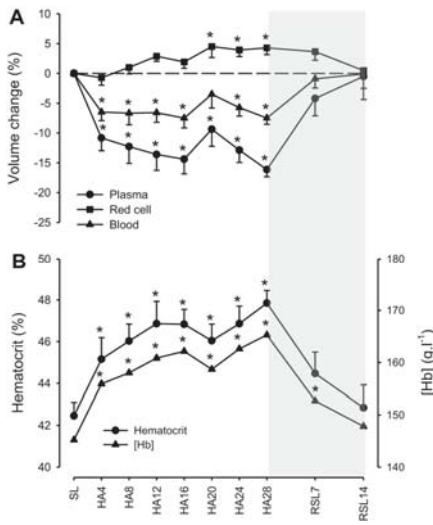
60 days on Mt. Everest
→ 25% increase
(AMREE Studie)

65 days at 5260 m
→ 35% increase
(Chacaltaya Study)

Milledge, Ward and West. High Altitude
Physiology and Medicine, Chapman and Hall



Changes in intravascular volumes (A) and hematocrit and Hb concentration in venous blood (B) during and after exposure to 3,454 m.



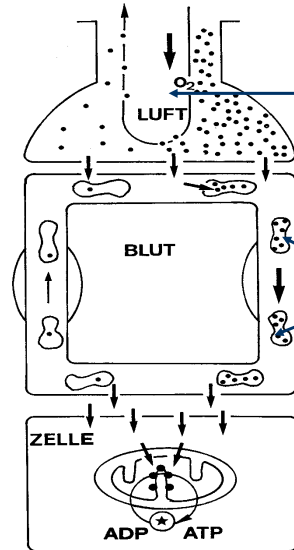
- Nach 3 Tagen CaO₂ im Blut gleich hoch wie im Tiefland, nach 12 Tagen ca. 15% höher
- Review: Siebenmann, JAP 2017 epub ahead of print

C. Siebenmann et al. J Appl Physiol 2015;119:1194-1201

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Effect of Acclimatization on O₂ Transport



Further increase of ventilation by ca. 50 % (4300 m)

Increase in [Hb] by < 30 % above 5000 m, depending on altitude and duration of exposure

At 4100 m completed in 2 weeks

Lundby, AJP 2004



Improved Performance after 10 wks at 5260 m

	ergometer: 10 min. 120 W		
	acute	after 9-10 weeks	
heart rate (min ⁻¹)	159	132	
perceived exertion	very hard	hard	
hemoglobin (g %)	14,0	18,5	RBC ↑ + PV↓
PaCO ₂ (mmHg)	27	21	ventilatory acclimat.
SaO ₂ (%)	63	75	ventilatory acclimat.
O ₂ content (ml/L blood)	124	196	> vs low altitude

Calbet, AJP 184:R304-316, 2003



3. HIF-dependent Gene Expression

hypoxia

prolyl-hydroxylase

O_2

Abbau

phosphorylation

nucleus

cytoplasm

200+ genes

HRE

Change of expression of about 1000 genes accounting for (amongst others):

- RBC ↑ (Erythropoietin)
- Ventilatory acclimatization
- Vessel growth and vascular permeability ↑ (VEGF)
- Shift fat → glucose metabolism
- Mitochondria ↓ → ROS ↓

Hofer et al., Pflügers Arch.Europ.J.Physiol. 443:503 (2002)
Semenza, Physiology 24:97 (2009)

Downsides of Acclimatization Processes

- **VEGF:** - BBB-leak with microhemorrhages in severe hypoxia/hypoxemia, prevention with in mice with VEGF neutralizing antibodies (Schoch, Brain 2002)

Schommer, Neurology 2014

Swenson, JAMA 2002

- Role in HAPE ? (no VEGF found in BAL fluid at 4559 m)
- **Ventilatory acclimatization** contributes to an increase of periodic breathing during sleep with acclimatization

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