High Altitude, High/Low Temperature

Marco Maggiorini
Medical Intensive Care Unit

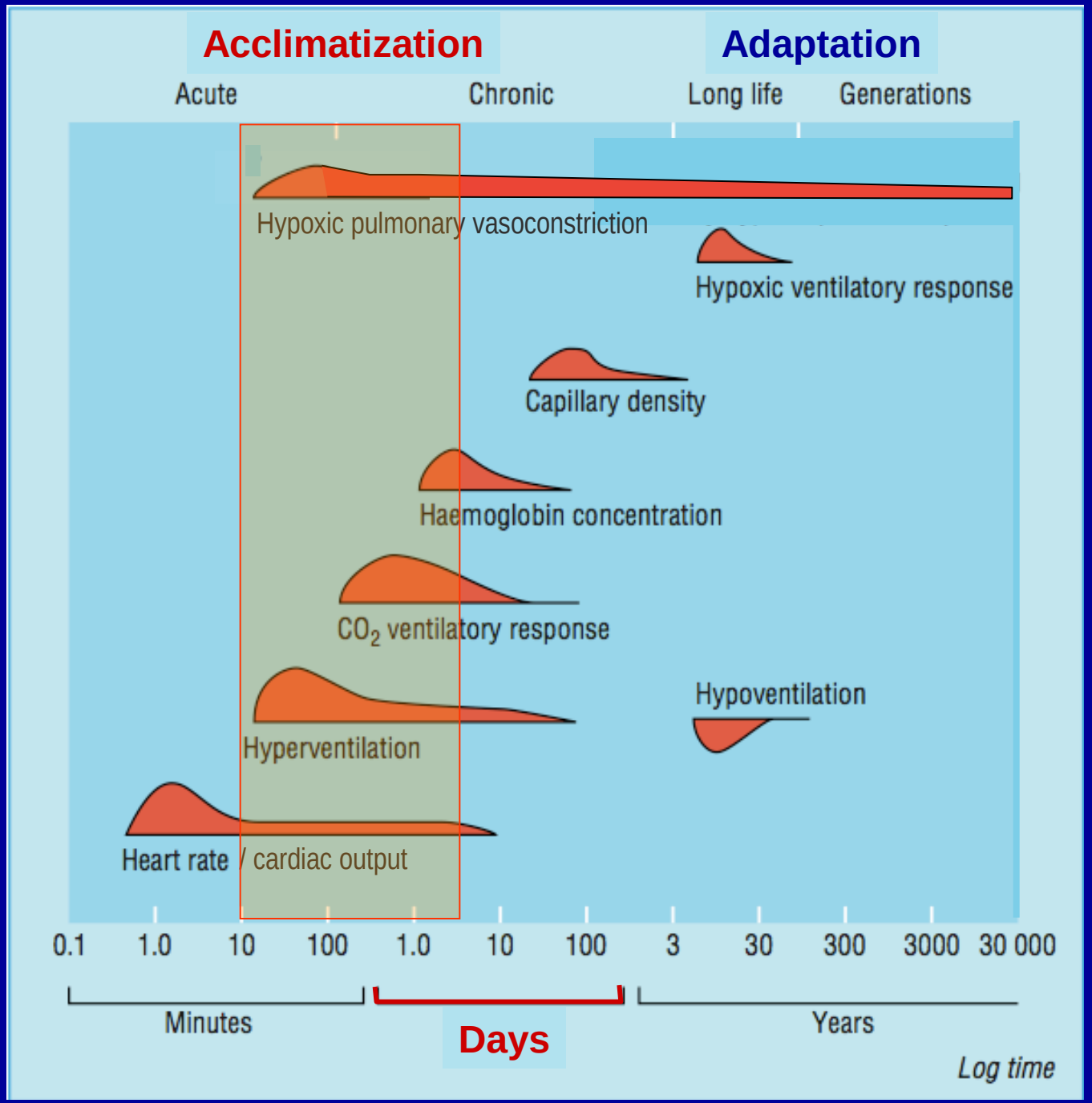
University Hospital Zürich

Illness of high altitude

- Individual inability to acclimatize
- Acute Mountain Sickness
- High Altitude Cerebral Edema
- High Altitude Pulmonary Edema

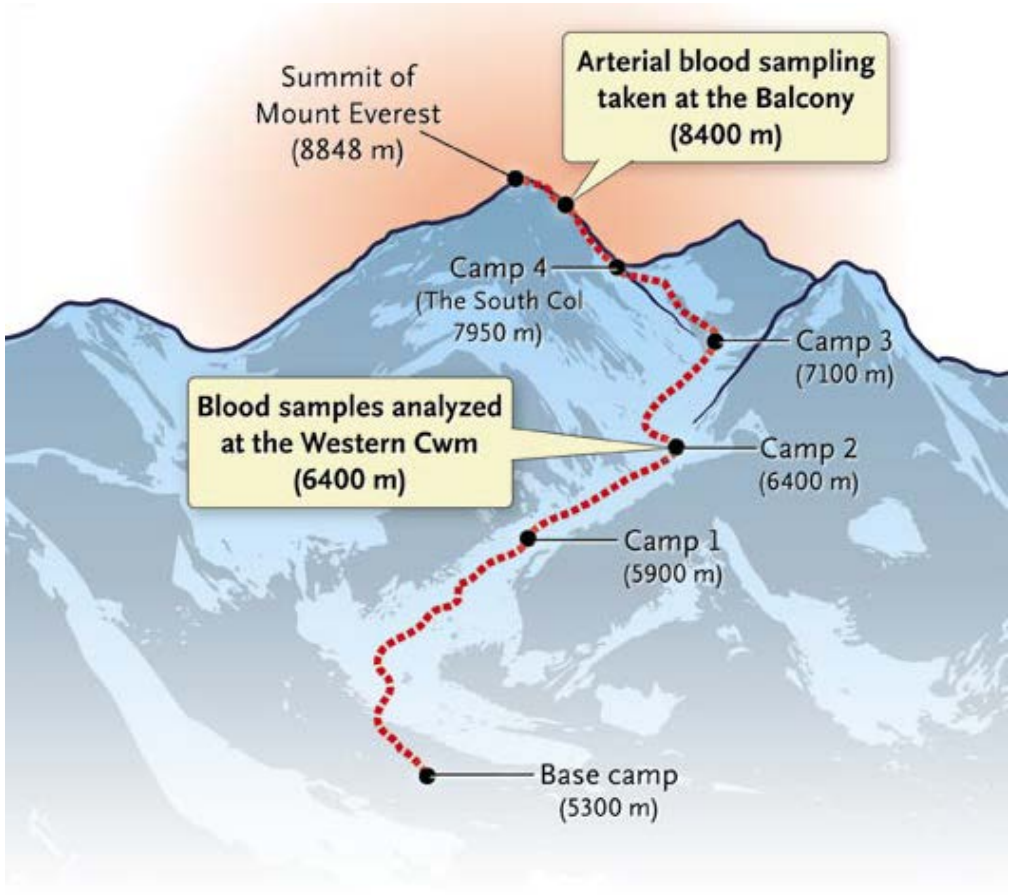
Alpubel plateau 3500m

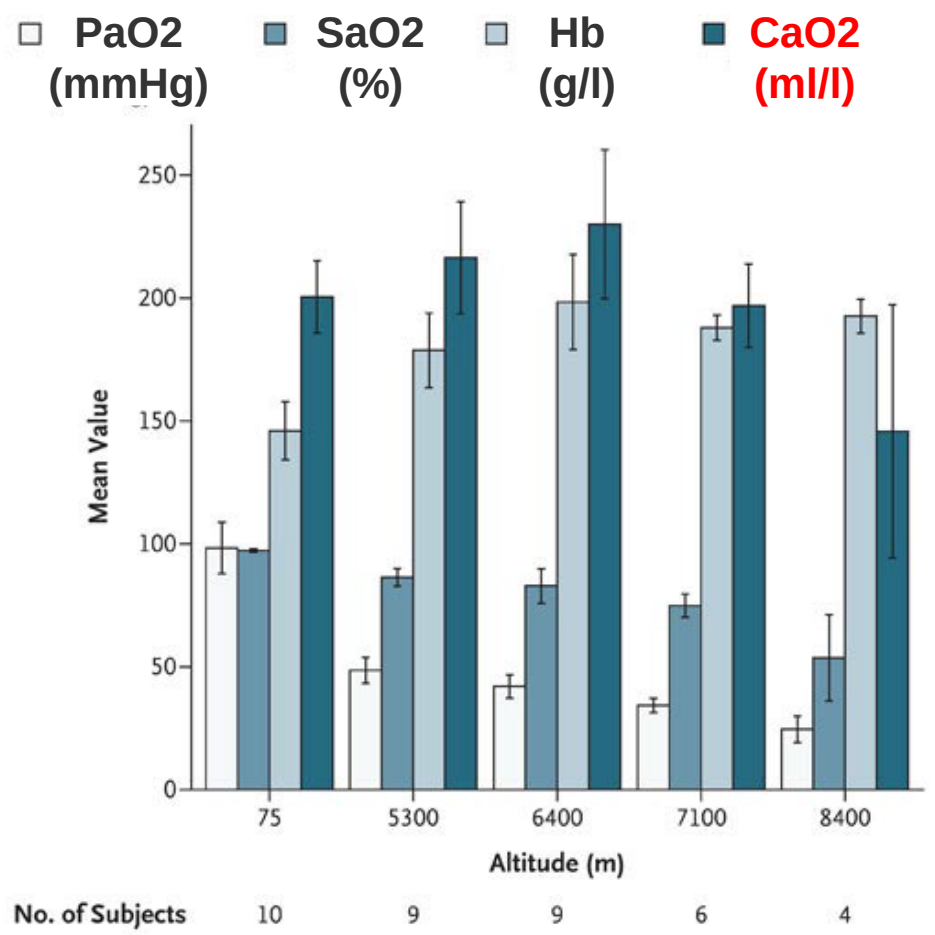
Physiologic response to hypobaric hypoxia



Oxygen transport at extreme altitude

$CaO_2 = SaO_2 \times Hb \times 1.39 + (PaO_2 \times 0.03)$





Grocott M. NEJM 2009 360:140

Headache mountains and fever slopes

Chinese Headache Mountain c. 30 BC

(Tseen Han Shoo Book 96)

"...Again passing the Great Headache Mountains, the Little Headache mountain, the Red Lands and the Fever Slope, men's bodies became feverish, they lose color and are attacked with headache and vomiting".

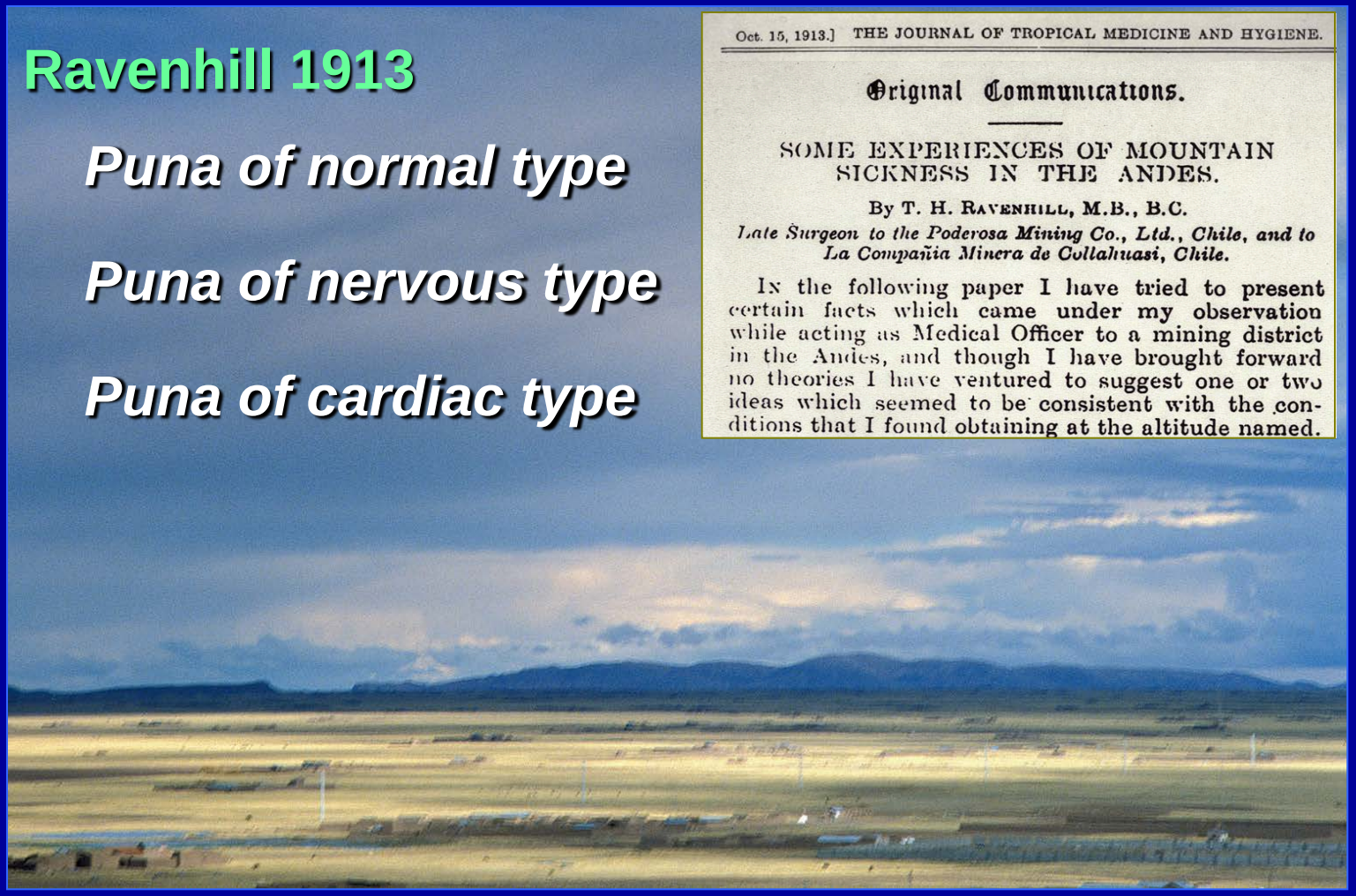
High altitude illnesses (Puna)

Ravenhill 1913

Puna of normal type

Puna of nervous type

Puna of cardiac type



Original Communications.

SOME EXPERIENCES OF MOUNTAIN SICKNESS IN THE ANDES.

By T. H. Ravenhill, M.B., B.C.

Late Surgeon to the Poderosa Mining Co., Ltd., Chile, and to La Compañia Minera de Collahuasi, Chile.

In the following paper I have tried to present certain facts which came under my observation while acting as Medical Officer to a mining district in the Andes, and though I have brought forward no theories I have ventured to suggest one or two ideas which seemed to be consistent with the conditions that I found obtaining at the altitude named.

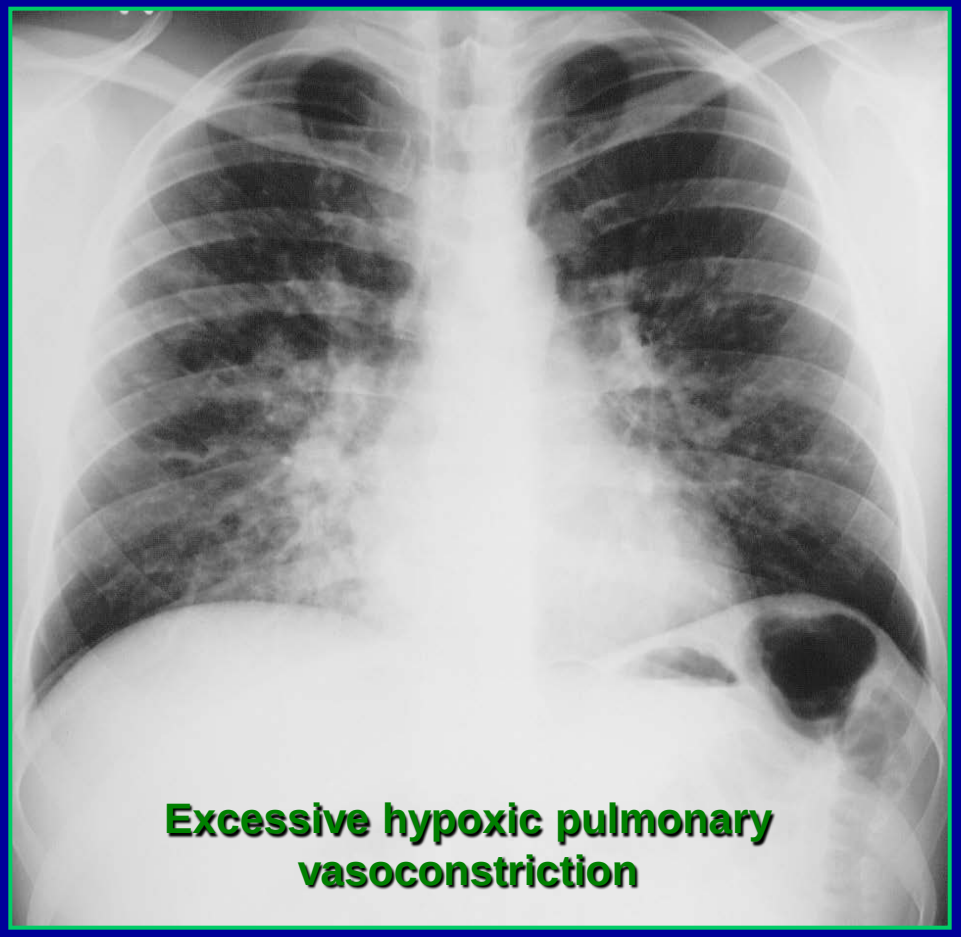
High altitude illnesses

Acute mountain sickness/HACE

Axiatl T_2-weighted MRI in HACE

Hackett et al JAMA 1998; 280: 1920-25

High altitude pulmonary edema



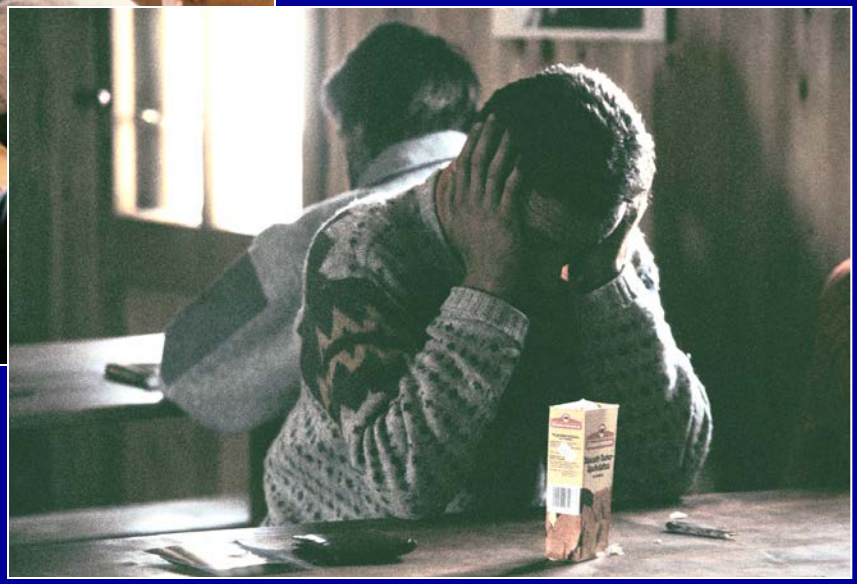
Symptoms of acute mountain sickness

Excessive fatigue

Lassitude

Nausea, Vomiting

Headache



Signs of acute mountain sickness

- Peripheral edema
  → Orbital, hands, feeds
- Lip cyanoses
- Mental dysfunction
- Ataxia

The Lake Louise consensus on definition of altitude illness

Acute mountain sickness (AMS)

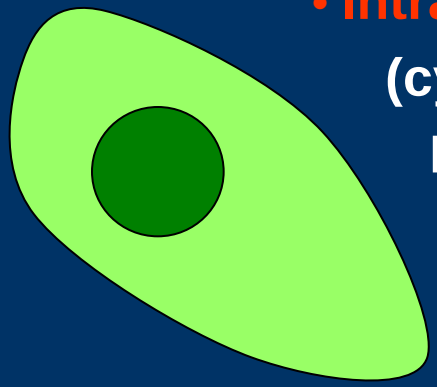
- Headache +
  - Gastrointestinal symptoms (anorexia, nausea, vomiting)
  - Fatigue or weakness
  - Dizziness or lightheadedness
  - Difficulty sleeping

- "Endstage" of AMS = High altitude cerebral edema (HACE)
  - Changes in mental status and/or
  - Ataxia in the presence of AMS

J.R. Sutton, G. Coats, C.S. Houston
Advances in the Biosciences: Hypoxia and Mountain Medicine Vol 84 1992

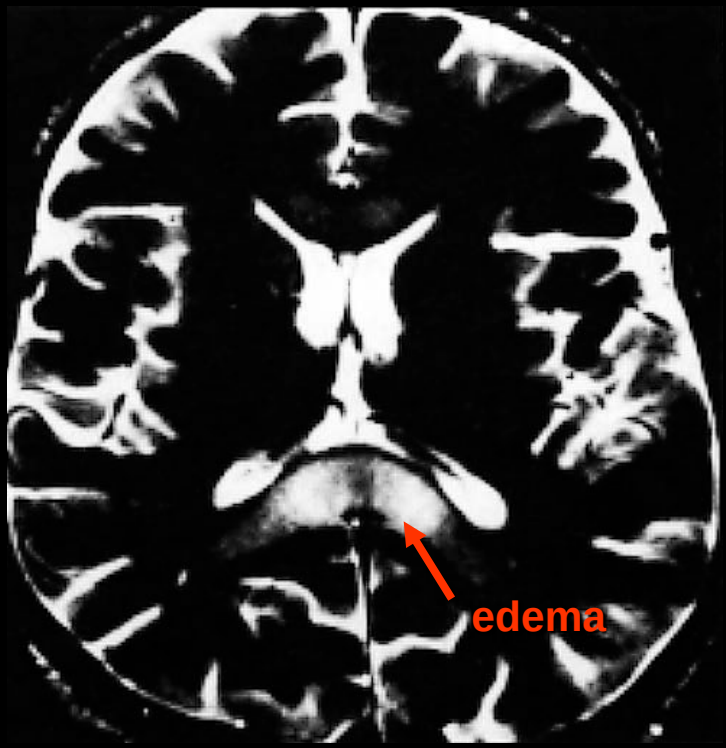
The brain in acute hypoxia

- ⇧ cerebral blood flow
- ⇩ impaired autoregulation
- ⇧ vessel permeability
  - vasogenic edema
  - ➔ edema corpus callosum and splenium



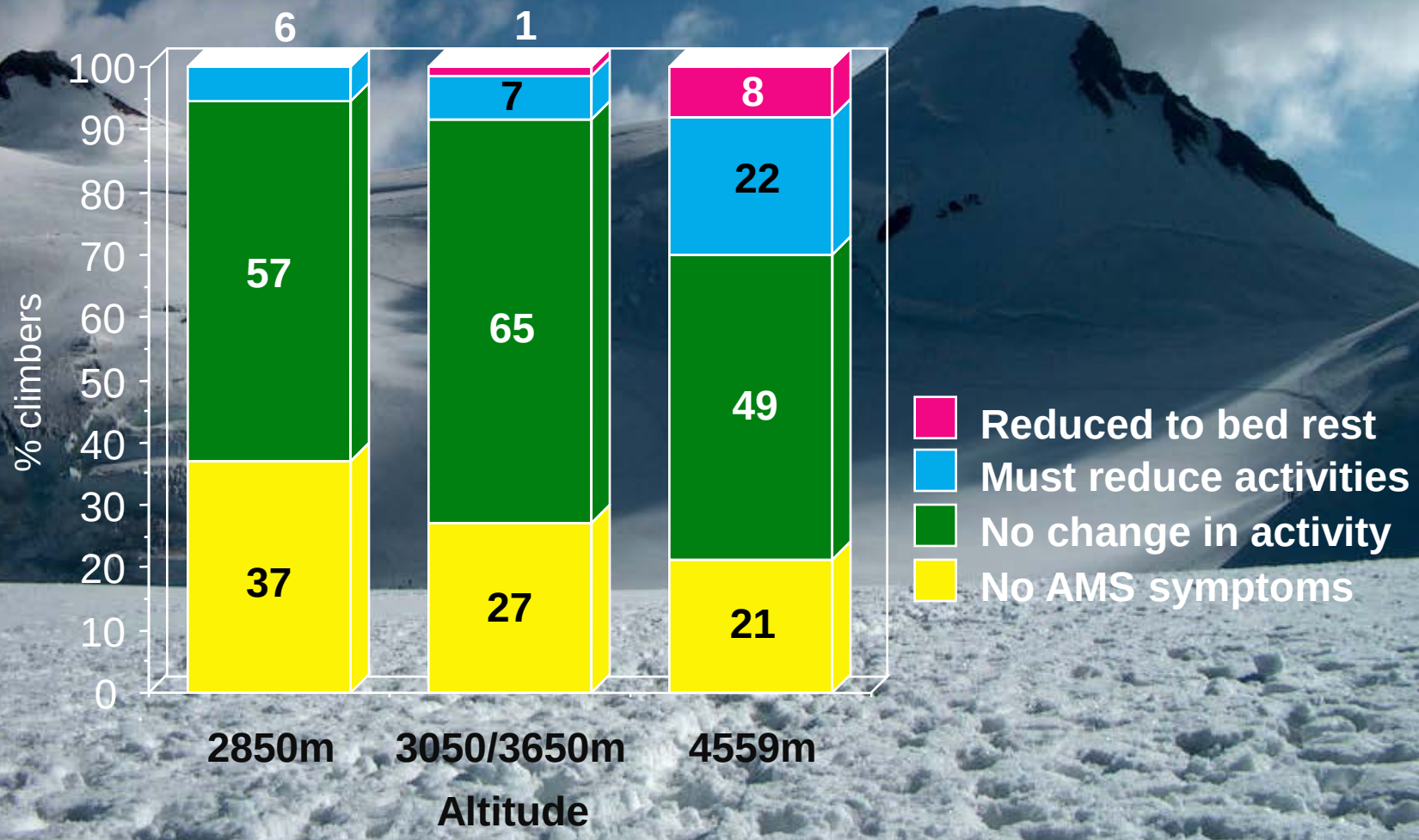
- Intracellular edema
  - (cytotoxic edema)
  - Mitocondrial dysfunction
  - Lactat-acidosis
  - O^{3-}, NOx

Axiatl T_2-weighted MRI in HACE

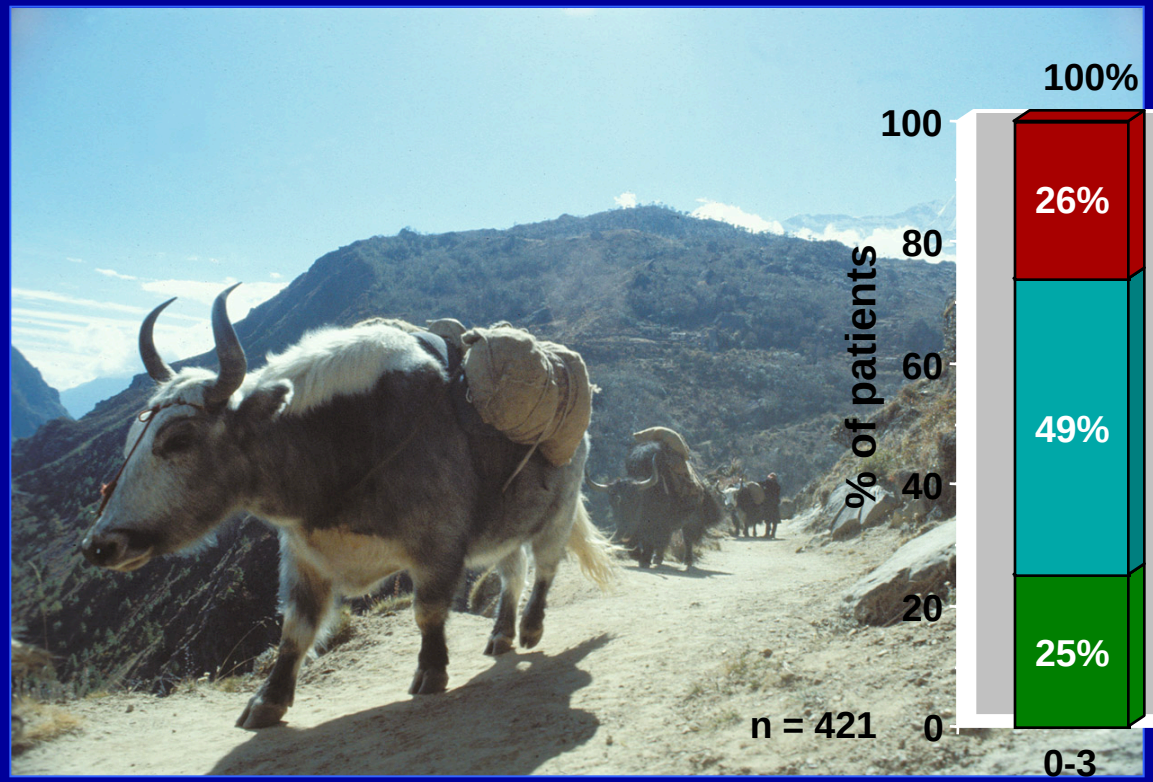


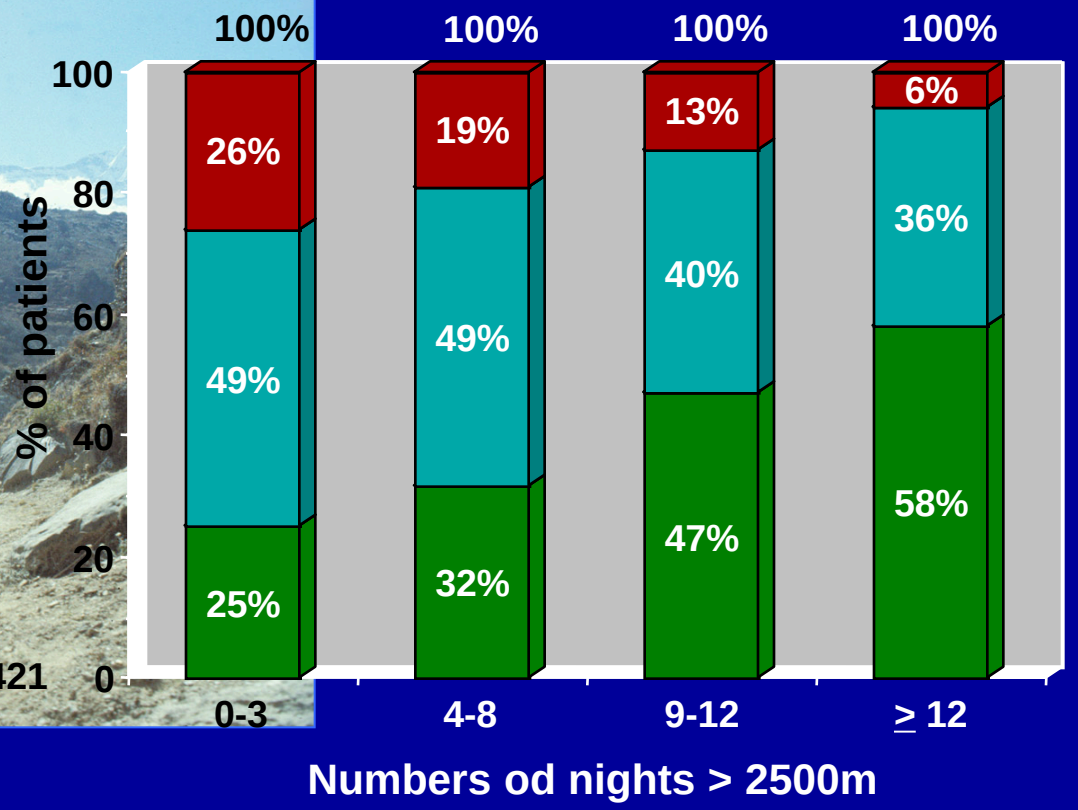
Hackett et al JAMA 1998; 280: 1920-25

Incidence of acute mountain sickness in the Swiss Alps



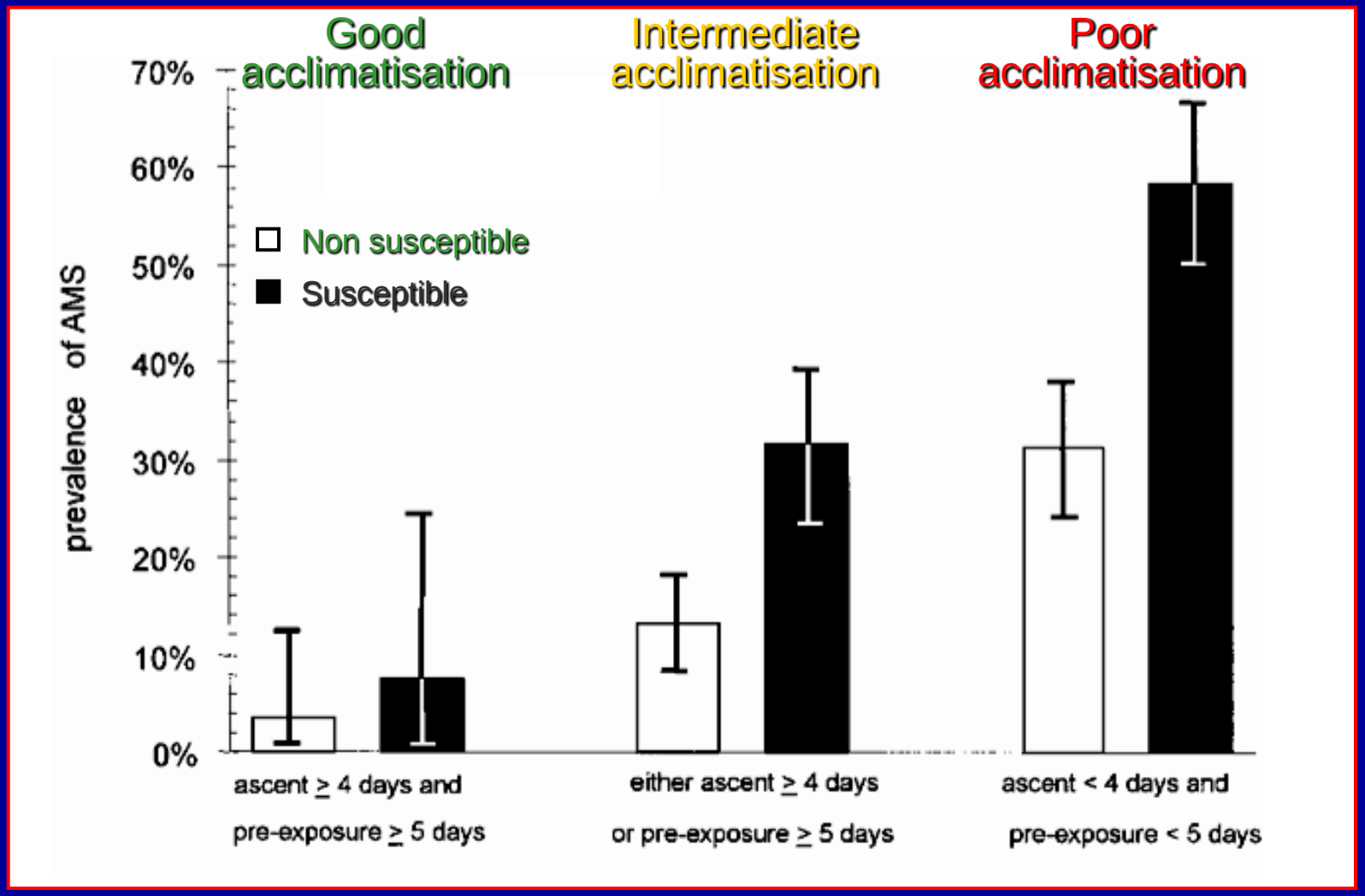
Prevention of high altitude illness





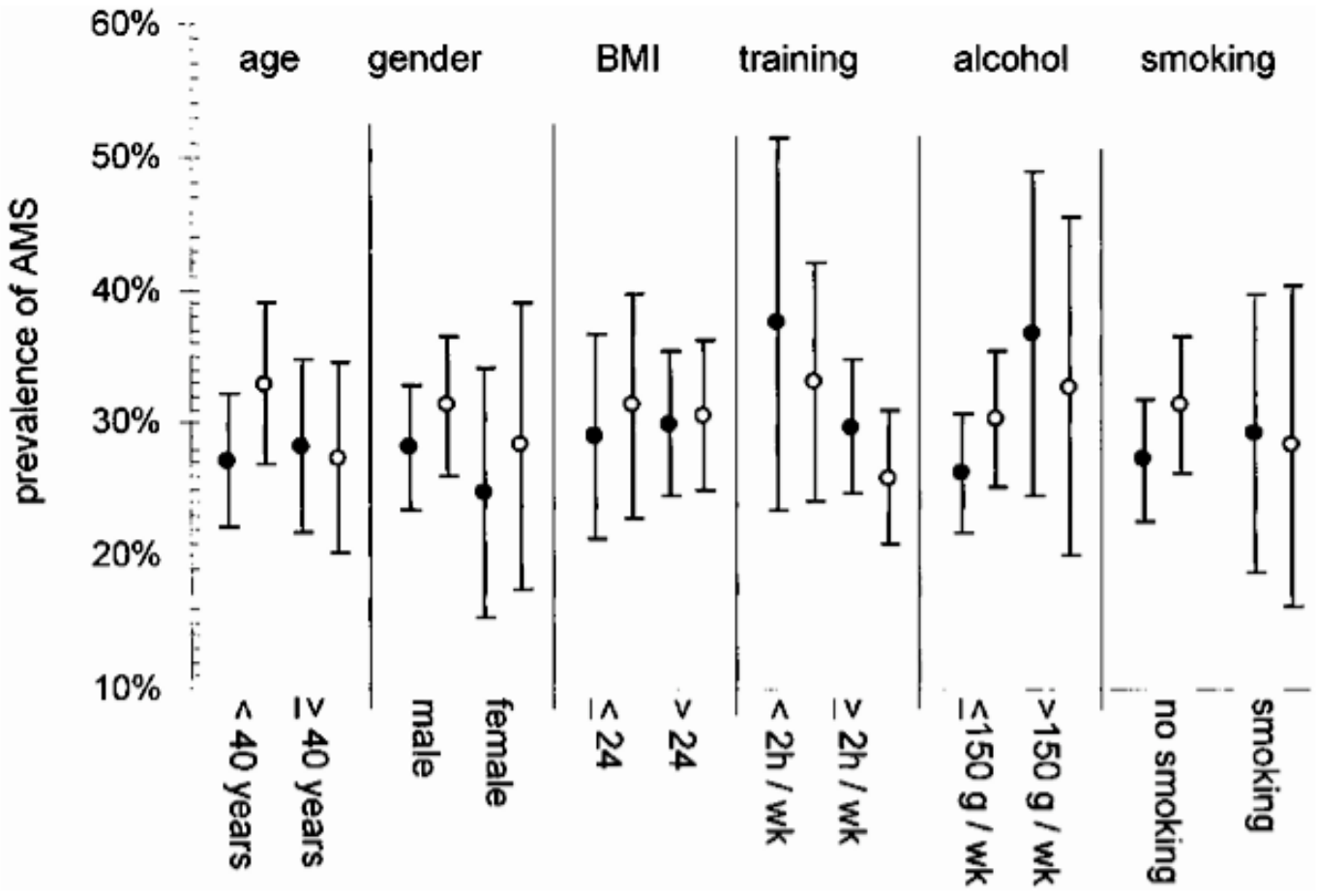
Rate of ascent < 600 m / day

Individual susceptibility is the major risk factor for AMS at 4559m



Schneider et al Med Sci Sports Exerc 2002;; 34:1886

Risk factors and prevalence of AMS during ascent to 4559m



Schneider et al
Med Sci Sports Exerc
2002,; 34:1886

Medical prophylaxis and treatment of AMS

Azetazoalmide

- **Mechanism**
  - Metabolic acidosis
- **Effect**
  - ⇧ Ventilation
  - ⇩ Periodic breathing

  ⇒ ⇧ PaO_2
- **Dosage**
  - 125 - 250 mg bid
- **Indikation**
  - AMS prophylaxis
  - Therapy of mild AMS

Dexamethasone

- **Mechanism**
  - ⇩ Cytoxines synthesis
  - ⇧ Cellular Na+-Transport
- **Effect**
  - ⇩ capillary leak
  - ⇧ diureses (Kidney tubuli)
  - ⇧ Water reabsorption (Alv. space)

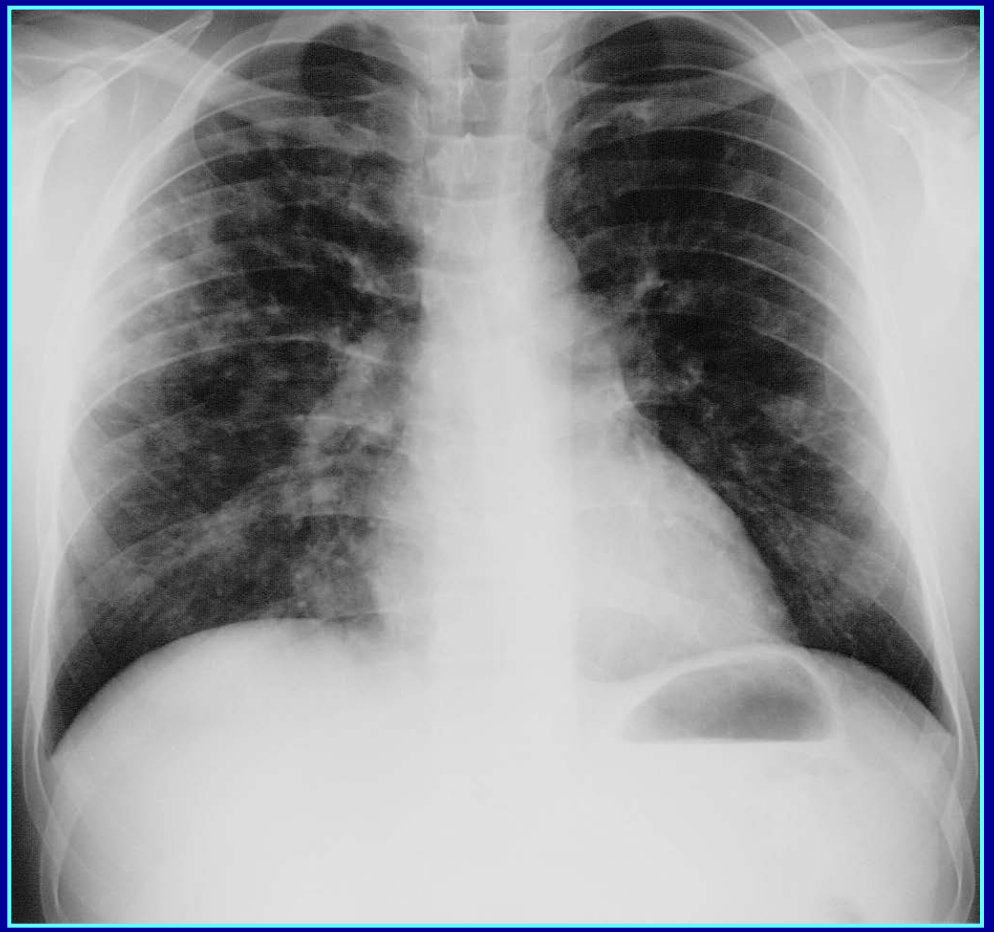
  ⇒ ⇩ Central dysfunction

  ⇒ ⇧ PaO_2
- **Dosage**
  - 8 - 16 mg per day
  - Therapy of moderate to severe AMS

High Altitude Pulmonary Edema

Central distributed infiltrates

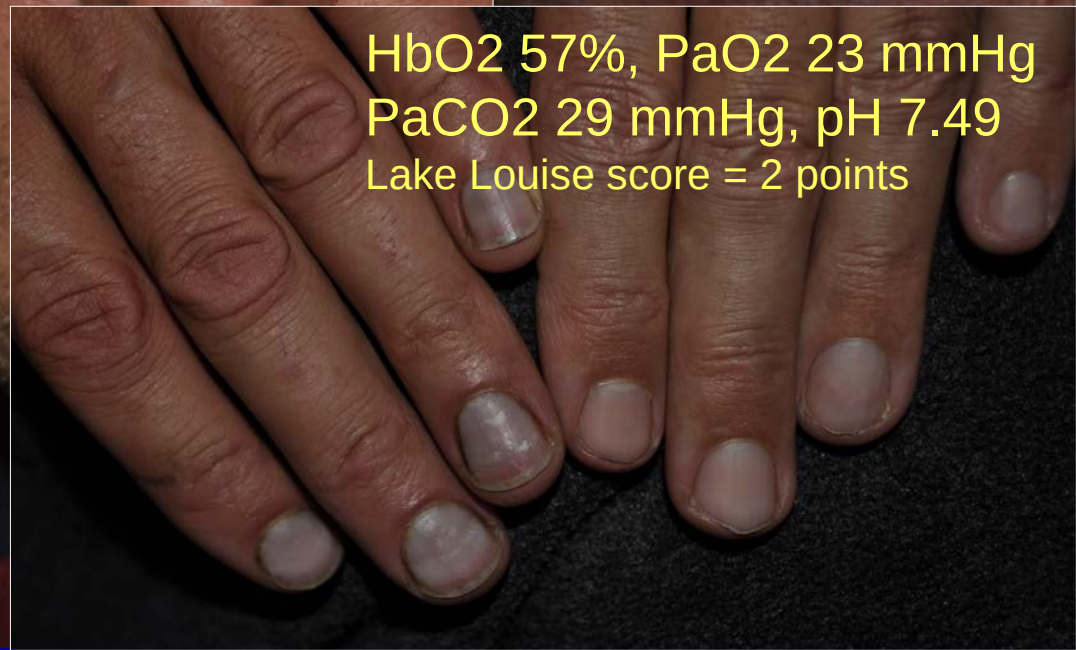
Peripheral distributed infiltrates



Clinical Presentation of HAPE

Symptoms and Signs

- Weakness / Decreased Exercise Performance
- Dyspnoe at Rest, Othopnoe
- Cough, Cracels bloody sputum
- Chest tightness or congestion
- Tachycarda > 90/min
- Tachypnoe > 25/min
- Cyanosis, SpO2 < 70% (4500m)
- Lung: Rales or wheezing
- Body Temperature > 37.4 ° C



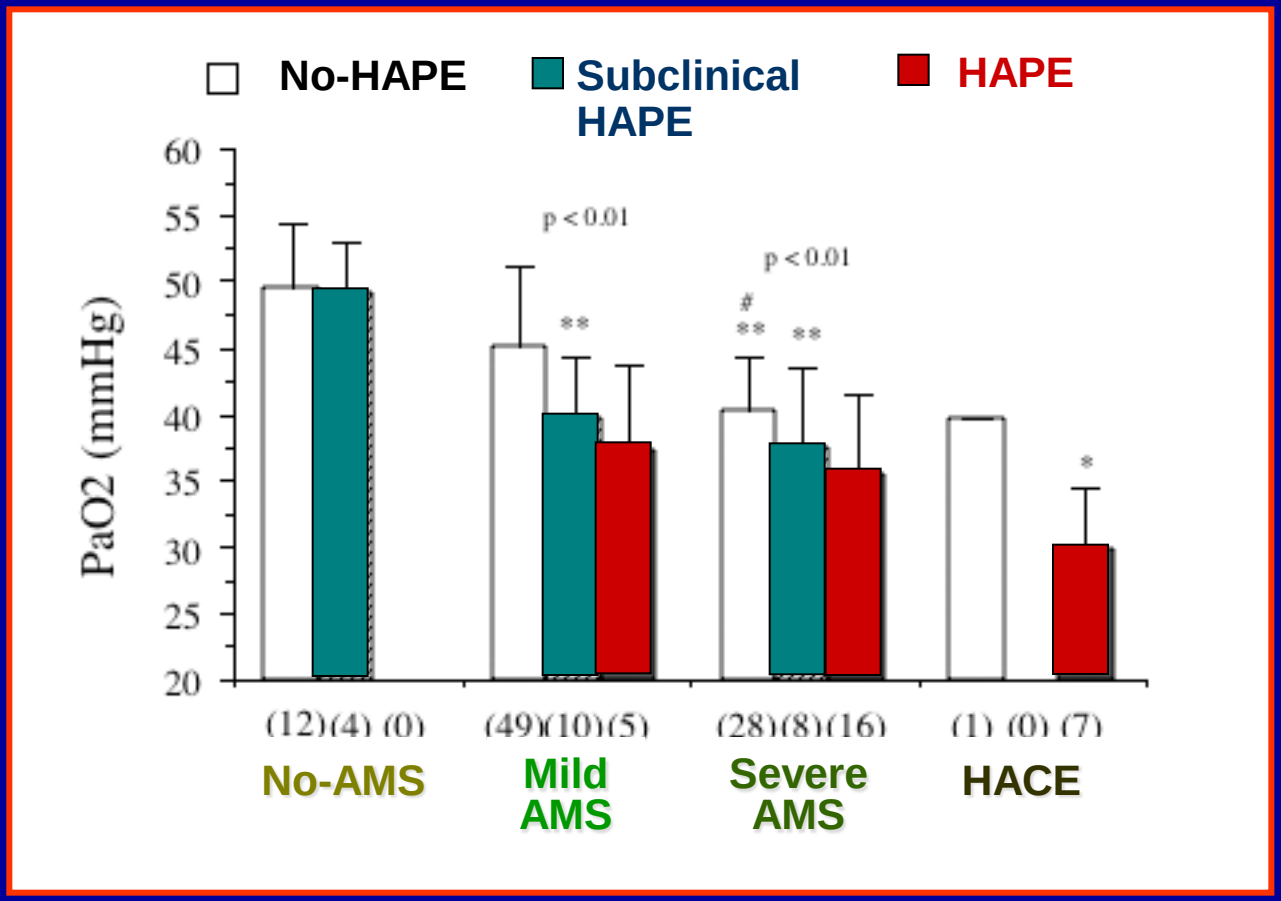
HbO2 57%, PaO2 23 mmHg
PaCO2 29 mmHg, pH 7.49
Lake Louise score = 2 points

Clinical diagnosis of high altitude pulmonary edema

		Rx's without HAPE 122	Rx's with HAPE 32
Dyspnea at rest	(11)	9%	91%
Tachypnea (> 25 breath/min)	(20)	55%	45%
Lung auscultation:			
no rales	(127)	85%	15%
rales +	(18)	61%	39%
rales ++	(9)	33%	67%

(Data were obtained from 60 subjects studied during 3 consecutive days at the altitude of 4559 m)

High altitude pulmonary edema may develop with only mild AMS



* p < 0.05 vs. mild and severe AMS; ** p < 0.01 vs. no-AMS; # p < 0.01 vs mild AMS

The Lake Louise consensus on definition of altitude illness

High altitude pulmonary edema (HAPE)

Symptoms: (at least two)

- Dyspnoe at rest
- Cough
- Weakness or decreased exercise performance
- Chest tightness or congestion

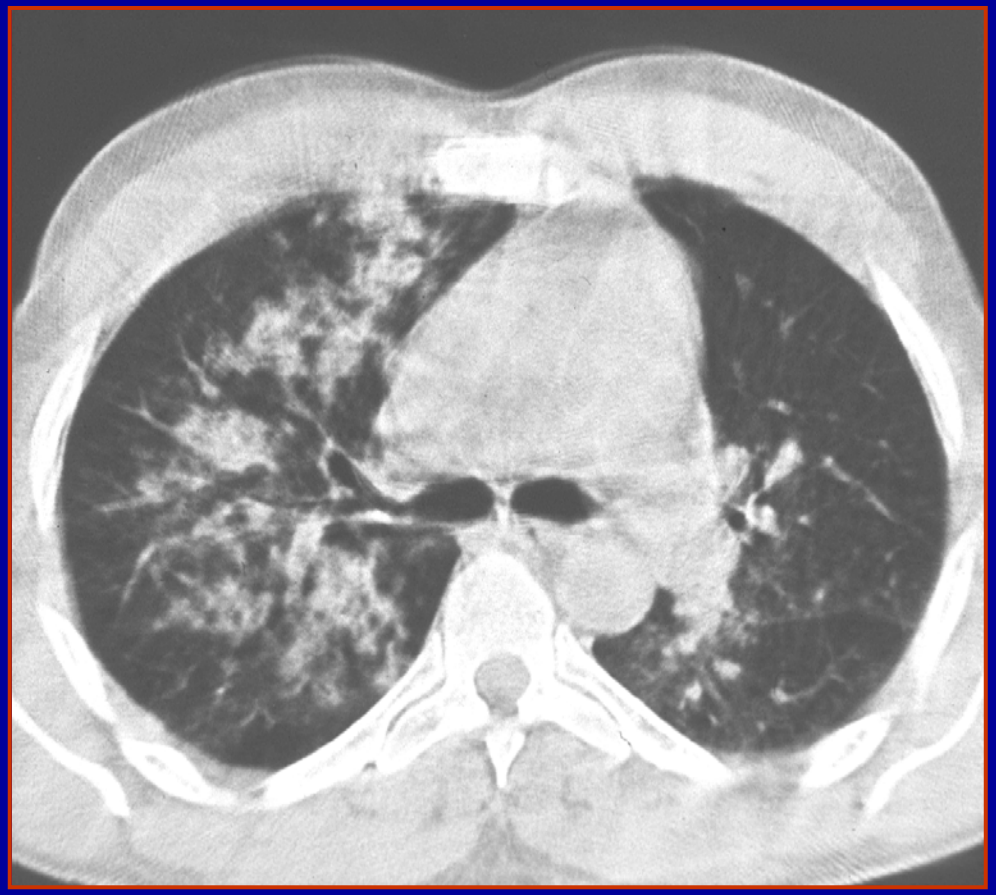
Signs: (at least two)

- Rales and wheezing in at least one lung field
- Central cyanosis
- Tachypnoe
- Tachycardia

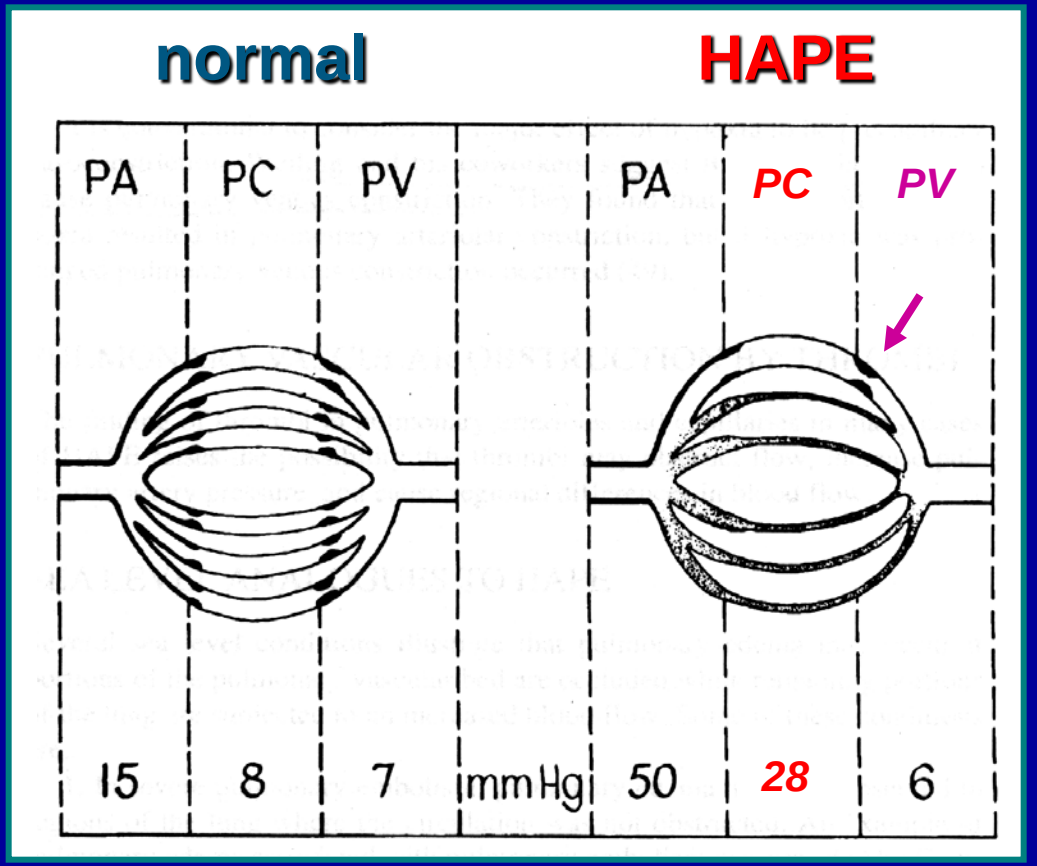
J.R. Sutton, G. Coats, C.S. Houston
Advances in the Biosciences: Hypoxia and Mountain Medicine Vol 84 1992

Pathophysiology of High Altitude Pulmonary edema: The overperfusion of PC and Venoconstriction

HAPE: patchy distributed infiltrates

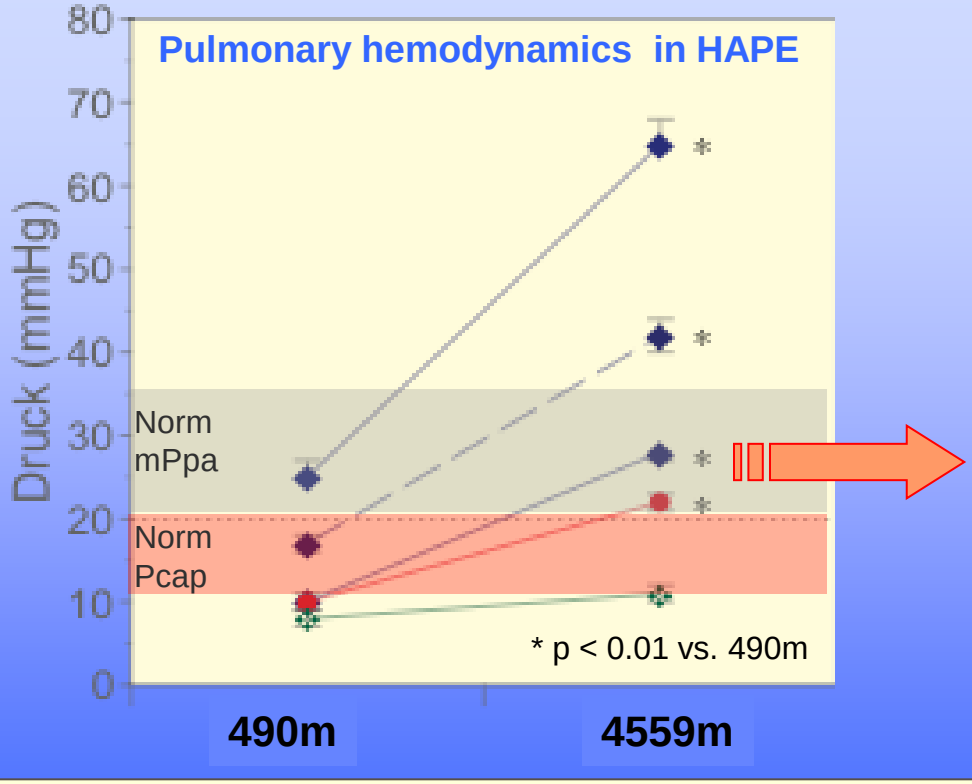


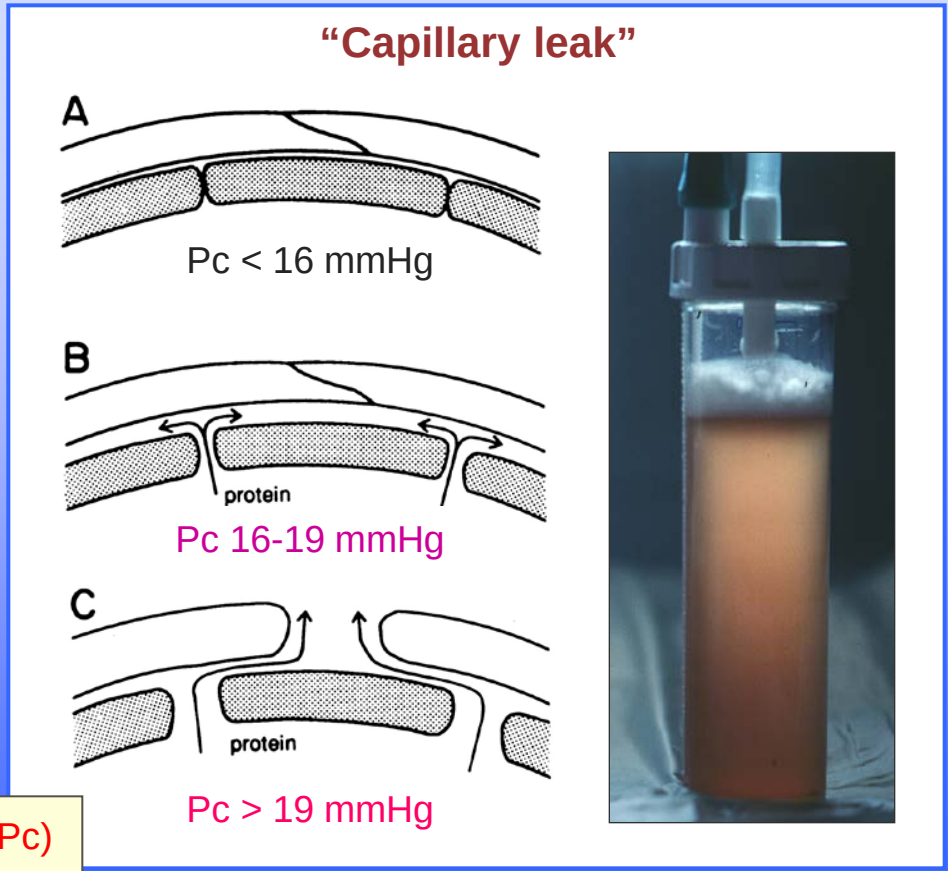
Uneven hypoxic vasoconstriction



Elevated pulmonary capillary pressure leads to a leakage of blood gas barrier

Excessive hypoxic pulmonary vasoconstriction





Pulonary artery pressure
- Systole
- Mean
- Diastole

- Pulmonary capillary pres. (Pc)
- Pulmonary aretry occluded pressure (Wedge pressure)

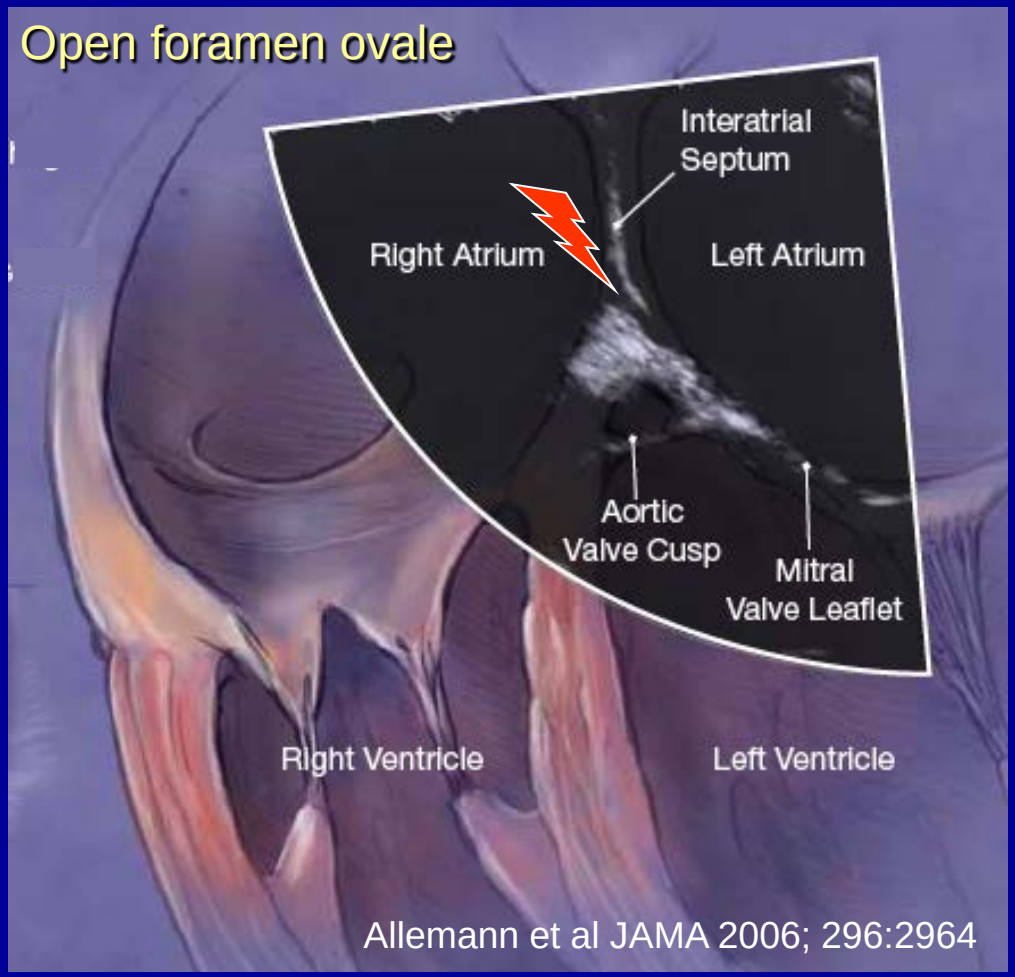
Maggiorini et al. Circulation 2001, 103: 2078
Swenson S et al. JAMA 2002, 287: 2226

Factors known to be associated with an increased risk of HAPE

Individual susceptibility

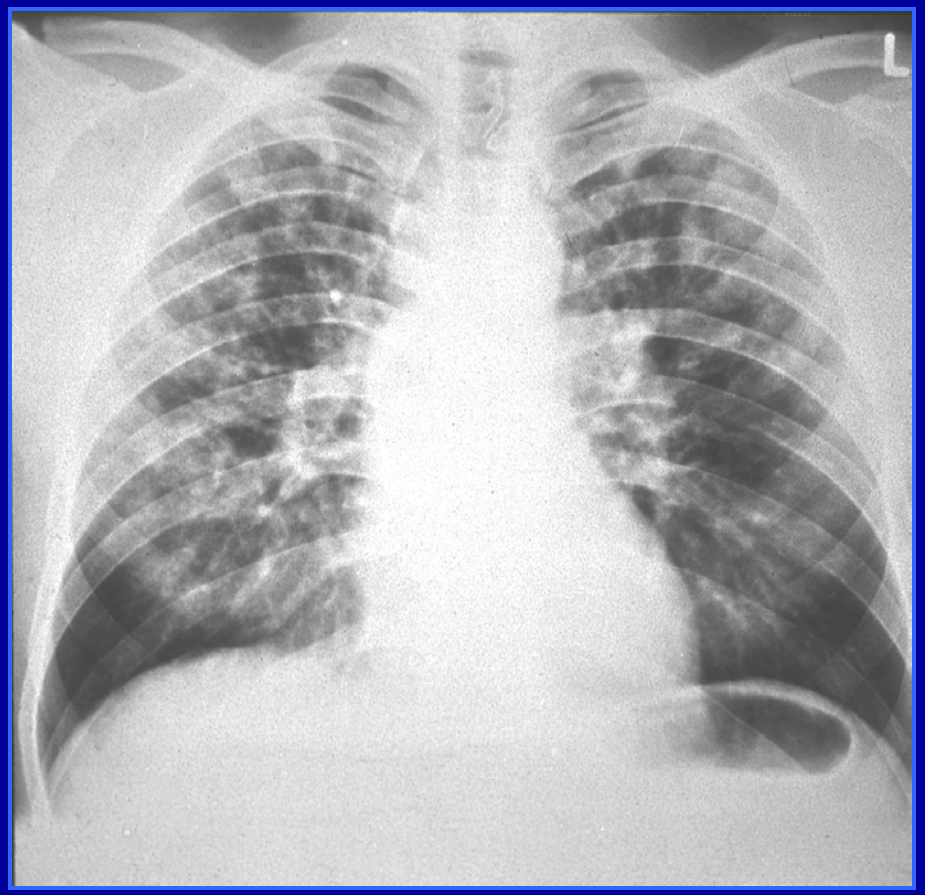
Additional risk factors

- Open foramen ovale
- Congenital atresia/hypoplasia of a pulmonary artery
- Pulmonary hypertension at low altitude
- Pulmonary embolism
- Systemic inflammation decreasing pulmonary capillaries edema formation threshold



Rationale for Prevention and Treatment Based on Pathophysiology

High Altitude Pulmonary edema



Inhibition of excessive hypoxic pulmonary vasoconstriction

- **Vasodilators**
  - Calcium channel blokers
  - Phosphodiestherase 5 inhibitors
- **Improve nitric oxide availability**
  - Phosphodiestherase 5 inhibitors
  - Glucocorticoids
- **Improve water reabsorption**
  - Beta-2-agonists
  - Glucocorticoids

Prophylaxis of High Altitude Pulmonary Edema (HAPE)

HAPE

Trekking/climbing above 2500m

Slow ascent
300 m/day
+

Nifedipine
CR30-60 every 24 h
Start
24h before ascent

or

Tadalafil
20 mg every 24 h
Start
24h before ascent

+ AMS > 2 AMS Symptoms

Azetazolamide
125 mg every 12 h

HAPE & AMS

Busienesstrip above 2500m

Rapid ascent with a short sojourn
1000 m/day + < 5 days above 2500m

Dexamethasone
4-8mg every 12 h
Start
24 h before ascent

Treatment of High Altitude Pulmonary Edema (HAPE)

HAPE

Mild-AMS

≤ 2 AMS Symptoms

Azetazolamide
125 mg every 12 h

4-6 l/min O_2
+
Nifedipin 20 mg
or
Sildenafil 50mg
every 8 h

Descent > 1000m

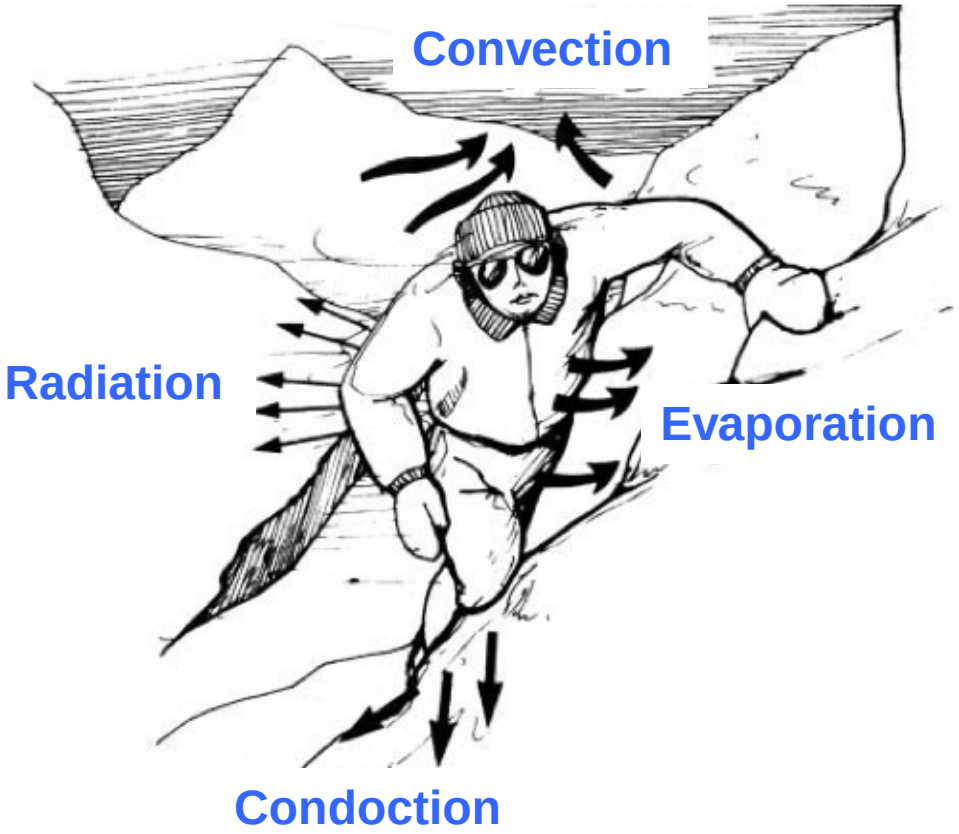
Mild/Severe AMS

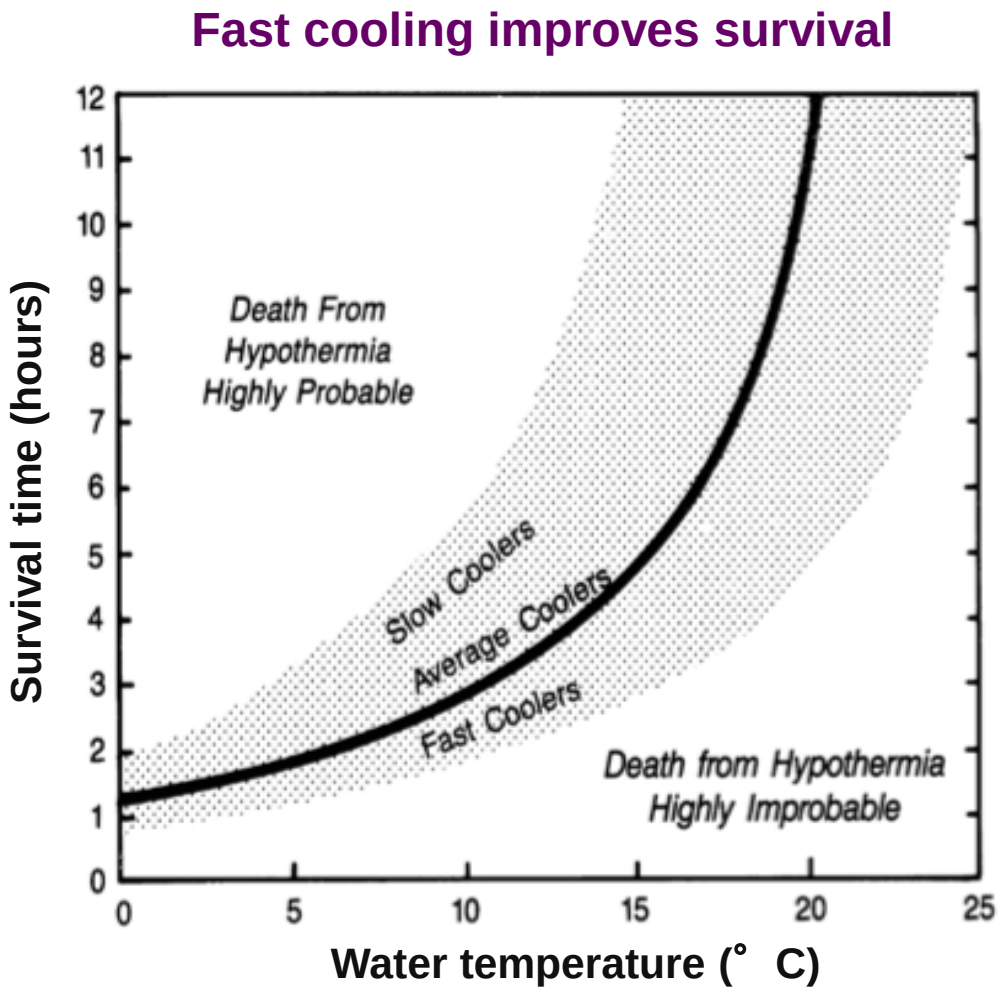
> 2 AMS Symptoms

Dexamethasone
8 mg loading dose
4 mg every 6 h

Hypothermia

Hypothermia mechanisms





Hypothermia Classification

Acute

- **Ice water, glacier crevasse**

Subacute

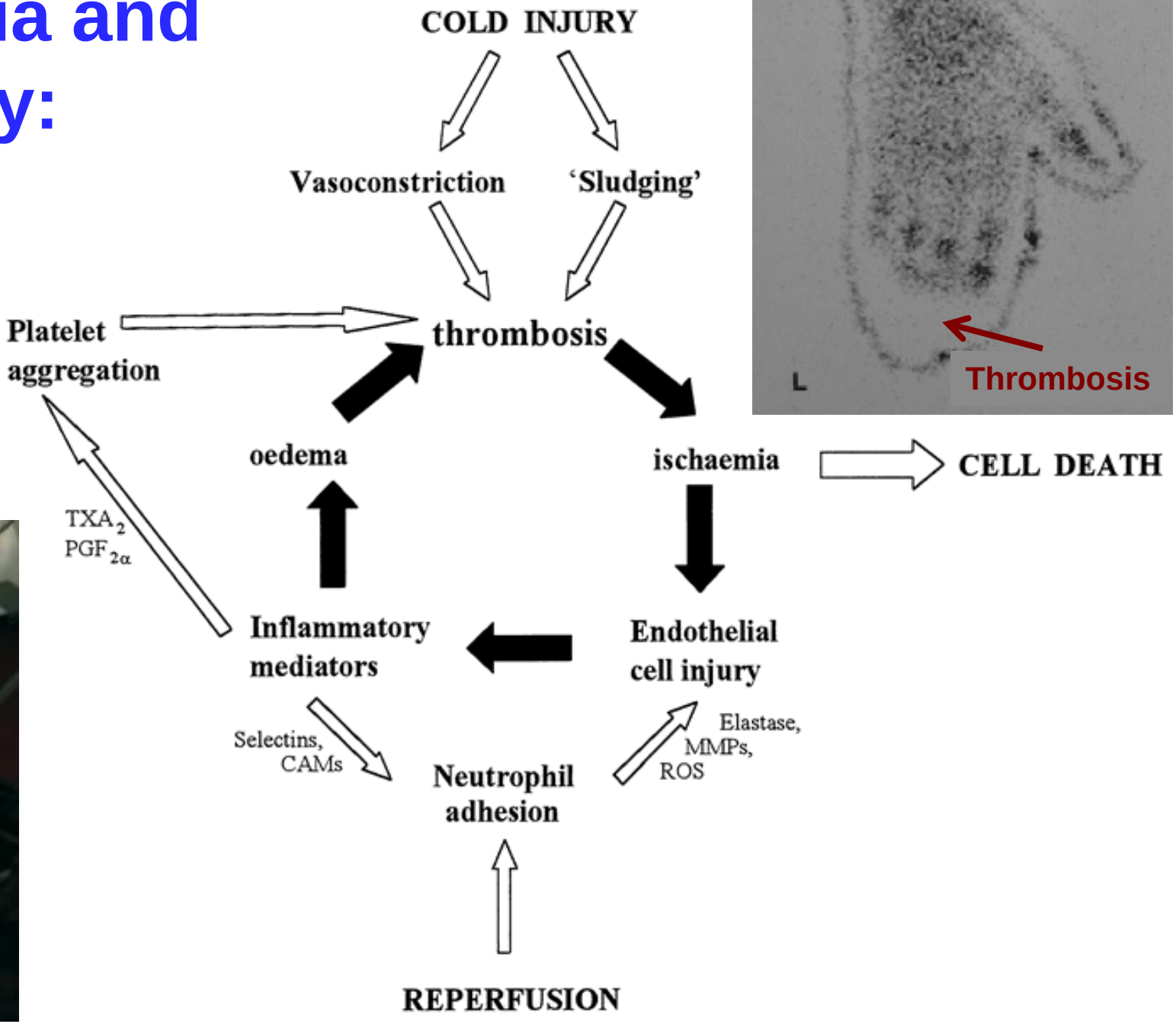
- **Avalange, snow and wind**

Chronic

- **Exhaustion**

Hypo-thermia stage	Core tempera-ture	Signs
I	35° - 32°	Patient alert, shivering
II	32° - 28°	Patient drowsy, nonshivering
III	28° - 24°	Patient unconscious
IV	< 24°	Patient not breathing

Hypothermia and tissue injury: Frostbite



Risk factors for cold injuries

Behavioural

- Inadequate clothing and shelter
- Alcohol and other drug use
- Psychiatric illness
- Smoking

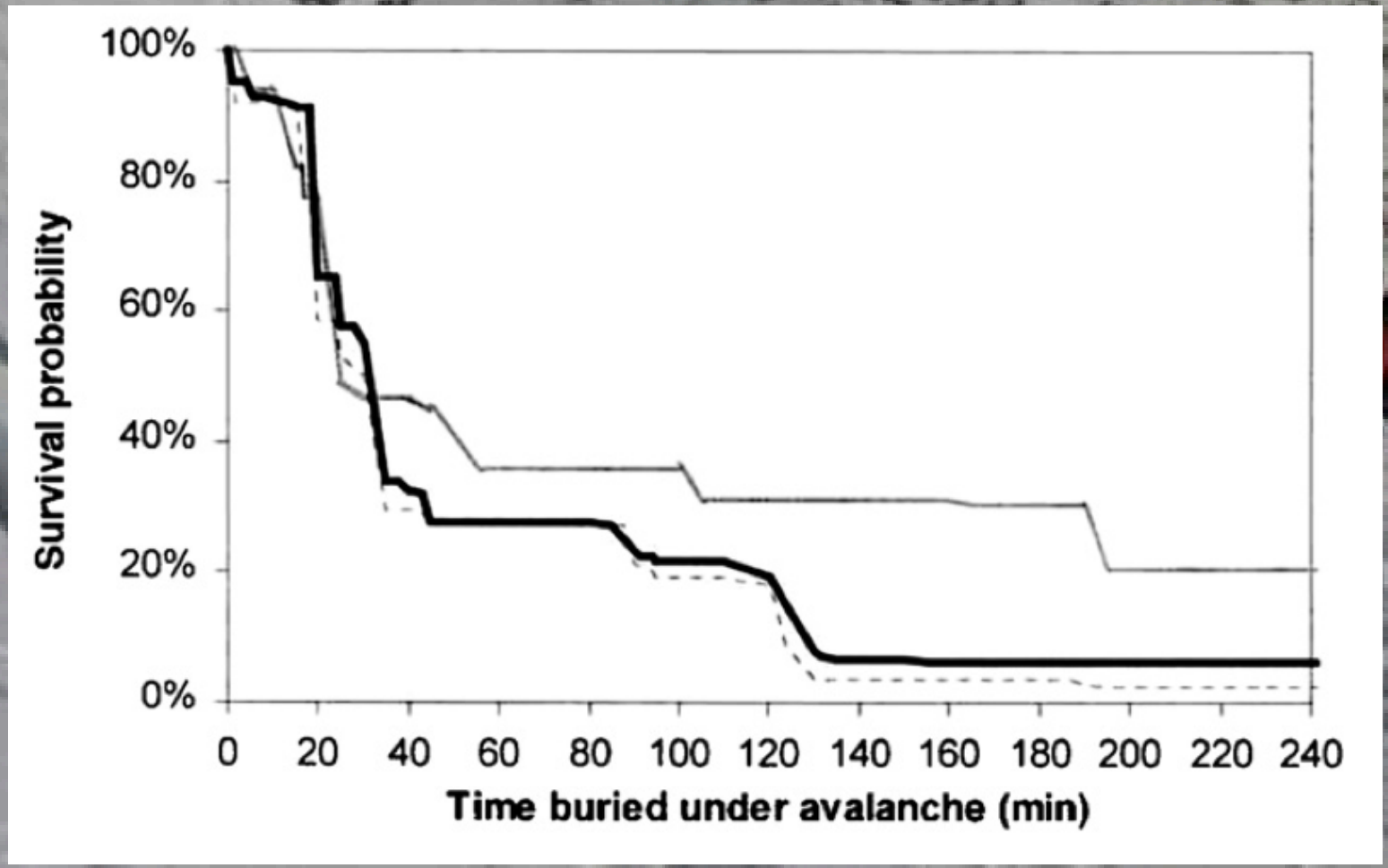
Mechanical

- Tightly constrictive clothing (too many socks)
- Contact with heat conductive materials
- Rings on fingers
- Immobility (bivouac, avalanche)

Physiological

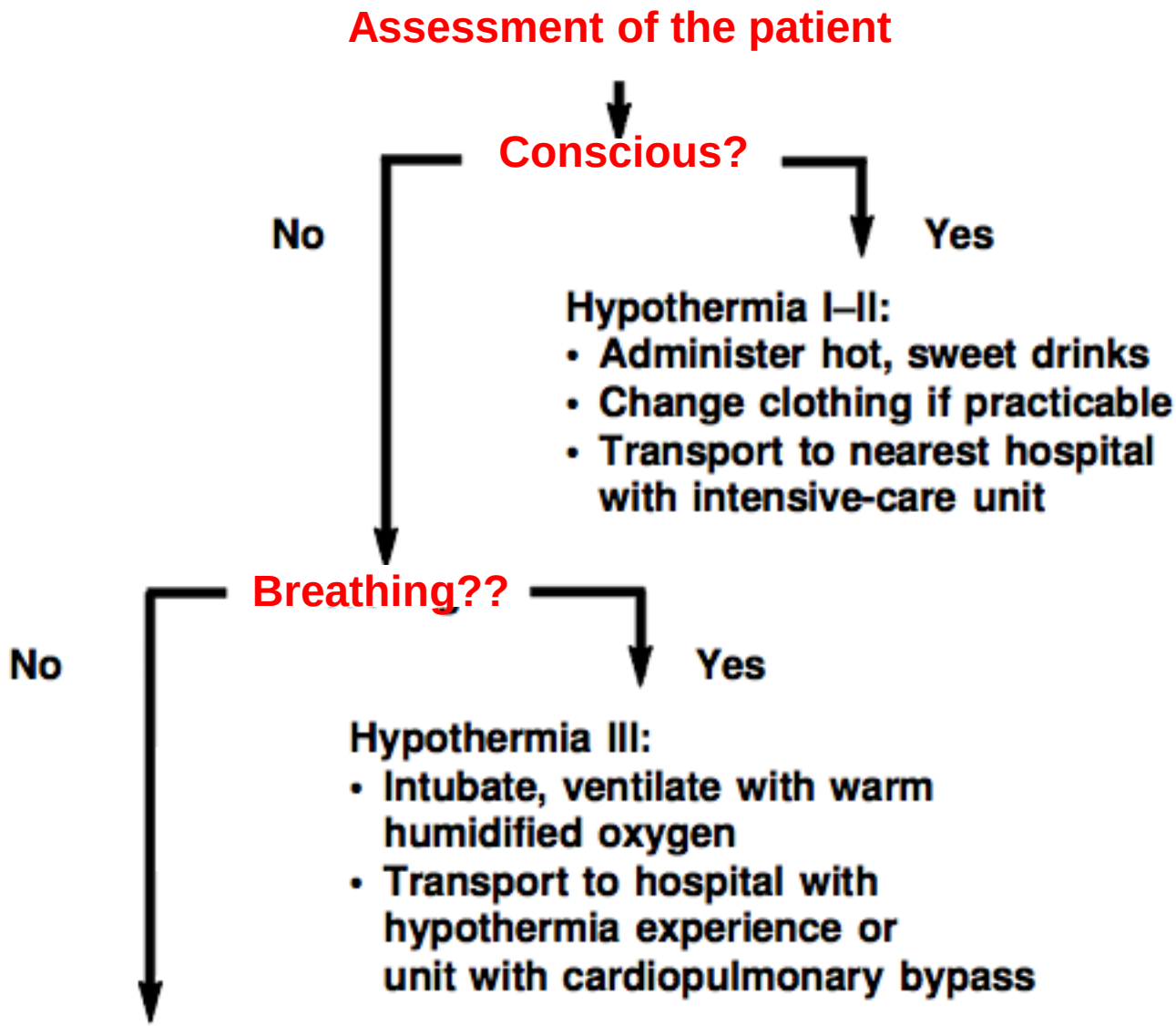
- Genetic susceptibility
- Dehydration and hypovolaemia
- Hypoxia and hypothermia
- Diabetes, atherosclerosis, vasculitis
- Raynaud’s phenomenon
- Vasoconstrictive drugs
- Sweating or hyperhydrosis (heat loss)
- Previous frostbite

Hypothermia in avalanche victims



Management of the hypothermic patient

Stage I, II and III



Management of the hypothermic patient stage III and IV

Obvious fatal injuries?

Yes

No

Start CPR, intubate

Check burial time and/or core temperature

≤35 min and/or ≥32°C

Continue resuscitation; follow standard ACLS protocol

>35 min and/or <32°C

ECG

Ventricular fibrillation

Asystole

No

Air pocket and free airways

Yes or uncertain

Pronounce patient dead

Hypothermia IV:

- Continue resuscitation
- VF: apply 3 DC shocks
- Transport to unit with cardiopulmonary bypass*

Hypothermia summary

- Prevention is vital non-freezing cold injury (Hypothermia) and for both frostbite.
- Early recognition and treatment will limit the extent of the injury.
- Hypothermia: warm slowly, Stage IV (Extra corporal circulation)
- Frostbite: warm quickly, defer surgery.
- Transfer to a referral center


At the end of the day

Elevated ambient temperature

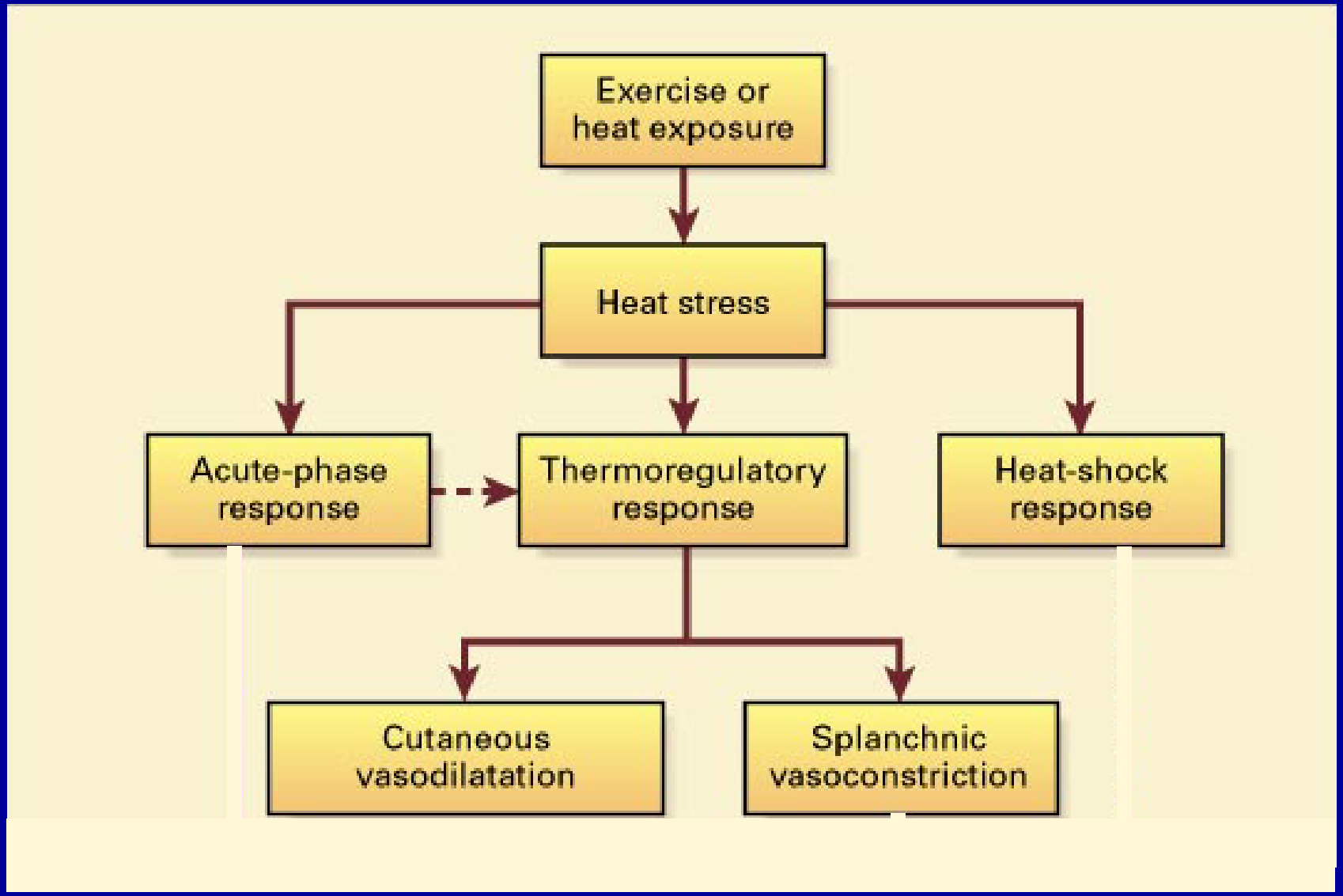
Heat Stress

Hyperthermia

Definition of hypertherima

Hyperthermia is a non-regulated elevation of core body temperature (heat stress, heat stroke) caused by the inability of the effector mechanisms to eliminate heat from the body adequately.

Response to heat exposure



Bouchama & Knochel, NEJM 2002, 346:1978

Heart related illness

Type	Causes	Clinical Presentation	Treatment
Heat edema	Vasodilation	Dependent edema BT normal	Elevate extremities
Heart rash	Sweating saturated skin surface and clogs sweat ducts	Pruritic rash BT normal	Cooling Mild antihistaminic
Heat cramps	Poor acclimatization, negative sodium balance	Twitches, fasciculations, painful spasms, sustained muscle contraction, BT normal	Appropriate water and sodium intake
Heat syncope	Dehydration, vasodilation, decreased cardiac output	Orthostatic hypotension, loss of consciousness, core BT normal	rehydration
Heat exhaustion	Compromised circulation and cooling mechanisms	Fatigue, malaise, headache, nausea, vomiting, muscle cramping, profuse sweating, hypotension, tachycardia	Stop exercise, remove clots, fluids, monitor vital signs

Relationship between ambient temperature and heat illness

Celsius	Comments
27–32 °C	***Caution*** — fatigue is possible with prolonged exposure and activity. Continuing activity could result in heat cramps
32–41 °C	***Extreme caution*** — heat cramps, and heat exhaustion are possible. Continuing activity could result in heat stroke
41–45 °C	***Danger*** — heat cramps, and heat exhaustion are likely; heat stroke is probable with continued activity
Over 45 °C	***Extreme danger*** — heat stroke is imminent

Heat stroke

Definition

- **Severe illness characterized by a core temperature > 40° C and central nervous system abnormalities such as delirium, convulsions or coma resulting from exposure to environmental heat or strenuous physical exercise**
  - It is a form of hyperthermia associated with systemic inflammatory response leading to a syndrome of multi-organ dysfunction in which encephalopathy predominates

Bouchama & Knochel, NEJM 2002, 346:1978

Heat stroke

Clinical and metabolic manifestations

- hyperthermia (40° C - 47° C) *
- central nervous system dysfunction (inappropriate behavior or delirium or coma) *
- Tachycardia & Hyperventilation (all patients)
- Hypotension (25% of the patients)
- Metabolic acidosis (exertional heat stroke)
- Rabdomyolasis (exertional heat stroke)

* Must be present

Bouchama & Knochel, NEJM 2002, 346:1978

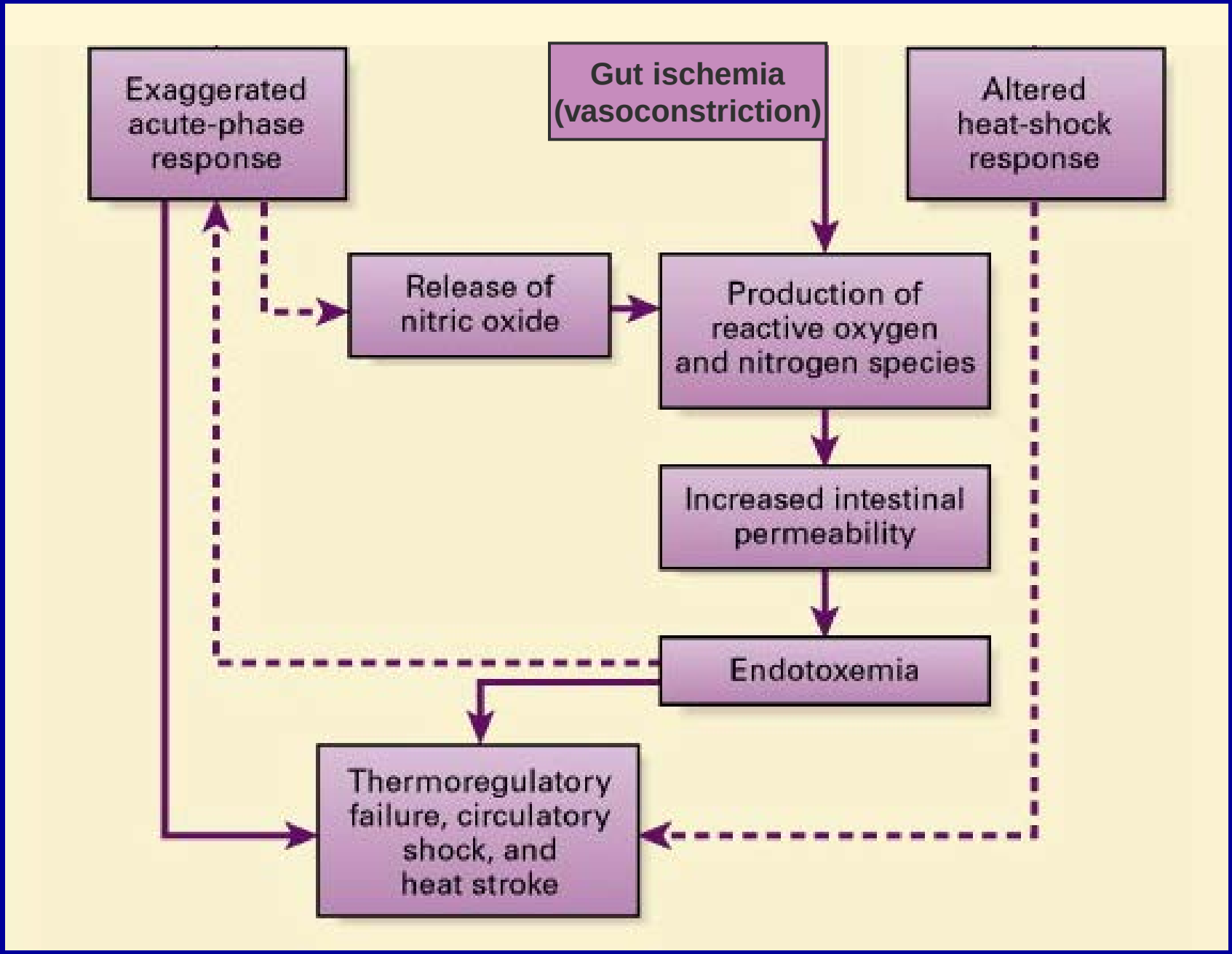
Heat stroke

Pathogenesis

- **Thermoregulatory failure: inability to maintain body temperature at 37° C because of insufficient adaptation to heat (several weeks)**
  - Inability to increase cardiac output to peripheral circulation
- **Exaggerated acute-phase response (systemic inflammatory response) following ischemia of the gut and intestinal hyperpermeability (endotoxies)**
- **Low level of expression of heat-shock proteins**
  - Aging, lack of acclimatization, genetic polymorphisms

Bouchama & Knochel, NEJM 2002, 346:1978

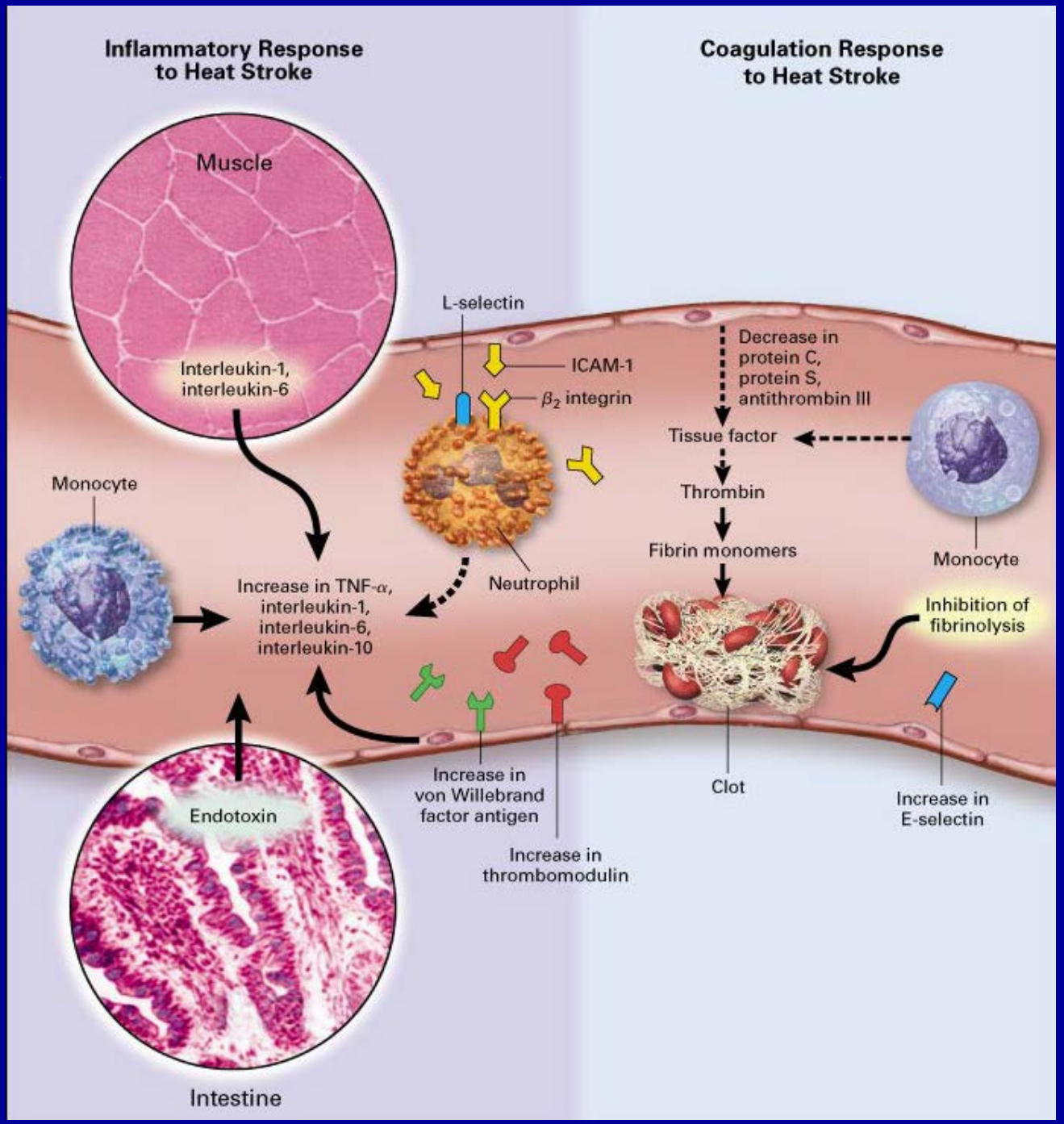
Heat stroke: Pathogenesis



Bouchama & Knochel, NEJM 2002, 346:1978

Heat stroke: Pathophysiology

- **Local inflammation**
  - Muscle
- **Systemic progression**
  - Monocyte, neutrophils, endothelial cells
  - Endotoxinemia following gut ischemia
  - DIC, microvascular thrombosis
- **Multi-organ failure**



Bouchama & Knochel, NEJM 2002, 346:1978

Heat Stroke

Treatment

- **Cooling (keep core temperature < 39.4˚ C)**
  - External: ice slush, cooling blankets or vest, cooling catheter, (hemofiltration)
  - Avoid shivering: sedation
- **Fluid resuscitation and vasopressors like in sepsis**
  - Prevent myoglobin induced renal failure
- **Pharmacologic agents are ineffective**
  - Dandrolene (randomized controlled trial)
  - Antipyretic agents

Bouchama & Knochel, NEJM 2002, 346:1978


Thank you for your attention
Dufourspitze 4680m