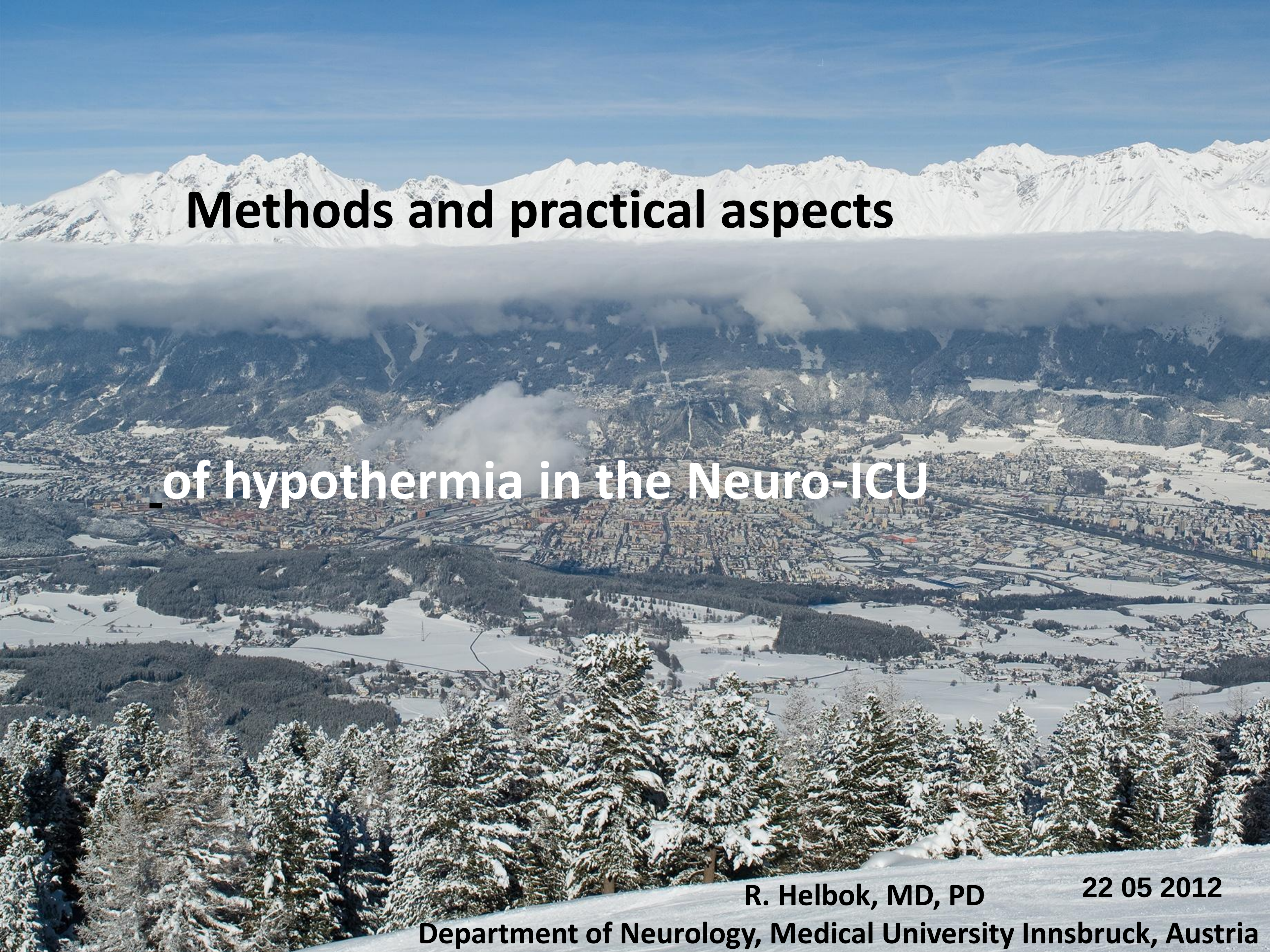

Methods and practical aspects of hypothermia in the Neuro-ICU

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22 05 2012

Disclosure

- None

Methods and practical aspects

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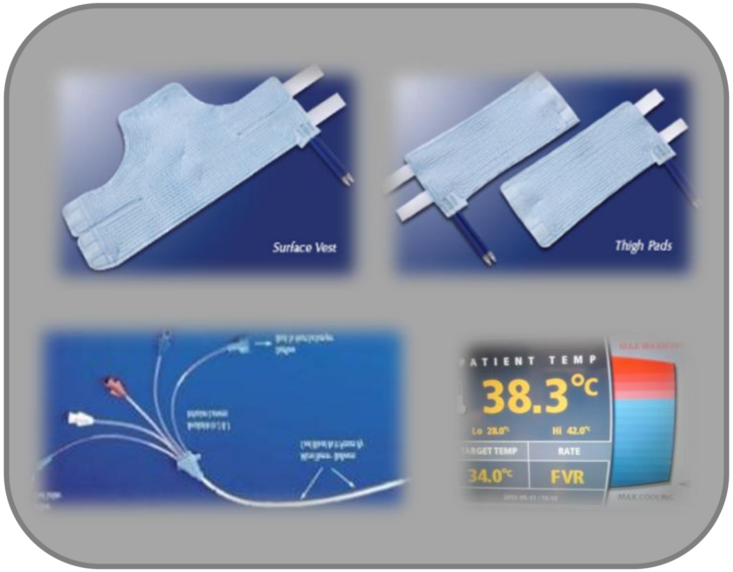
Outline

- ➢ **How to achieve hypothermia**

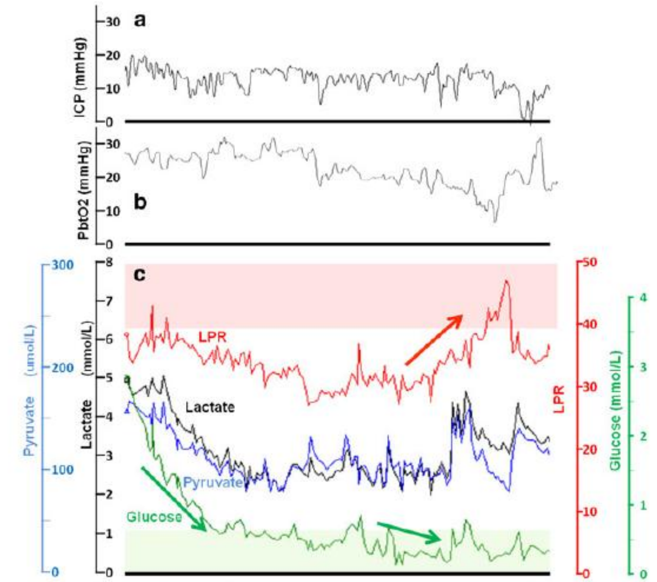
- ➢ **How to maintain hypothermia**
- ➢ **What-s important for the clinician**

Outline

- How to achieve hypothermia
- **How to maintain hypothermia**
- What-s important for the clinician



- ➢ How to achieve hypothermia
- ➢ How to maintain hypothermia



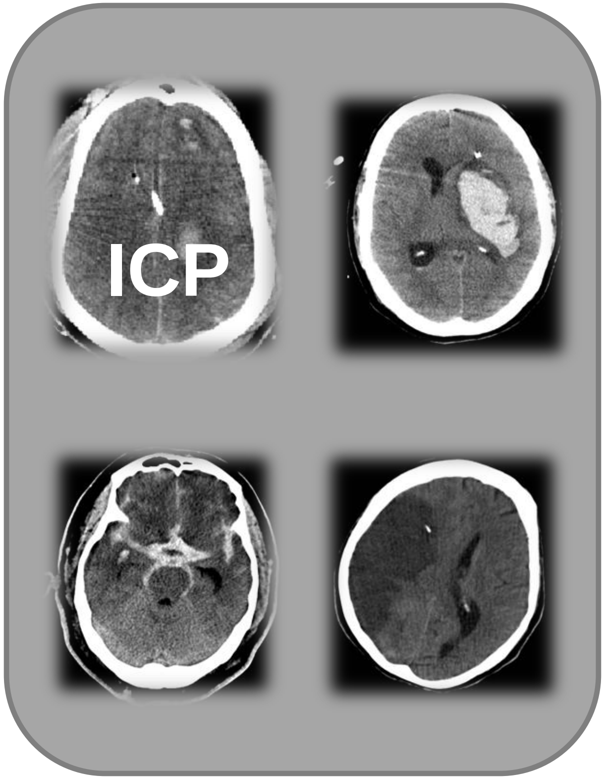
day post SAH	0	1	2	3	4	5	6	7
ipsilateral MCA	ND	50	60	75	90	130	210	200
ipsilateral ACA	ND	45	50	70	80	100	170	160
Lindegard Index	ND	1	1	1	1.4	1.8	4	3.2
Creatinine / BUN	1.1 / 22	1.3 / 43	2.5 / 92	2.0 / 78	1.2/ 44	1.1 / 39	1.1/ 4 2	1.0 / 41

- ➢ **What-s important for the clinician**

Therapeutic hypothermia

- *Evidence (RCT)* *cardiac arrest*

- *Small trials*



How to cool ?

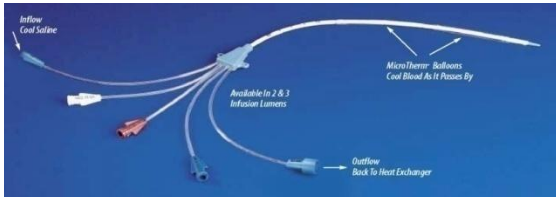
- Ice bags

- Fans

- Intravenous Cooling

- Mechanical Cooling

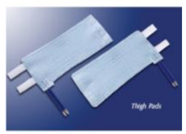
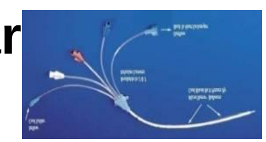
- Endovascular Cooling*!*



Cooling methods

	Pros	Cons
Ice bags 	inexpensive widely available	messy, difficult to control temp
Intravenous Fluids 	inexpensive widely available	need to determine way to keep fluids cold

Cooling methods

	Pros	Cons
Surface cooling  	fair control of patient temp easy to use	variety of systems/costs not easily transportable
Endovascular cooling 	reliable control fast no risk of skin lesions	expensive large invasive line infection risk

Keep Track of Temperature

- **Bladder**
- **Rectal**
- PA Catheter
- Esophageal
- Tympanic
- Axilla

Continuous **monitoring** (or q15min) during induction until stabilized at goal temperature 32-34°C

Hypothermia

- **mild**

  34-35,9º C

- **moderate**

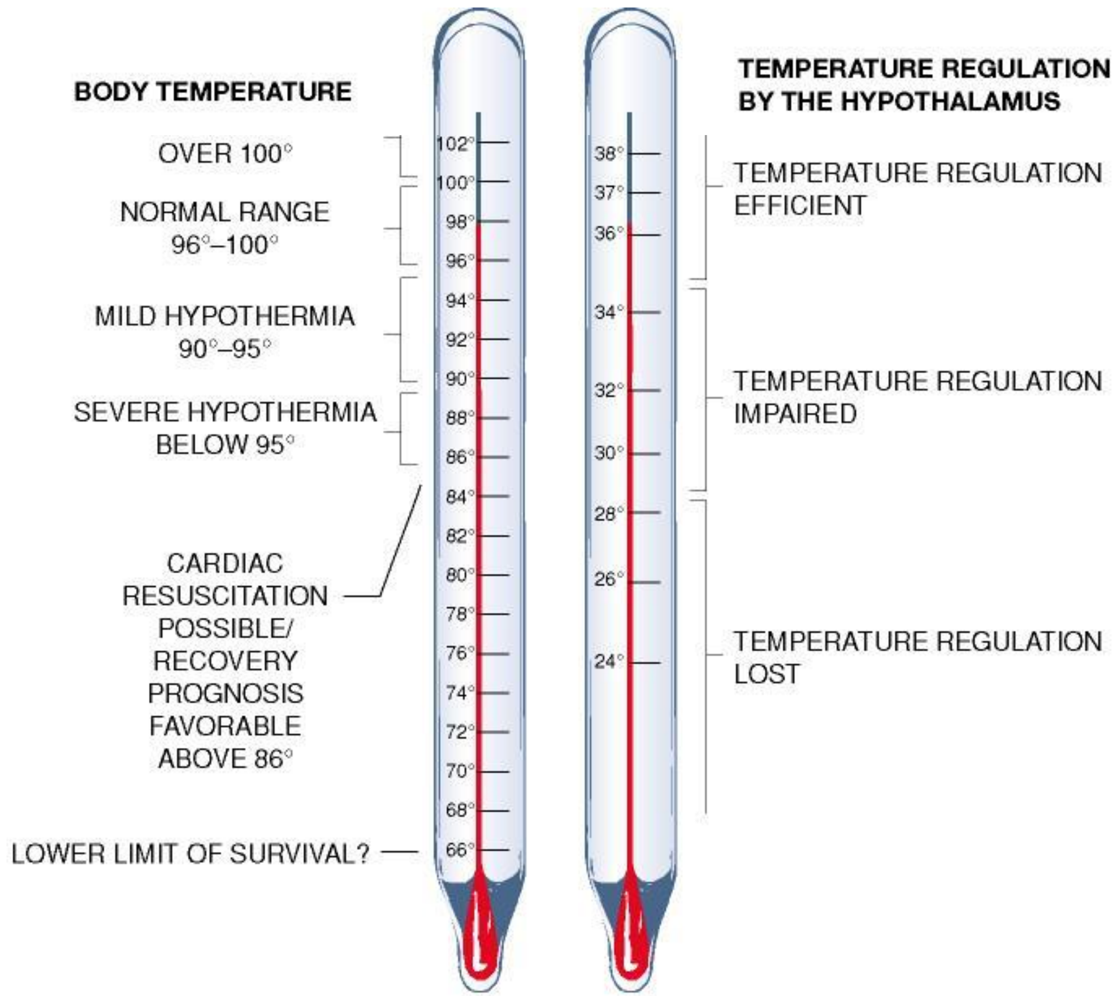
  32-33,9º C

- ~~**moderate deep**~~

  ~~30-31,9º C~~

- ~~**deep**~~

  ~~<30º C~~



Polderman et al CCM 2009 ***37:****1101-1120*

Success with induced hypothermia requires

- Understand processes at the cellular level in the minutes to hours following an initial injury
  - postresuscitation disease
  - reperfusion injury
  - secondary brain injury

- Understand physiological effects pathophysiological mechanisms of hypothermia

- Apply adequate monitoring in intensive care units

Hypothermia for acute brain injury —mechanisms and practical aspects

H. Alex Choi, Neeraj Badjatia and Stephan A. Mayer

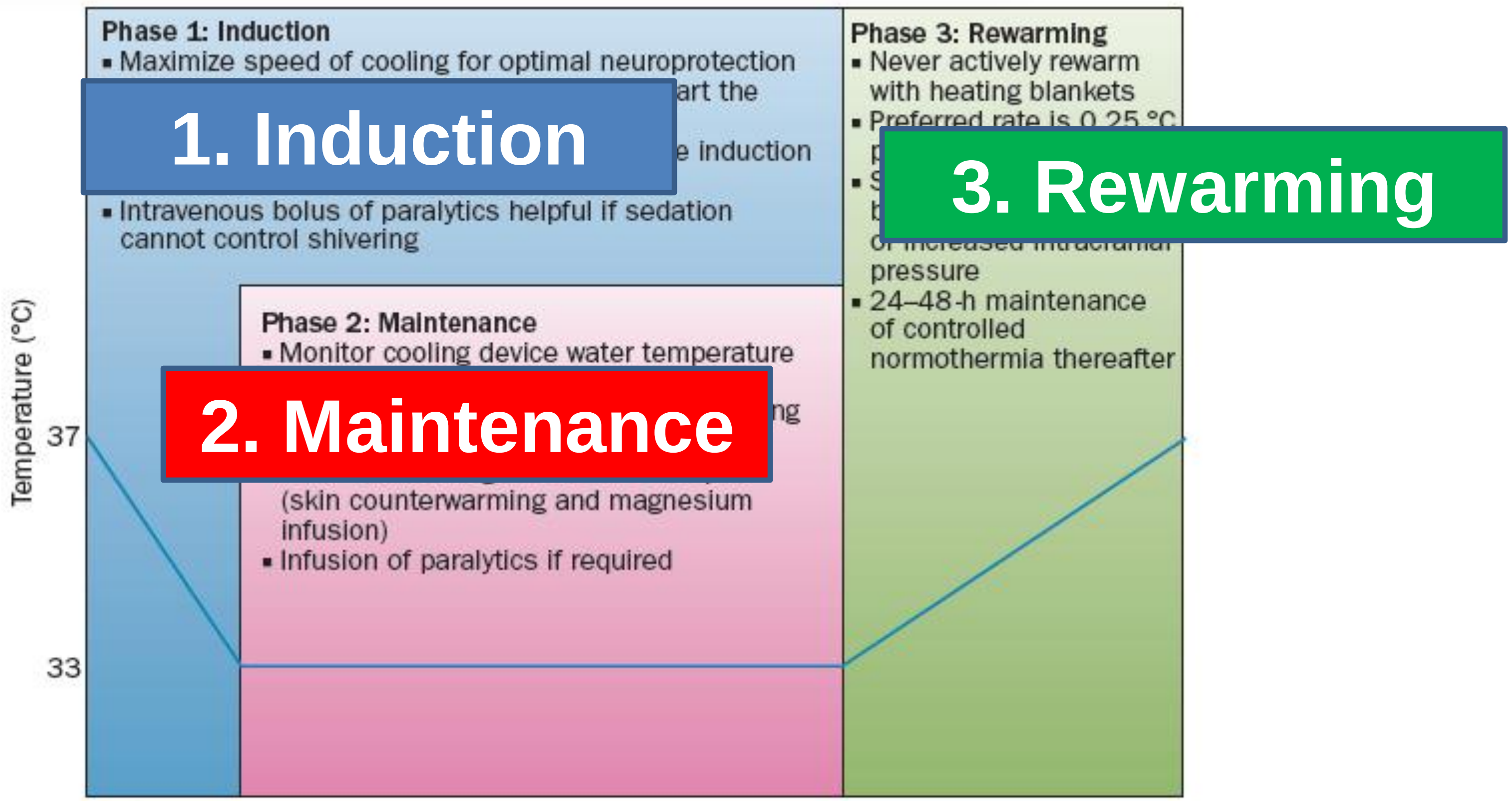
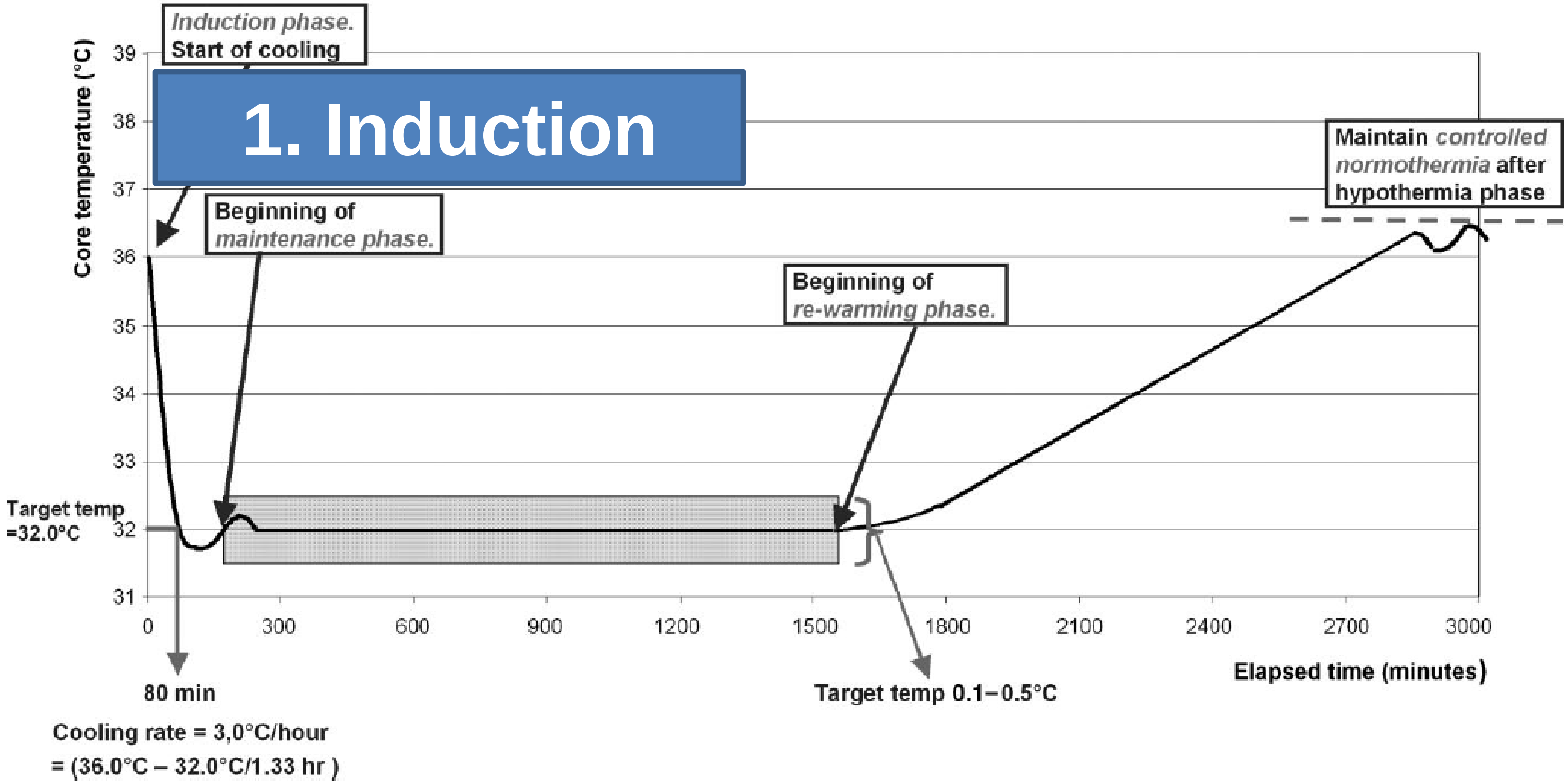


Figure 1 | Key management points during the three phases of therapeutic hypothermia.

Choi et al, Nat Rev Neurol. 2012 28;8:214-22

Mechanisms of action, physiological effects, and complications of hypothermia



Polderman et al CCM 2009 ***37:****1101-1120*

1. Induction

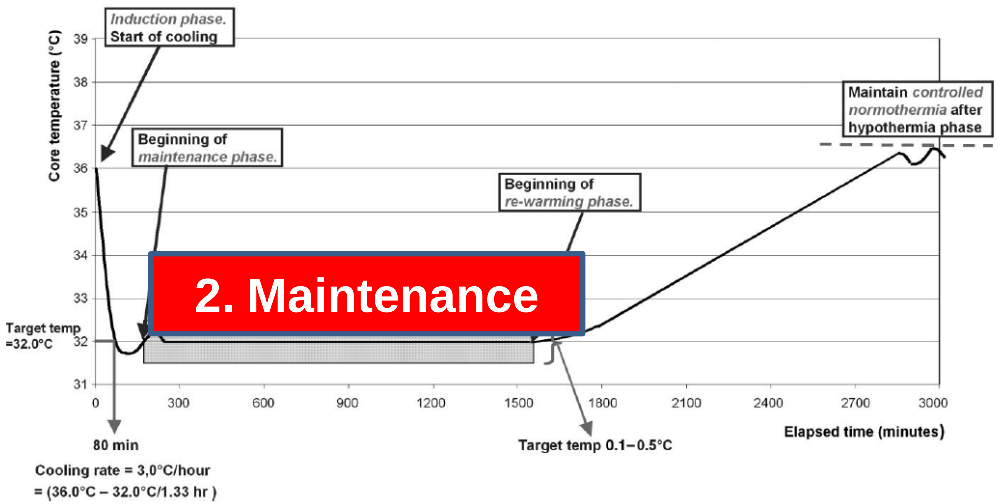
- ➢ Goal: Reach target within 2 hours → **RAPID**
  - ✓ Intravenous cold saline (kept at 1-4°C (30cc/kg)
    - peripheral or femoral line
    - decrease by 2°C after 1h-infusion
  - ✓ Ice bags
    - axilla, groin and sides of neck
  - ✓ Expose the skin
  - ✓ Water and alcohol sprays

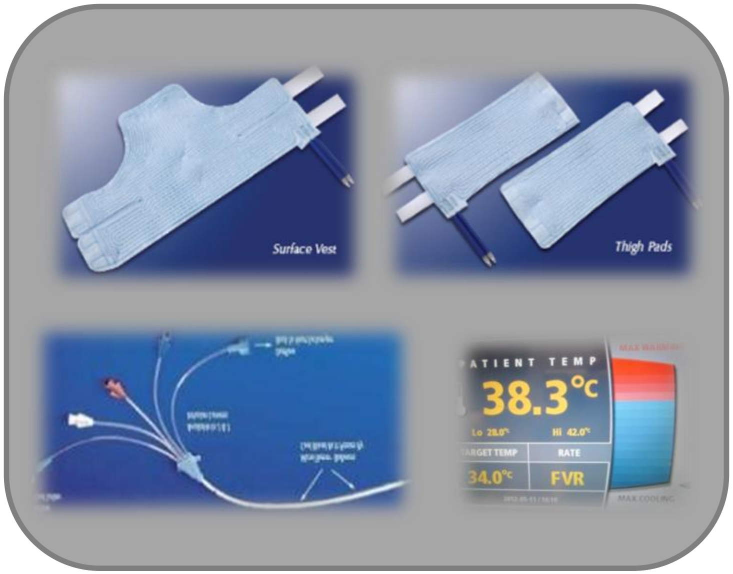
- ➢ Surface/intravscular cooling devices

✓ Avoid temperature overshoot !

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

2. Maintenance

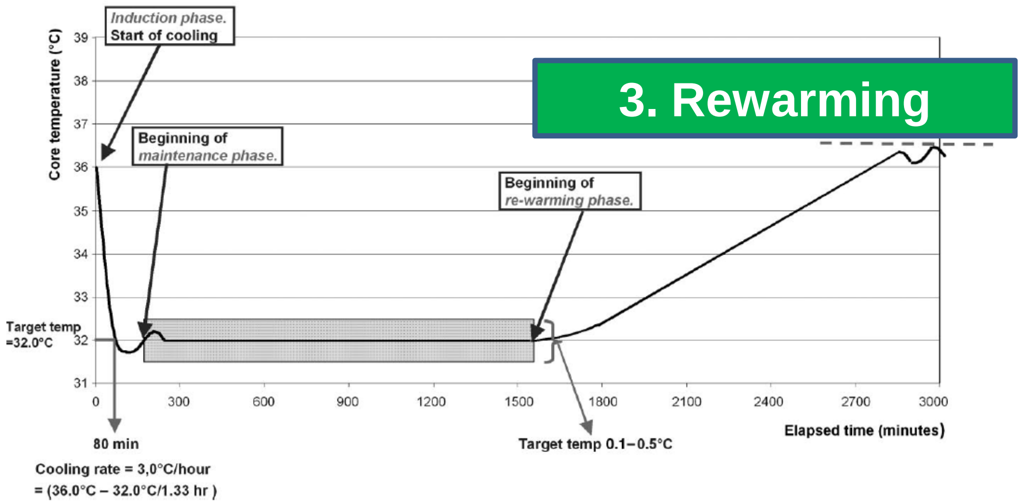


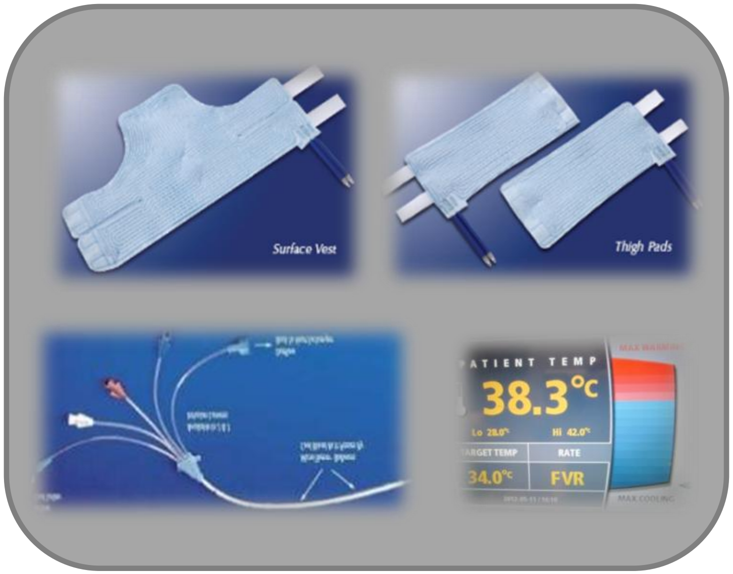


- only minor fluctuations, 0.2°C
  - Advanced cooling technologies

Polderman et al CCM 2005; 33:2744–2751;
Polderman et al CCM 2009 ***37:****1101-1120 ;*
Choi et al, Nat Rev Neurol. 2012 28;8:214-22

3. Rewarming





- should be contolled
  - Advanced cooling technologies

- go slow!
  - 0.25°C/hr for postcardiac arrest
  - Severe brain injury: 0.05-0.1°C/hr

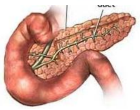
Polderman et al CCM 2005; 33:2744–2751; Polderman et al CCM 2009 ***37:****1101-1120 ; Choi et al, Nat Rev Neurol. 2012 28;8:214-22*

1. Induction

Risk for


- ✓ **hypovolemia**


- ✓ **electrolyte disorders**


- ✓ **hyperglycemia**


- ✓ **CO_2 production ↓**


- ✓ **shivering**

→ start adequate monitoring

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

Renal changes Temp < 35°C

- Tubular dysfunction
- Diuresis

  ➢ Hypovolemia, Hypotension

- Intracellular shifts
- Electrolyte loss

  ➢ Mg, K, Phosphate ↓

Polderman, KH et al, 2001, JNS, 94, 697–705
Polderman, KH, ICM 2004,30, 757–769
Choi et al, Nat Rev Neurol. 2012 28;8:214-22

TH - Fluid balance and electrolytes

- **<u>GOAL</u>**

  - Aggressive replacement (Mg, K) with goal high normal ranges

  - Multiple boluses / supplements to infusions

  - Careful monitoring, especially during re-warming

Polderman, KH et al, 2001, JNS, 94, 697–705
Polderman, KH, ICM 2004,30, 757–769
Choi et al, Nat Rev Neurol. 2012 28;8:214-22

TH: Metabolism

- **Metabolism** ↓ (cerebral ↓ by 6-10%/1°C)
- **Oxygen consumption** ↓

- Insulin resistance → **Hyperglycemia**
  - Secondary to decreased insulin sensitivity and secretion
  - Rewarming: insulin sensitivity increases → hypoglycemia!

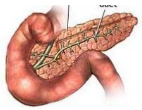
➢ Goal is normoglycemia
- Resultant higher insulin rates (lower K+)

Polderman, KH, ICM 2004,30, 757–769

1. Induction

Risk for

- ✓ hypovolemia
- ✓ electrolyte disorders



- ✓ hyperglycemia

- ✓ **CO_2 production ↓**

- ✓ shivering

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

HT and blood gas (ABG)

- Man, 45 y
- Severe TBI, ICP crisis →start hypothermia (cold saline, intravascular), maintain at 33 °C
- ICP~~18mmHg
- Acid-base status?
- Technician asks you if he should warm the blood before analysis…

A) Don't warm it : 33°C

B) Warm it to 37°C

C) Both and I'll pick the best one.

HT and blood gas (ABG)

ABG (37°C)	temp-corrected (33 ° C)
• pH = 7.45	pH = 7.50
• pCO_2 = 35	pCO_2 = 27
• pO_2 = 90	pO_2 = 70

- Everything’s perfect, I don’t touch the ventilator ?
- Will you try to ↓ RR or ↓V_T to ↑ pCO2 ?

HT and blood gas (ABG)

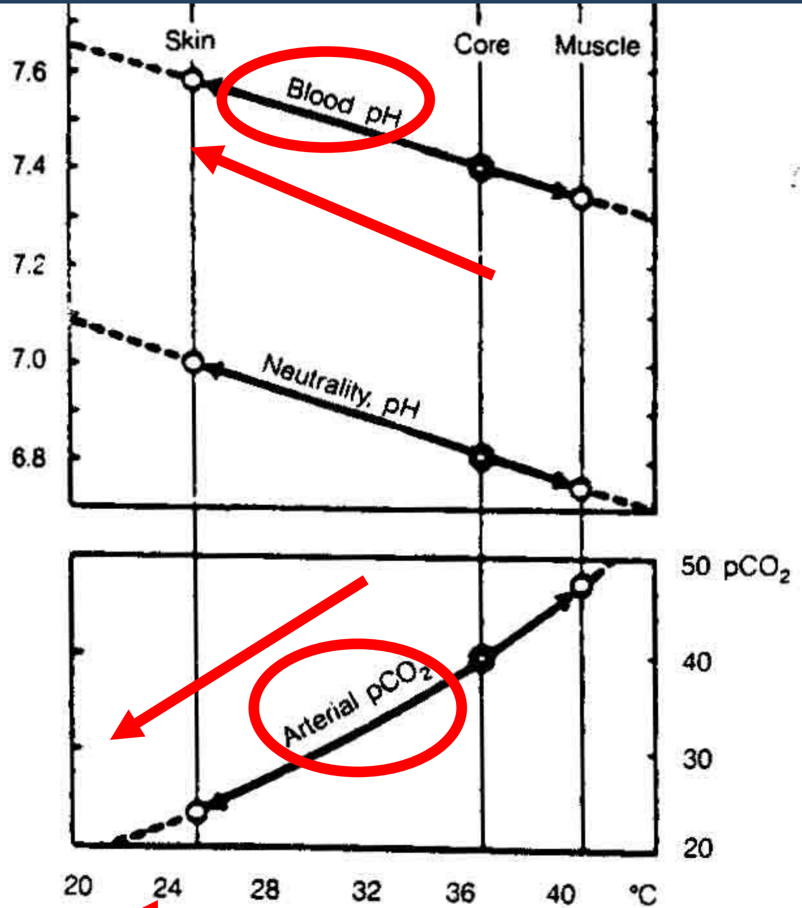
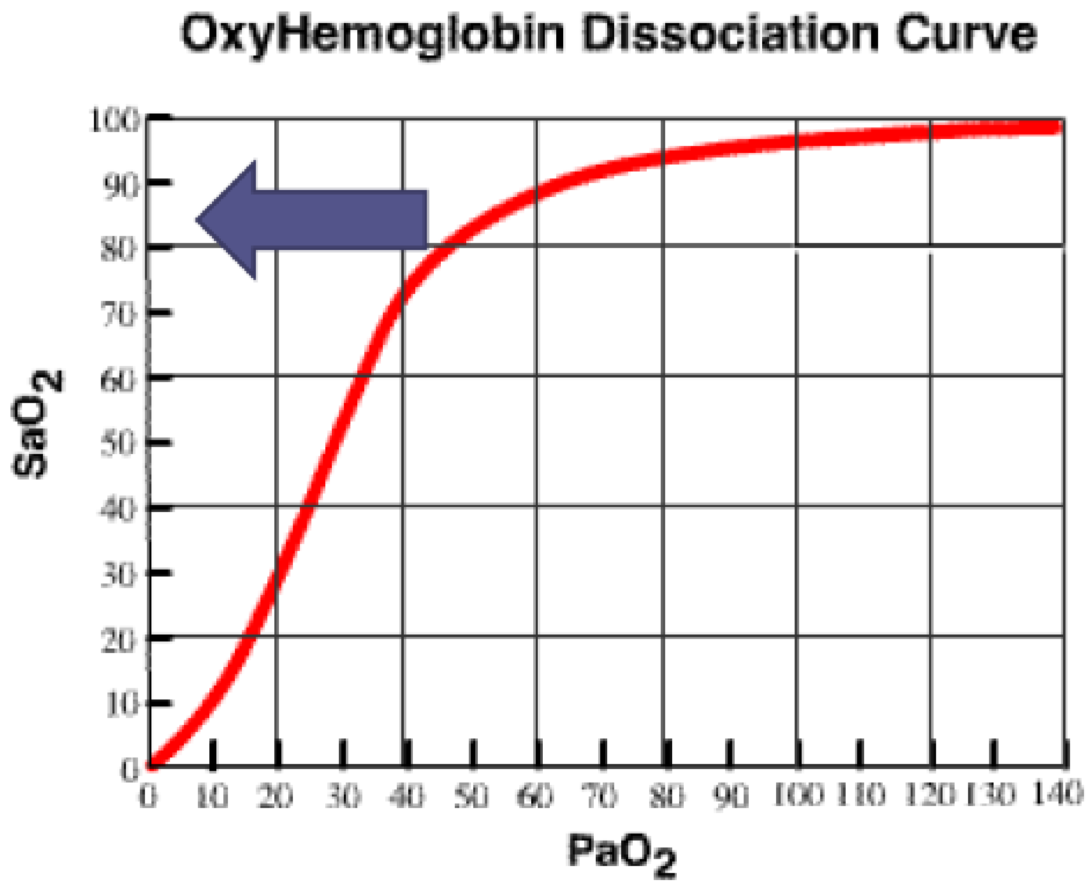


FIGURE 4. *pH-temperature relation of blood in various capillary beds of a person exercising in a cold environment. CO_2 remains constant. All of these measurements are pH of 7.40 and pCO_2 of 40 mm Hg in the blood gas machine at 37 C. (Reprinted with permission from Rahn.[11])*

HT and blood gas (ABG)

- Solubility of gases:
  - temperature dependent
- Left shift due to cooling
  - Dec. O2 consumption
- ABGs warmed to 37C:
  - Solubility of CO2 increases -- higher PCO2/lower pH……….



Polderman, KH et al, 2001, JNS, 94, 697–705
Polderman, KH, ICM 2004,30, 757–769

HT and blood gas (ABG)

ABG (37°C)	temp-corrected (33 ° C)
pH = 7.45	pH = 7.50
pCO_2 = 35	pCO_2 = 27
pO_2 = 100	pO_2 = 80

pO_2 and pCO_2 overestimated , pH underestimated

RISK

- **Hyperventilation**
- **cerebral vasoconstriction**

- **Hypoventilation**
- **cerebral vasodilation**
- **ICP**

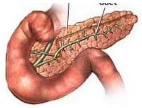
We use temperature corrected ABG values

→ monitor ICP, check TCD
→ ↓ RR or ↓VT to ↑ pCO2
→ target pCO2 values 32 to 36 mm Hg

Risk for

- ✓ hypovolemia

- ✓ electrolyte disorders



- ✓ hyperglycemia

- ✓ CO_2 production ↓

- ✓ **shivering**

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

TH - shivering

Physiological attempts to increase temperature

- Temperature 30-35°C

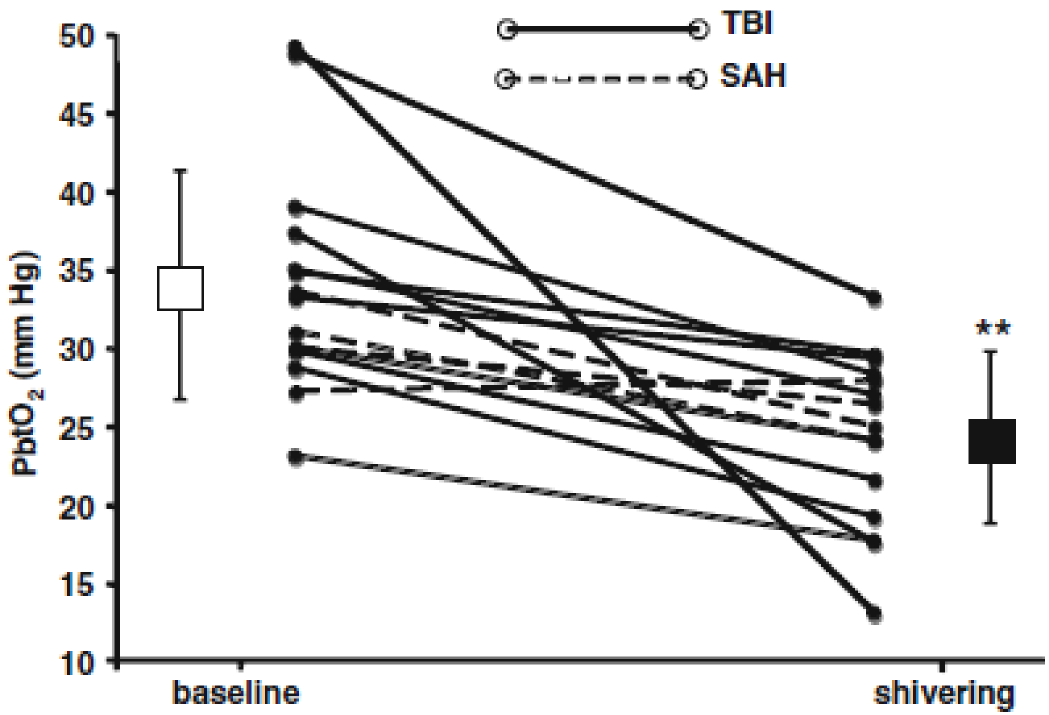
  - Shivering
  - Peripheral vasoconstriction
  - Increased muscle activity
  - Increased oxygen consumption (40-100%)
  - Increased metabolism

Physiologic changes of induced hypothermia

Effect of Shivering on Brain Tissue Oxygenation During Induced Normothermia in Patients With Severe Brain Injury

Mauro Oddo · Suzanne Frangos · Eileen Maloney-Wilensky · W. Andrew Kofke · Peter D. Le Roux · Joshua M. Levine

Neurocrit Care (2010) 12:10–16



Shivering – assess and treat!

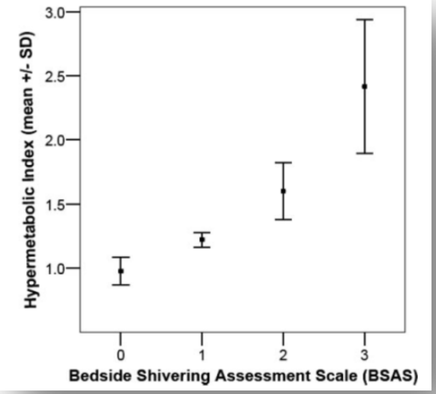
Hypothermia for acute brain injury —mechanisms and practical aspects

H. Alex Choi, Neeraj Badjatia and Stephan A. Mayer

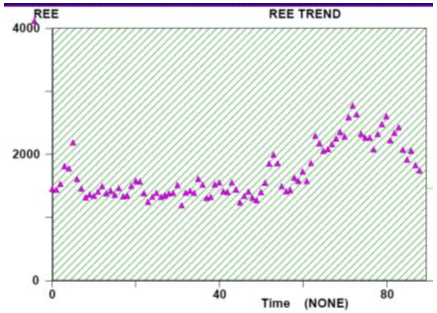
Table 2 | The Columbia Anti-Shivering Protocol

Step	Level of sedation	Intervention for shivering	Dosage
0	None	Acetaminophen Busiprone Magnesium sulphate Skin counterwarming	650–1000 mg every 4–6 h 30 mg every 8 h 0.5–1 mg/h i.v. (goal: 3–4 mg/dl) Maximum temperature 43 °C
1	Mild	Dexmedetomidine	0.2–1.5 μg/kg/h
2	Moderate	Opioids	Fentanyl, starting dose: 25 μg/h Meperidine 50–100 mg i.m. or i.v.
3	Deep	Propofol	50–75 μg/kg/min
4	Neuromuscular blockade	Vecuronium	0.1 mg/kg i.v.

Abbreviations: i.v., intravenously; i.m., intramuscularly. Adapted from Choi, H. A. *et al.* Prevention of shivering during therapeutic temperature modulation: the Columbia Anti-Shivering Protocol. *Neurocrit. Care* 14, 389–394 (2011).



Badjatia et al, Stroke. 2008;39:3242-3247



Helbok et al, CCM, under review

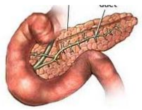
Badjatia et al, Stroke. 2008;39:3242-3247

Choi et al, Nat Rev Neurol. 2012 28;8:214-22

1. Induction

Risk for

- ✓ **hypovolemia** ➢ fluid management
- ✓ **electrolyte disorders** ➢ electrolyte administration



- ✓ **hyperglycemia** ➢ insulin

- ✓ **CO2 production ↓** ➢ adjust ventilator settings

- ✓ **shivering** ➢ treat!

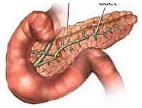
→ start adequate monitoring

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

Risk for

✓ hypovolemia

✓ electrolyte disorders

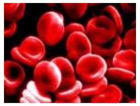


✓ hyperglycemia

✓ CO_2 production ↓

✓ shivering

➢ **heart**



➢ **blood**

➢ **infections**

➢ **GI**

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

TH: Cardiovascular system

≤35°C: Negative chronotropic effects

Polderman, K. H, ICM 2004,30, 757–769 ; Bergman, R. et al. Eur. J. Anaesthesiol.2010.27, 383–38

TH: Cardiovascular system

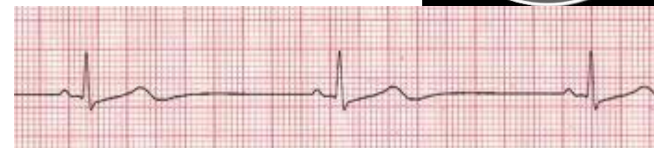
≤35°C: Negative chronotropic effects

≤32°C Prolonged PR, QT intervals

- ≤ 28°C Atrial fibrillation
- Ventricular arrhythmias at temps <28-30° C)

Polderman, K. H, ICM 2004,30, 757–769 ; Bergman, R. et al. Eur. J. Anaesthesiol.2010.27, 383–38

TH: Cardiovascular system



≤35°C: Negative chronotropic effects

≤32°C Prolonged PR, QT intervals

- ≤ 28°C Atrial fibrillation
- Ventricular arrhythmias at temps <28-30° C)

≥33°C: generally well tolerated

- Bradycardia (↓ CO) increased myocardial contractility
- BP (cold diuresis, endocrine)

33°C safe lower limit in critically ill pts

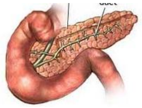
Polderman, K. H, ICM 2004,30, 757–769 ; Bergman, R. et al. Eur. J. Anaesthesiol.2010.27, 383–38

1. Induction

2. Maintenance

Risk for

- ✓ hypovolemia
- ✓ electrolyte disorders

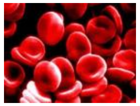


- ✓ hyperglycemia

- ✓ CO2 production ↓

- ✓ shivering

- ➢ heart



- ➢ **blood**

- ➢ infections

- ➢ GI

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

TH: Hematological abnormalties

- **Platelet** dysfunction and thrombocytopenia (33-35°C) immediately reversed with restoration of temperature

Spiel AO, eta l Resuscitation. 2009;80:762-5

- **Coagulation** tests prolonged (PTT, ROTEM)

Poldermann KH et al, Lancet 2008;371:1955-69

- The risk bleeding is very low
- No significant bleeding complications seen in trials

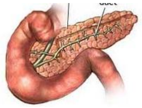
Hemmen TM et al, Stroke 2010 ;41:2265-70

> ➢ *Risks of bleeding does not prevent treatment*
> ➢ *Concomitant use of thrombolytics, anticoagulation, antiplatelets acceptable*

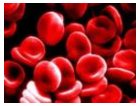
CAVE: combination with acidosis

Hemmen TM et al, Stroke 2010 ;41:2265-70

Risk for

- ✓ hypovolemia
- ✓ electrolyte disorders
- ✓ hyperglycemia
- ✓ CO2 production ↓
- ✓ shivering

- ➢ heart
- ➢ blood
- ➢ **infections**
- ➢ GI

Polderman et al CCM 2005; 33:2744–2751; Choi et al, Nat Rev Neurol. 2012 28;8:214-22

TH - infections

< 35°C **Immune suppression**

Impaired neutrophil and macrophage function

Inhib release of pro-inflammatory cytokines

Insulin resistance and hyperglycemia

< 33°C WBC, impaired leukocyte function < 33°C

➢ Increased risk of infections

Kimura A at al , 2002 CCM30:1499–1502; Aibiki M et al, 1999, J Neurotraum 16:225–232; Salman H et al, 2000, Acta Physiol Scand 168:431–436; Polderman, K. H, ICM 2004,30, 757–769

TH: Infections

Infectious complications in out-of-hospital cardiac arrest patients in the therapeutic hypothermia era*

Nicolas Mongardon, MD; (Crit Care Med 2011; 39:1359–1364)

Table 1. Baseline admission characteristics and outcome of patients admitted after cardiac arrest, classified according to the use of therapeutic hypothermia

	Therapeutic Hypothermia (n = 334)	No Therapeutic Hypothermia (n = 87)	*p*
Age, yr	60 (50–73)	60 (49–71)	.86
MacCabe score			
0	288	69	.2
1–2	47	17	
Male, n (%)	240 (72)	71 (82)	.08
Simplified Acute Physiology Score II	64 (56–75)	63 (53–77)	.41
No-flow (min)	5 (0–10)	3 (0–10)	.07
Low-flow (min)	15 (8–25)	10.5 (5–26)	.17
Shockable rhythm, n (%)	160 (48%)	40 (46%)	.75
Cardiac etiology, n (%)	209 (63%)	38 (44%)	.002[a]
Postresuscitation shock, n (%)	180 (54%)	42 (49%)	.35
Infectious complication, n (%)	230 (69%)	51 (59%)	.03[a]
Cerebral performance category 1–2, n (%)	120 (36%)	29 (33%)	.66
Intensive care unit mortality, n (%)	208 (62%)	58 (67%)	.45

Table 2. Source of infections and causative agents in successfully resuscitated cardiac ar

	Early-Onset Pneumonia	Late-Onset Pneumonia	Bloodstream Infection	Cath Rela Infec
Gram-positive bacteria				
Staphylococcus aureus	42	8	6	
Streptococcus pneumoniae	26	1	1	
Streptococcus species	3		3	
Staphylococcus epidermidis			3	
Enterococcus faecalis			1	
Clostridium difficile				
Corynebacterium jeikeium			1	
Gram-negative bacteria				
Escherichia coli	28	10	8	
Haemophilus influenzae and *parainfluenzae*	36	2		
Klebsiella pneumoniae	13	3	1	
Pseudomonas aeruginosa	5	11	2	
Enterobacter cloacae	4	4	2	
Proteus mirabilis	7	2	1	
Moraxella catarrhalis	5			
Acinetobacter baumannii		1		
Stenotrophomonas maltophilia		1		
Other enterobacteriaceae species	19	7	5	
Others				
Candida albicans			1	
Polymorph flora	24			
No growth	52			
Total	264	50	35	1

Infections and Normothermia

Prophylactic, Endovascularly Based, Long-Term Normothermia in ICU Patients With Severe Cerebrovascular Disease

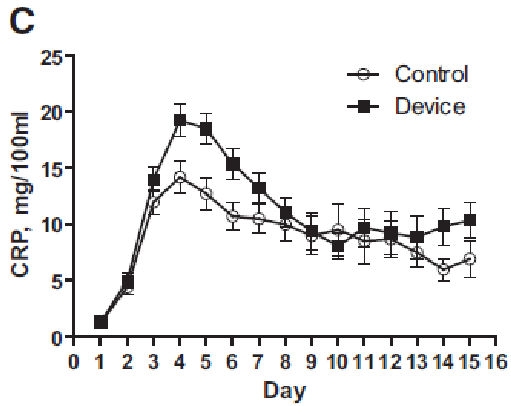
Broessner. (*Stroke*. 2009;40:e657-e665.)

- N = 102

Influence of Prophylactic, Endovascularly Based Normothermia on Inflammation in Patients With Severe Cerebrovascular Disease

Broessner. (*Stroke*. 2010;41:2969-2972.)

	Through Neuro-ICU Discharge		
Infection Type	CoolGard n (%)	Control n (%)	*P* Value
Overall	48 (94)	43 (84)	0.20
Infectious	48 (94)	40 (78)	0.04
Noninfectious	19 (37)	20 (39)	1.00



Baseline Variable	CoolGard (n=51)	Control (n=51)	*P*
Longitudinal data of inflammatory parameters			
C-reactive protein, mg/100 mL (mean±SD)	10.8±6.0	8.6±5.6	0.03
WBCs, G cells/L (mean±SD)	10.3±3.3	10.5±2.8	0.84
IL-10, pg/mL (mean±SD)	11.3±17.2	10.9±16.5	0.72
IL-6, pg/mL (mean±SD)	95.2±82.2	72.7±83.8	0.03
Procalcitonin, μg/L (mean±SD)	0.4±1.1	0.7±1.4	0.60

Infections- what to do?

high vigilance of infections in TH- patients is needed

- ✓ Microbiological surveillance
    - ✓ blood, urine, respiratory specimen
- ✓ Radiological pneumonia surveillance
- ✓ Check lab parameters
    - ✓ CRP, PCT, leukocytes
- ✓ Check catheter insertion sites
    - ✓ timely catheter replacement
- ✓ Avoid hyper and hypoglycemia

TH: GI changes

Usually occur < 35°C

- Impaired bowel function
- Impaired intestinal motility
- Potential for ileus
- Mild pancreatitis (occurs frequently!)
- Liver enzymes ↑

Decreased drug metabolism by the liver

- vasoactive drugs
- opiates
- sedatives
- barbiturates
- neuromuscular blocking
- antiepileptic drugs
- some beta-blockers

3. Rewarming

Most dangerous phase of induced hypothermia

Concerns/Precautions

– Rebound ICP

– Vasodilatation

  - Dramatic changes in hemodynamic profile

– SIRS type syndrome

  - increased catecholamines, O_2 consumption

– Rebound electrolytes (hyperkalemia)

– Cardiac arrhythmias

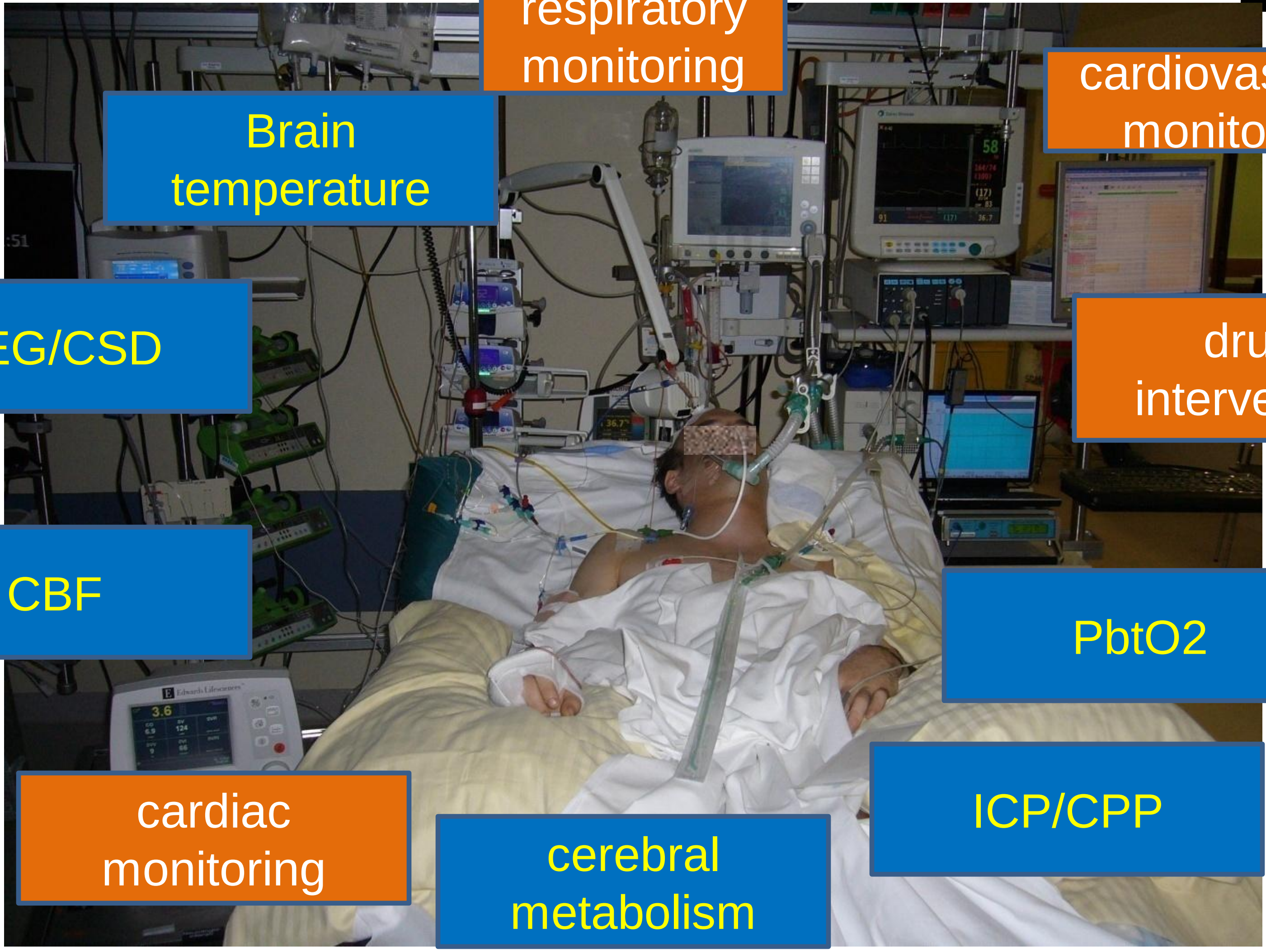
>>>>> monitor and go slow <<<<<

TH: Neurological changes

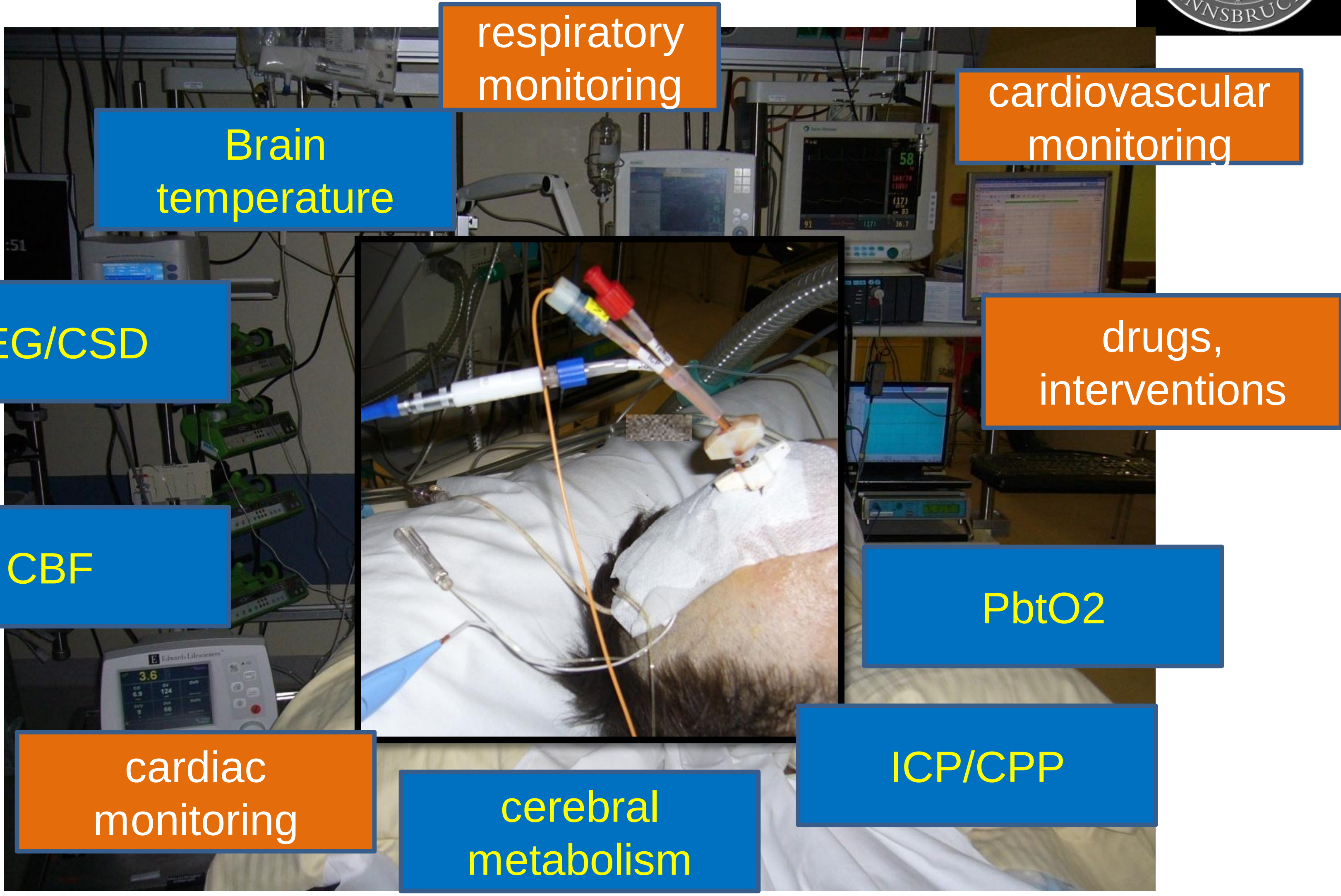
- Neurological Changes
    - Consciousness
    - Lethargy
    - Coma
- Requires intubation, mechanical ventilation, sedation
- Sometimes paralysis
- Neuro exam?

what's the best monitoring?

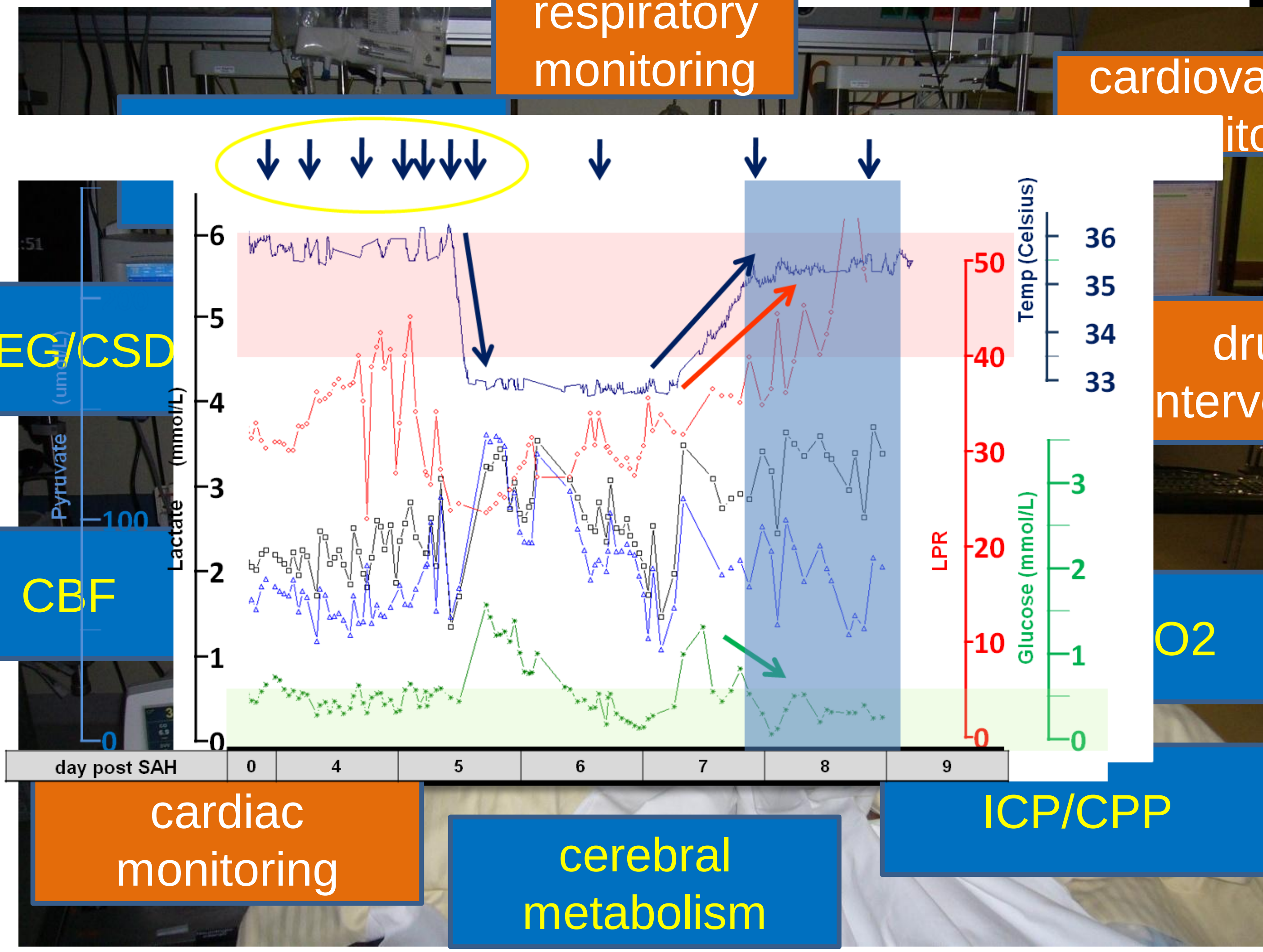
Multimodal Neuromonitoring



Multimodal Neuromonitoring



Multimodal Neuromonitoring



respiratory monitoring

cardiovascular monitoring

EEG/CSD

drugs, interventions

CBF

O2

ICP/CPP

cardiac monitoring

cerebral metabolism

Intracerebral monitoring in comatose patients treated with hypothermia after a cardiac arrest

J. Nordmark[1], S. Rubertsson[1], E. Mörtberg[1], P. Nilsson[2] and P. Enblad[2]
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Table 1

Intracranial pressure (ICP) and cerebral perfusion pressure (CPP) during induced hypotherma and re-warming in four patients with restoration of spontaneous circulation after cardiac arrest.

	ICP						CPP						
	mmHg		Proportion of monitoring time* (%)				mmHg		Proportion of monitoring time* (%)				
	Mean $\pm$ SD	Median (10th–90th percent.)	>15	>20	>25	>30	Mean $\pm$ SD	Median (10th–90th percent.)	<60	<55	<50	<45	<40
Pat 1	14 ± 4	14 (11–18)	30	2.7	1.8	0.9	51 ± 10	47 (42–66)	80	58.2	56.4	20.9	3.6
Pat 2	11 ± 3	11 (8–15)	9.2	1.7	0	0	67 ± 10	66 (56–79)	20.8	7.5	1.6	0	0
Pat 3	5 ± 3	5 (1–9)	0	0	0	0	63 ± 12	61 (50–80)	38.7	22.8	9.5	2.5	0
Pat 4	15 ± 3	16 (11–19)	43.4	2.2	0	0	60 ± 11	58 (47–73)	58.1	46.4	29.6	3.9	0

*Proportion of monitoring time (whole monitoring period; see Figs 1–4) with measurements above or below the stated thresholds. The measured values were registered after every 15 min.

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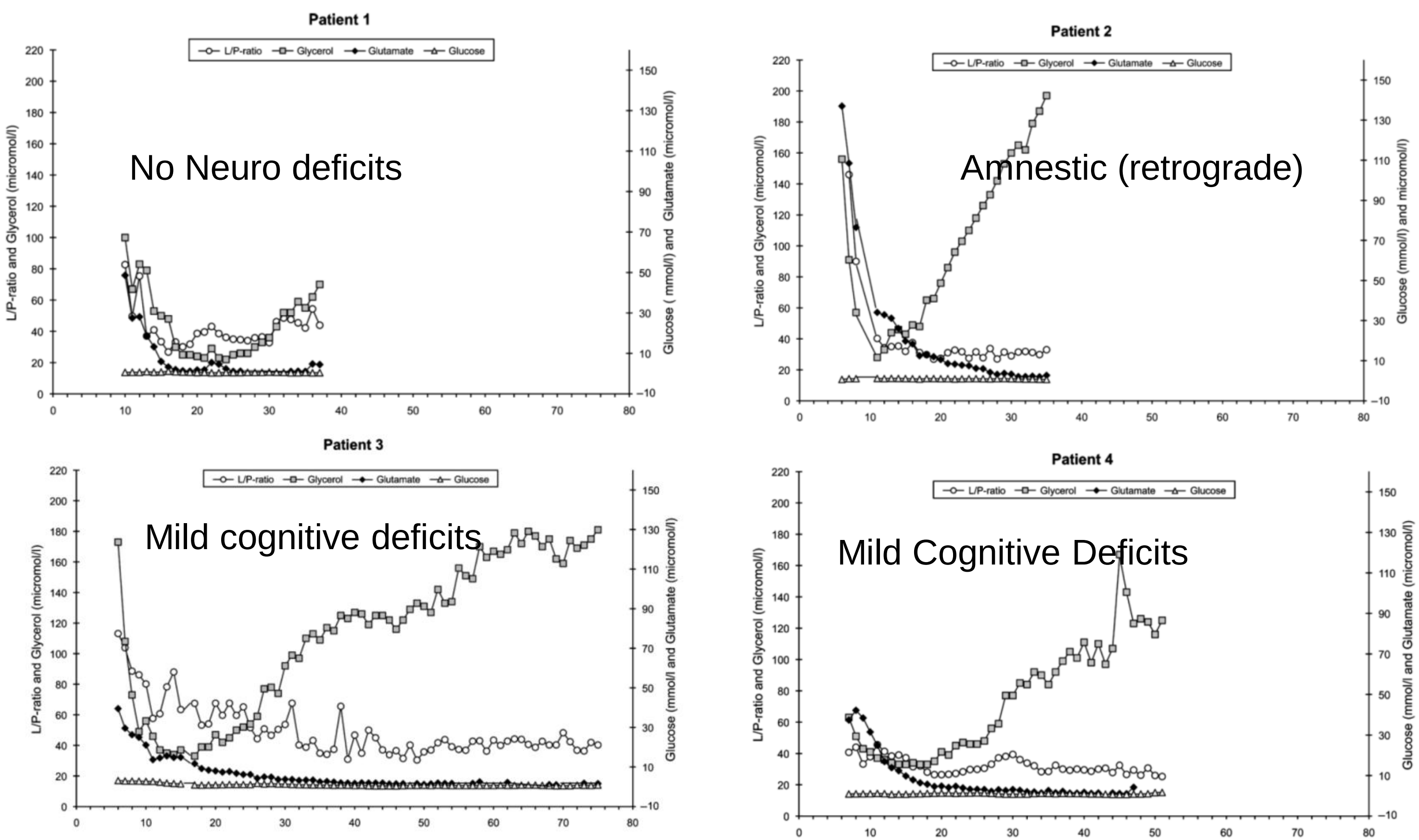

successful application of hypothermia requires

- Team effort
- Requires vigilance, experience
- Guidelines and protocols
- Provide training for the team

Questions?

Neurological ICU Innsbruck…