Pediatric cardiopulmonary challenges of altitude

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Switzerland
No conflict of interest.
Introduction
High Altitude

Introduction
### Introduction

Höhenluft bzw. „Hypoxie“

<table>
<thead>
<tr>
<th>Höhe (m)</th>
<th>p Luft (hPa)</th>
<th>p O₂ (hPa)</th>
<th>O₂ Vol (%)</th>
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<td>4.000</td>
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<td>20,9</td>
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<td>212</td>
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</tbody>
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100.00 mm Hg $\rightarrow$ 133.32 hPa
Introduction
Introduction

Copacabana – Titicaca, 3812m
Introduction

Copacabana – Titicaca, 3812m
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Little Matterhorn – Wallis, 3883m
Introduction

Little Matterhorn – Wallis, 3883m
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Introduction
Introduction
High altitude (>2500m)

Oxygen saturation of hemoglobin is < 90%

Tissues are hypo-oxygenated
Adaptation

Hypoxia/Hypoxemia stimulate the cardiovascular system to adapt in order to maintain a sufficient oxygenation of the tissues.
Adaptation to altitude

- Erythrocytosis
- Increased affinity of oxygen-hemoglobin
- Pulmonary vasoconstriction, cerebral vasodilation
- Increased ventilation and cardiac output
Adaptation and acclimatization

Changes from low altitude [%]

Days at altitude

- Sympathetic activity
- Pulmonary artery pressure
- Mean systemic blood pressure
- Heart rate
- Cerebral blood flow
- Cardiac output
- Stroke volume
Interindividual variability

Changes from low altitude [%]

Days at altitude

Pulmonary artery pressure

Sympathetic nerve activity

Blood pressure
Alterations observed at 2500 m

- Mood, impulse control
- Personnality trait
- Sense of reality
- Visual sensitivity
- Balance
- Concentration
- Memory
- Orientation
- Decision making
- Reaction time
- Hearing sensitivity
- Judgment
- Behavior
- Manual ability
- Affect
- Character
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Acute and Chronic Altitude-Induced Cognitive Dysfunction in Children and Adolescents

Stefano F. Rimoldi, MD¹, Emrush Rexhaj, MD¹, Hervé Duplain, MD², Sébastien Urban, MD³, Joël Billieux, MD⁴, Yves Allemann, MD¹, Catherine Romero, RN⁵, Alejandro Ayaviri, MD⁵, Carlos Salinas, MD⁵, Mercedes Villena, MD⁵, Urs Scherrer, MD¹,⁶, and Claudio Sartori, MD²

**Digit Span (# digit)**

<table>
<thead>
<tr>
<th></th>
<th>Sea Level</th>
<th>Acute Altitude</th>
<th>Chronic Altitude</th>
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<td>A</td>
<td>6</td>
<td>6</td>
<td>6</td>
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<tr>
<td>B</td>
<td>12</td>
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<td>12</td>
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**Corsi Block (# items)**

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<tr>
<td>D</td>
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**CVLT (# words)**

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<tr>
<td>D</td>
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**TMT part A (msec)**

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<td>D</td>
<td>25</td>
<td>25</td>
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</table>
What may happen?

1. **AMS** – acute mountain sickness

2. **HACE** – high altitude cerebral edema

3. **HAPE** – high altitude pulmonary edema

4. **Re-Entry HAPE** – high altitude residents HAPE

5. **CMS** – Chronic Mountain sickness (Monge)
What may happen?

1. **AMS** – acute mountain sickness

2. **HACE** – high altitude cerebral edema

3. **HAPE** – high altitude pulmonary edema
AMS

- Irritability
- Headache
- Anorexia
- Dizziness
- Nausea, vomiting
- Sleep disturbances
- Asthenia

(CAUTION! YOU ARE AT 17586 FT (5360 M)  
  ✓ Do not exert  
  ✓ Try not to spend more than 20 minutes here  
  ✓ Refrain from smoking  
  ✓ In case of breathlessness and/or chest pain, seek medical attention immediately  
  ✓ Protect your eyes from sunlight by wearing goggles)
AMS Incidence

Children and Adolescents 22% to 27%

↓↑

Adults 48% to 62%


AMS Treatment

- Recovery
- Symptomatic treatment
- Acetazolamide 2.5mg/kg/dose 2-3x/d
- Descent when symptoms persist
HACE

- Irritability
- Headache
- No appetite
- Dizziness
- Nausea
- Sleep disturbances
- Asthenia
- Severe headache
- Ataxia
- Coordination disturbances
- Consciousness ↓
- Loss of focal neurologic functions
- Dyspnea
- Tachypnea
- Tachycardia
- Dry or productive cough
HACE

Never been reported in children

Low incidence (0.3%) – high mortality

The cerebral effects of ascent to high altitudes Mark H Wilson, MRCS, Stanton Newman, DPhil, Chris H Imray, FRCS The Lancet Neurology Volume 8, Issue 2, Pages 175-191 (February 2009)
Figure 1: Proposed pathophysiology of AMS and HACE
HACE Treatment

- Urgent evacuation
- Oxygen
- Decompression chamber
- Dexamethasone 0.15mg/kg 4x/d
HAPE

Dyspnea
Tachypnea
Tachycardia
Dry or productive cough
Hemoptysis
HAPE Incidence

Adults 1%
Children 0%

↓↑

Adolescents 17%
(re-entry HAPE)
HAPE Clinic

Tachypnea, Cough, Tachycardia

36 to 72 hours after arrival at high altitude
HAPE

Pathophysiology

1. Exaggerated pulmonary arterial hypertension
2. Decreased alveolar fluid clearance

Patient at risk

1. Congenital heart disease
2. Pulmonary disease
3. Trisomy 21
4. Epigenetics (perinatal Hypoxia, Preeclampsia, IVF)


But...

Exaggerated pulmonary arterial hypertension is not sufficient to trigger pulmonary oedema in humans

Trisomy 21

P < 0.05
The Barker hypothesis
Developmental origin of adult diseases

Environmental insults occurring during the fetal / perinatal period

Low birth weight

Augmented risk of cardiovascular diseases in adulthood
Coronary heart disease, Hypertension, Diabetes

Systemic vascular dysfunction
Transient perinatal hypoxia predisposes to exaggerated hypoxic pulmonary hypertension later in life.

Sartori et al, Lancet 1999;353:2205-07
Offspring of preeclampsia, a novel risk factor for hypoxic pulmonary hypertension?

<table>
<thead>
<tr>
<th></th>
<th>Incidence of HAPE (%)</th>
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<tbody>
<tr>
<td>Preeclampsia</td>
<td>100</td>
</tr>
<tr>
<td>No preeclampsia</td>
<td>0</td>
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</table>

(n=4)
Preeclampsia

Maternal circulation

Vasoactive substances

Long-term vascular dysfunction in the offspring?
Offspring of mother with preeclampsia display pulmonary hypertension at high altitude
Vascular dysfunction later in life

Premature cardiovascular diseases
Assisted Reproductive Technologies

Have been done for almost 3 decades
Account for a steadily increasing number of births
Make up for 1-4% of the population in developed countries
Assisted reproductive technology (ART)
Hypothesis

Early embryonnaal

ART

Long-term vascular dysfunction?
Methods

65 healthy children (11±2 y) born by ART
57 age-, sex-, birth weight- and gestational age-matched controls

3450 m for 72 hours

Pulmonary and systemic vascular function
Pulmonary-artery pressure
Flow-mediated vasodilation
Pulse wave velocity
Exaggerated hypoxic pulmonary hypertension in children born from ART

Scherrer et al., Circulation 2012; 125:1890-1896
Vascular dysfunction in ART children is induced by ART per se and not to parent related factors.
Vascular dysfunction later in life

Premature cardiovascular diseases
<table>
<thead>
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Risk factors for AMS

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<tr>
<th>Risk Factor</th>
<th>Description</th>
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<tbody>
<tr>
<td>Rate of ascent</td>
<td>In adults, rapid ascent is associated with a higher incidence of AMS</td>
</tr>
<tr>
<td>Absolute altitude gained</td>
<td>In adults, the incidence of altitude illness increases with increasing altitude and with height gain from previous sleeping altitude.</td>
</tr>
<tr>
<td>Exertion</td>
<td>Possible factor in adults</td>
</tr>
<tr>
<td>Cold</td>
<td>Risk factor for HAPE</td>
</tr>
<tr>
<td>Preceding viral respiratory infections</td>
<td>May increase the incidence of HAPE among native-lowland children who ascend to high altitude.</td>
</tr>
<tr>
<td>Unilateral absence of the right pulmonary artery or primary pulmonary hypertension</td>
<td>Increases the risk of HAPE</td>
</tr>
<tr>
<td>Perinatal pulmonary hypertension</td>
<td>Perinatal hypoxia and pulmonary hypertension may cause an increased risk of pulmonary hypertension at altitude; this has not yet been associated with HAPE.</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>Common lesions such as ASD, PDA, and VSD may increase the risk of altitude illness, especially HAPE.</td>
</tr>
<tr>
<td>Individual susceptibility</td>
<td>Some individuals develop recurrent HAPE that relates to exaggerated hypoxic pulmonary vasoconstriction. It is possible that this may be an inherited susceptibility. A low hypoxic ventilatory response may possibly be a risk factor for HAPE. Impaired alveolar liquid clearance also may contribute to the pathogenesis of HAPE. There are likely to be factors that increase susceptibility to AMS and HACE.</td>
</tr>
<tr>
<td>Reascent to altitude</td>
<td>Children who normally reside at altitude, who reascend to altitude after a trip to sea level, are at increased risk of HAPE.</td>
</tr>
<tr>
<td>Organized groups</td>
<td>Travelers in organized parties may be at an increased risk of dying from altitude illness, probably as a result of reduced flexibility in the itinerary.</td>
</tr>
</tbody>
</table>

Pollard A. and al.,
High Altitude Med Biol 2001;2:389
Prevention of high altitude sickness

1. Planning and education

1. Steady ascent above 3000m
   (300-400m/day)

3. First day – keep it quiet!

4. Hydration and nutrition

5. Sun protection APF 30-50
Prevention of high altitude sickness

http://www.kardiologie.insel.ch/de/spezial-sprechstunden/hoehenmedizinsprechstunde/
Ignacio, 5 months old

Born full term, no complications
Breast feeding, gaining weight
The family wants to go to Bogota, altitude 2640 m, to meet the grand parents. Should they:

  Cancel the trip because the baby is too young?
  Take an oxymeter with them?
  Advise and go
AMS is not specific in children!

- Increased fuzziness
- Decreased play
- Decreased appetite
- Poor sleep
Modified Lake Louise Score

1. Amount of unexplained fussiness when awake during the past 24 hours
   (0) No fussiness
   (1)
   (2)
   (3) Intermittent fussiness
   (4)
   (5)
   (6) Constant fussiness

2. Intensity of fussiness when awake
   (0) No fussiness
   (1)
   (2)
   (3) Moderate
   (4)
   (5)
   (6) Very strong

3. How well has your child eaten today?
   (0) Normal
   (1) Slightly less than normal
   (2) Much less than normal
   (3) Vomiting or not eating

4. How playful is your child today?
   (0) Normal
   (1) Playing slightly less
   (2) Playing much less than normal
   (3) Not playing

5. The ability of your child to sleep today is
   (0) Normal
   (1) Slightly less or more than normal
   (2) Much less or more than normal
   (3) Not able to sleep

Total Activity Score = (3+4+5)=

Total Fussiness Score = (1+2)=

- Is the Fussiness Score 4 or higher?
- Is the Activity Score 3 or higher?

If you answered ‘Yes’ to both questions, then AMS is the diagnosis.
Ignacio, 5 months old

Born full term, no complications
Breast feeding, gaining weight
The family wants to go to Bogota, altitude 2640 m, to meet the grand parents. Should they:
  Cancel the trip because the baby is too young?
  Take an oxymeter with them?

Advise and go

Barben J, Paediatrica 2010;21:1
Hutter D, Paediatrica 2006:17:1
Clara, 12 years old

Cystic fibrosis DF 508 homozygote diagnosed at 13 months of age
Chronic colonisation with S. aureus
Infection with M. abcessus, under treatment
$\text{FEV}_1$ 29%, $\text{SpO}_2$ on room air 94%
A trip to Brazil is scheduled; what should we do?

- Nothing, let her go as she is
- Do a hypoxic challenge test
- Do a 6 minute walk test
- Give her oxygen for the flight anyways
What happens in flight?

Cabin pressure ≈ altitude 1’400-2’500 m
- FiO₂ and gas volume
- PaO₂ and SpO₂, even in healthy subjects

Who needs O₂ during a flight?

**NO**
- SpO₂ > 95%
- SpO₂ 92-95% no risk factors

**YES**
- SpO₂ < 92%
- Already on O₂

**MAYBE**
- Do a hypoxic challenge test
Hypoxic challenge test

Who?
- Ex premature baby < 1 y old at the time of travel, BPD
- Severe CF (FEV$_1$ < 50%)
- Severe restrictive lung disease
- Cardiac disease

How?
- Measure SpO$_2$ while breathing a gas mixture with 15.1% O$_2$
- No routine blood gas or ECG in children

Normal hypoxic challenge if SpO$_2$ > 85% during the test
What happens in flight?

Cabin pressure ≈ altitude 2’500 m

- FiO$_2$ and increased gas volume
- PaO$_2$ and SpO$_2$ even in healthy subjects

Who needs O$_2$ during a flight?

*Anyone with a SpO$_2$ < 85% or SpO$_2$ < 75% during > 1 minute*
Oxygen on board

Prepare well ahead of departure date!
Medical certificate
Enough medication supply
Compressed and liquid oxygen are prohibited on board aircraft (FAA, may 2016)

→ Portable oxygen concentrator (POC)
### Medical certificate template

<table>
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<th>Date: ____________________________</th>
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<tr>
<td>Patient name: ____________________</td>
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<td>Date of birth: ____________________</td>
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**Diagnosis:**
- COPD
- Interstitial lung disease
- Pulmonary hypertension
- Other ____________

- The use of supplemental oxygen at ____ L/min is required at all times. This includes the use of oxygen while in the airport terminal, during take-off and landing, and also while moving about in the aircraft cabin.

- The use of supplemental oxygen at ____ L/min is required only during flight.

- The patient (or caregiver) may adjust the oxygen flow setting to a maximum of ____ L/min, as needed during the flight to compensate for variance in symptoms, activity, or cabin pressure.

- The patient will be using a portable oxygen concentrator and will ensure that he/she is carrying an adequate supply of batteries.

- The patient or caregiver is able to see, hear, and respond to portable oxygen concentrator alarms, as needed.

**Physician signature:** ____________________________

**Physician name:** ____________________________

**Physician telephone number:** ____________________________
Kiara, 2 years old

Ex 28 WGA premie, twin, severe BPD
Severe RSV bronchiolitis (ICU) just before her 2\textsuperscript{nd} birthday

1 month later, the mother wants to go to Portugal by plane

Resting $\text{SpO}_2$ 97%, hypoxic challenge test $\text{SpO}_2$ 75%

Repeated HCT 5 months later, $\text{SpO}_2$ 87%
Ben, 17y

Wants to go ski with his dad
Previous episode of malaise while skiing in Saas Fee
  AMS prevention with acetazolamide 2.5mg/kg/d 2-3x/d
Severe cyanosis with tachypnea dyspnea, malaise
Did we miss something?
  Cardiac work up and hypoxic test
  ASD! Failed hypoxic test!
So double the acetazolamide dose?
Close the ASD?
Children at altitude

• Be sure this is a sensible holiday for children

• Young children can’t tell you how they feel

• Treatment for children with altitude illness is the same as for adults (but, smaller doses, prefer syrups!)

• Remember descent is the best treatment!

• When in doubt, refer to a specialised consult
Thanks

Research Group of Urs Scherrer
Yves, Stefano, Emrush, Rodrigo
Claudio Sartori
Audience
Thanks for listening to me...