Poikilothermia is Not Fun!

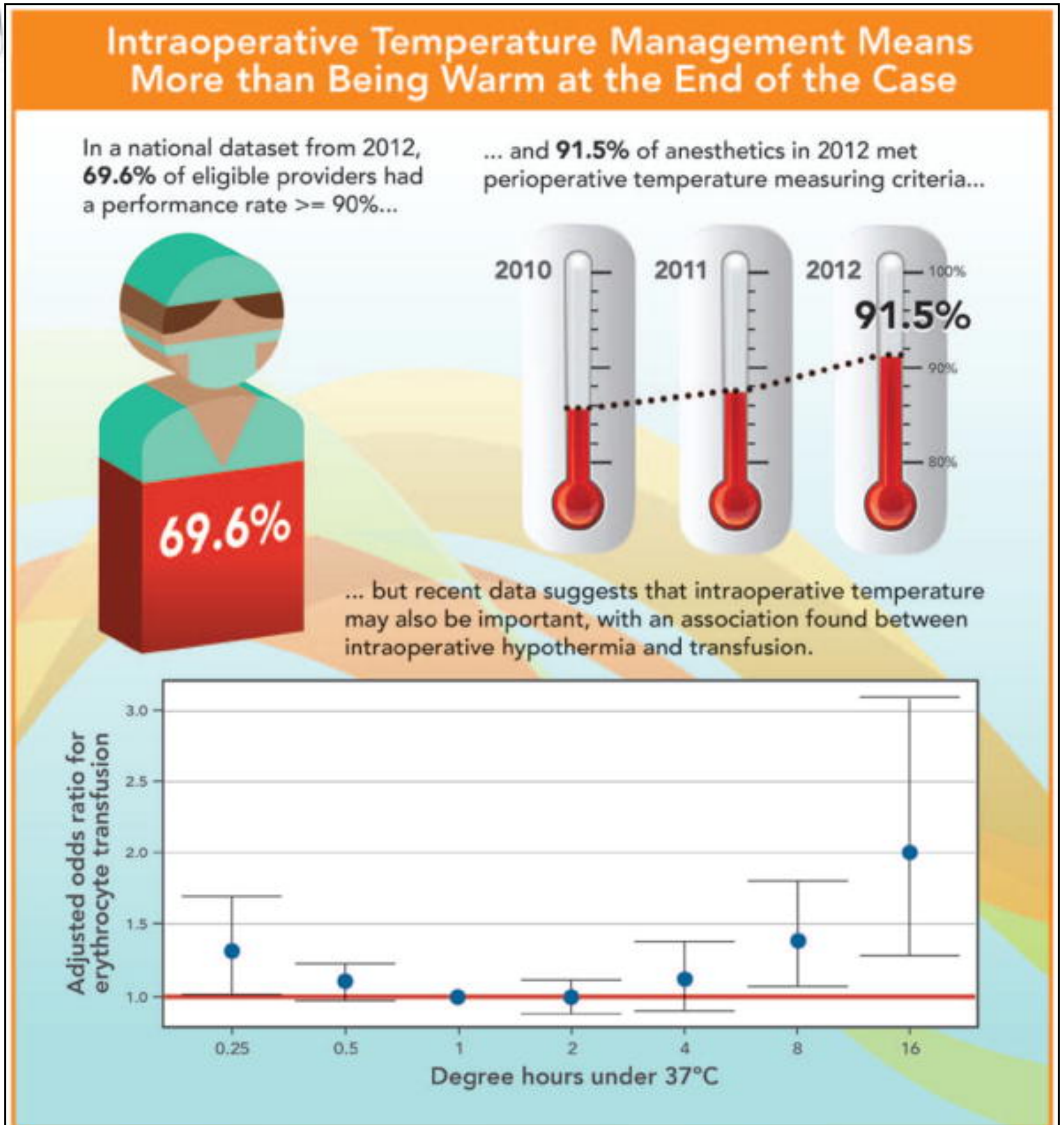
Richard N. Merchant MD FRCPC

OBJECTIVES

- Define and understand
  - … **poikilothermia and hypothermia**
  - … **How thermal homeostasis is normally maintained**
  - … **How body heat is lost in anesthesia**
  - … **What the consequences of hypothermia are**
  - … **How body heat can be maintained**

CONFLICTS OF INTEREST

- 3M Canada has provided a grant for the research project that I will describe, and I have received financial support for my time in preparing and giving this presentation.

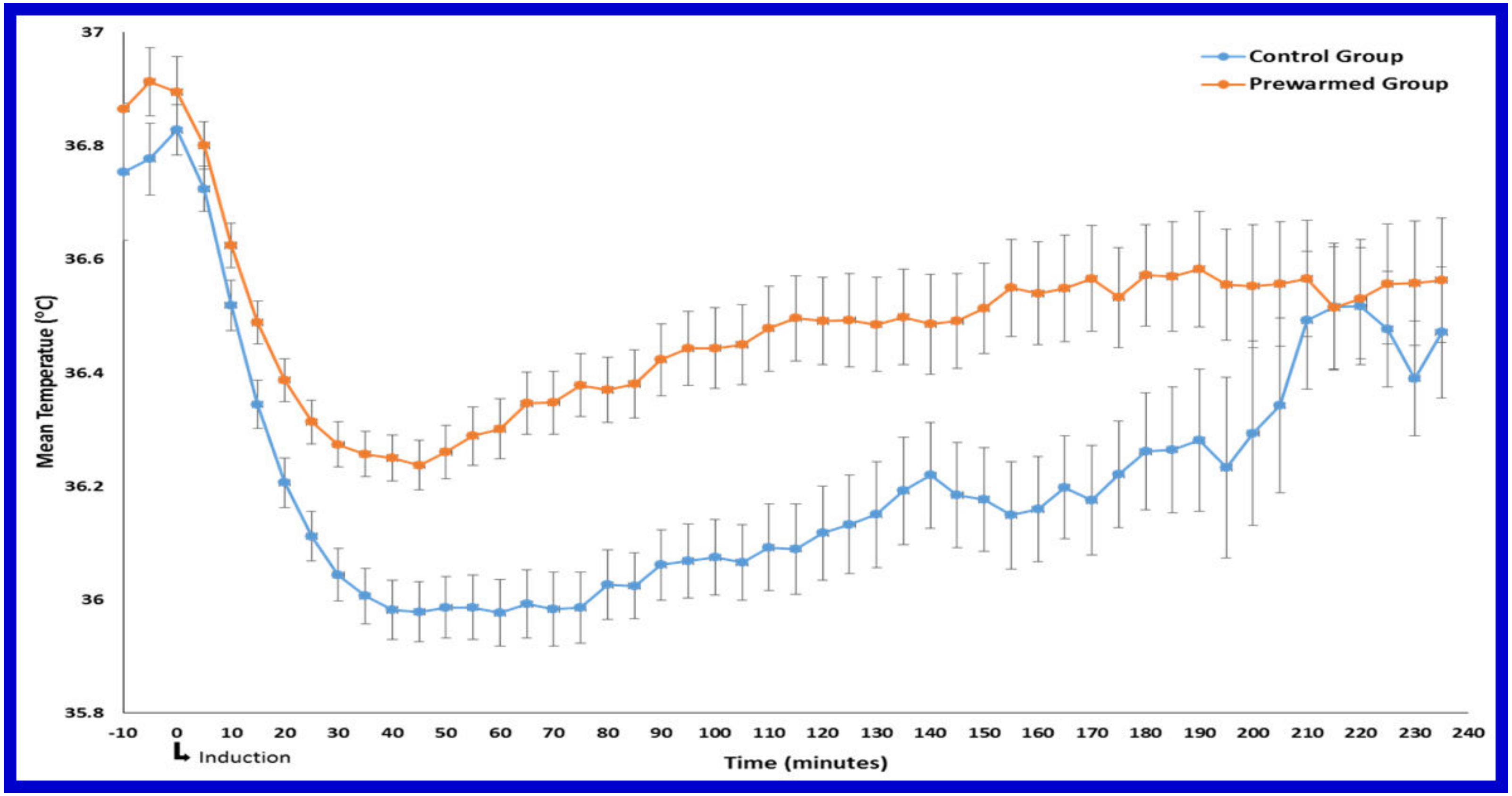


Intraoperative Temperature Management Means More than Being Warm at the End of the Case.

Wanderer, Jonathan; Rathmell, James

Anesthesiology. 122(2):A23, February 2015. DOI: 10.1097/01.anes.0000459438.03762.ee

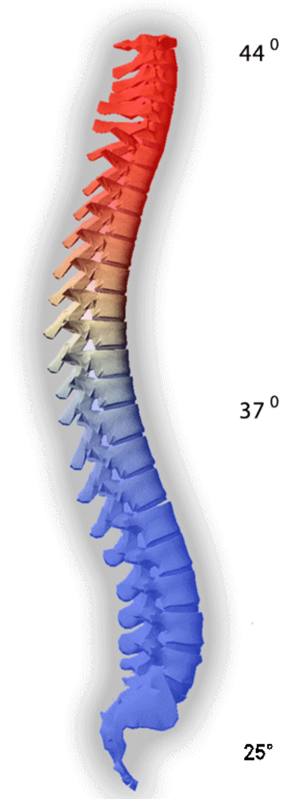
POWS RESULT1



Clem

POIKILOTHERMIA

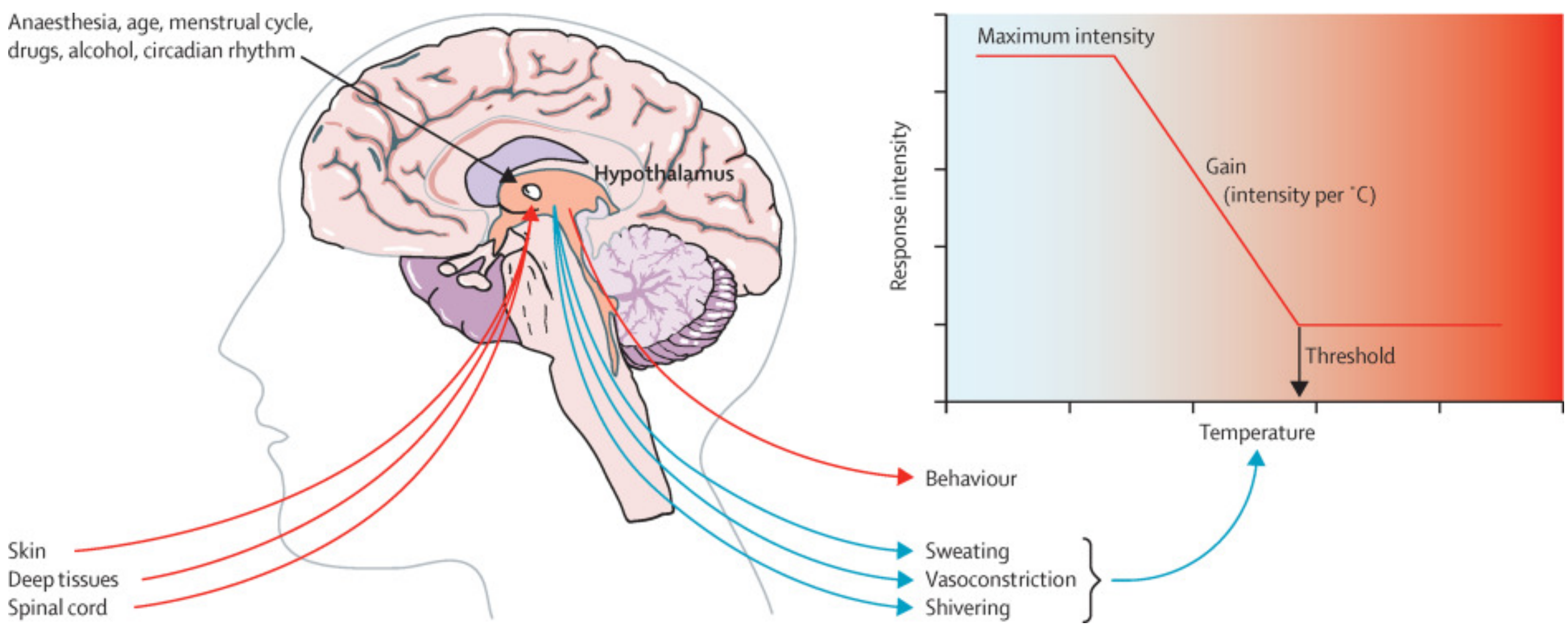
- the inability to regulate core body temperature (as by sweating to cool off or by putting on clothes to warm up), found especially in some spinal cord injury patients and in patients under general anesthesia.
- (poikilothermia. Dictionary.com. Dictionary.com Unabridged. Random House, Inc. http://www.dictionary.com/browse/poikilothermia (accessed: November 26, 2016).
- Hypothermia is core body temperature less than 36.0°C

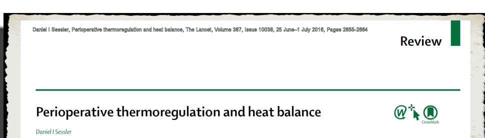


Maximum & Minimum Body Temperature

THERMOREGULATION

- **major thermoregulatory defenses in humans are…**
  - … **sweating,**
  - … **arteriovenous shunt vasoconstriction,**
  - … **shivering.**
  - … **(Non-shivering thermogenesis (activation of brown fat by an uncoupling protein, thermogenin15) is used in preference to shivering in infants)**




Daniel I Sessler, Perioperative thermoregulation and heat balance, The Lancet, Volume 387, Issue 10038, 25 June–1 July 2016, Pages 2655-2664

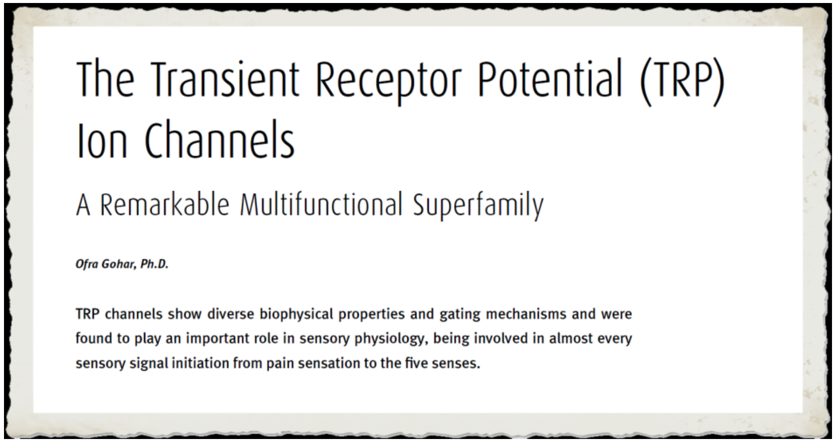
Review

Perioperative thermoregulation and heat balance

Daniel I Sessler

TRANSIENT RECEPTOR PROTEINS

- Transient receptor potential (TRP) channels are a group of unique ion channels that serve as cellular sensors for a wide spectrum of physical and chemical stimuli (23,25,142). They respond with exquisite sensitivity to fundamental cell signaling elements such as PIP2, Ca2+, cyclic nucleotides, phosphorylation potential, temperature, and osmotic pressure, as well as environmental inputs that can be either beneficial or harmful. Activation of TRP channels changes the membrane potential, translocates important signaling ions cross the cell membrane, alters enzymatic activity, initiates endocytosis/ exocytosis, and so on.

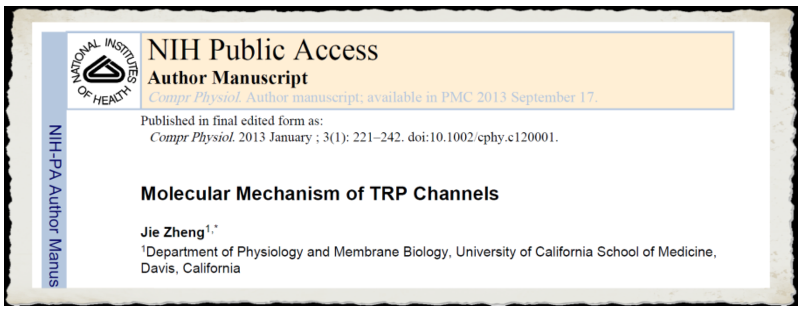


The Transient Receptor Potential (TRP) Ion Channels

A Remarkable Multifunctional Superfamily

Ofra Gohar, Ph.D.

TRP channels show diverse biophysical properties and gating mechanisms and were found to play an important role in sensory physiology, being involved in almost every sensory signal initiation from pain sensation to the five senses.



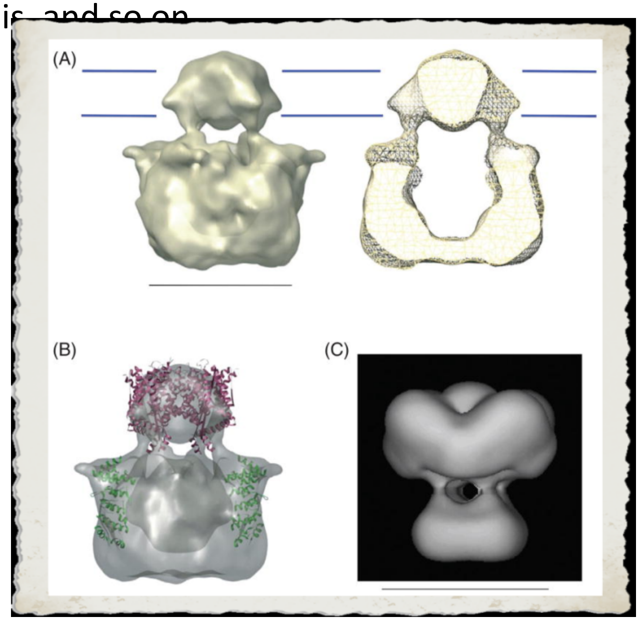
NIH Public Access
Author Manuscript
Compr Physiol. Author manuscript; available in PMC 2013 September 17.

Published in final edited form as:
Compr Physiol. 2013 January ; 3(1): 221–242. doi:10.1002/cphy.c120001.

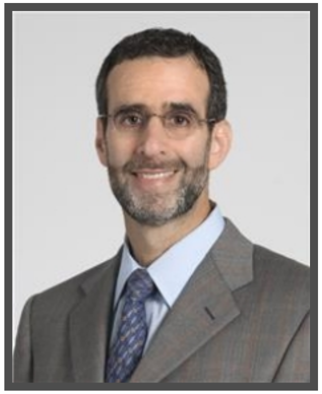
Molecular Mechanism of TRP Channels

Jie Zheng[1,*]
[1]Department of Physiology and Membrane Biology, University of California School of Medicine, Davis, California

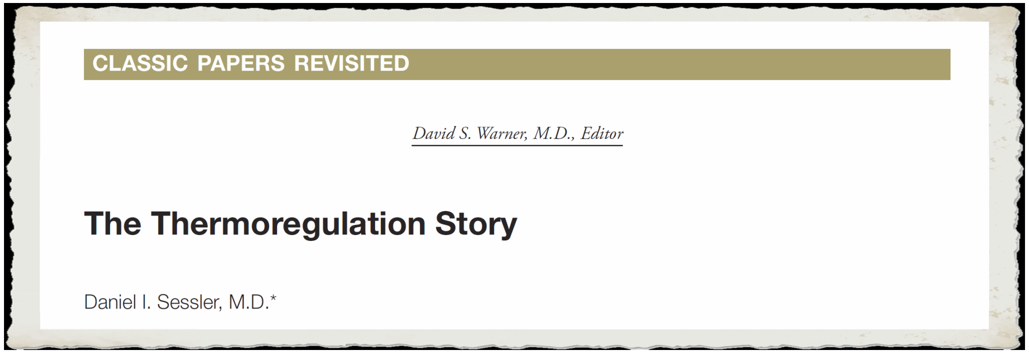
NIH-PA Author Manus



THERMOREGULATION



- Sessler DI, Olofsson CI, Rubinstein EH, Beebe JJ: The thermoregulatory threshold in humans during halothane anesthesia. Anesthesiology 1988; 68:836–42
- Matsukawa T, Sessler DI, Sessler AM, Schroeder M, Ozaki M, Kurz A, Cheng C. Heat flow and distribution during induction of general anesthesia. Anesthesiology. 1995 Mar;82(3) 662-673.
- Andrea Kurz, MD, Daniel I. Sessler, MD, Richard Christensen, BA, Martha Dechert, BA; Heat Balance and Distribution during the Core-Temperature Plateau in Anesthetized Humans. Anesthesiology 1995;83(3):491-499
- …and on for another 390 articles in PubMed

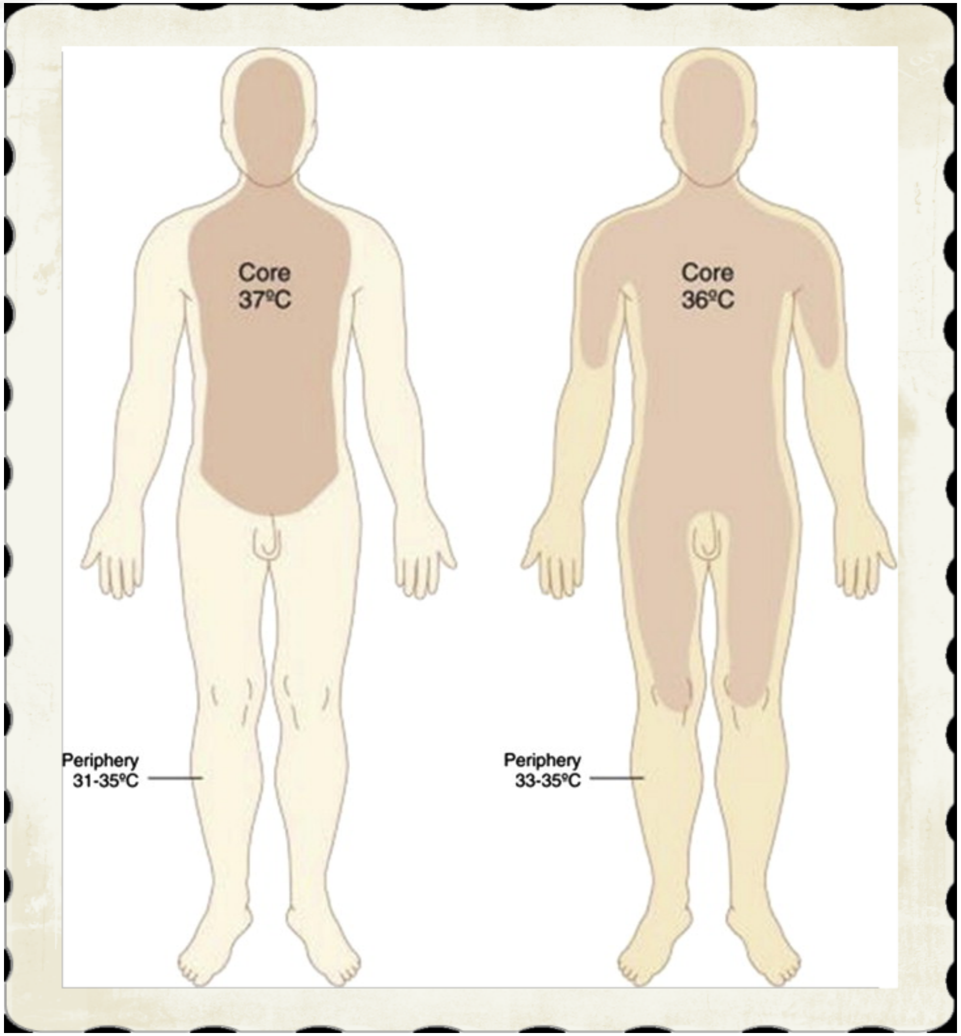

CLASSIC PAPERS REVISITED

David S. Warner, M.D., Editor

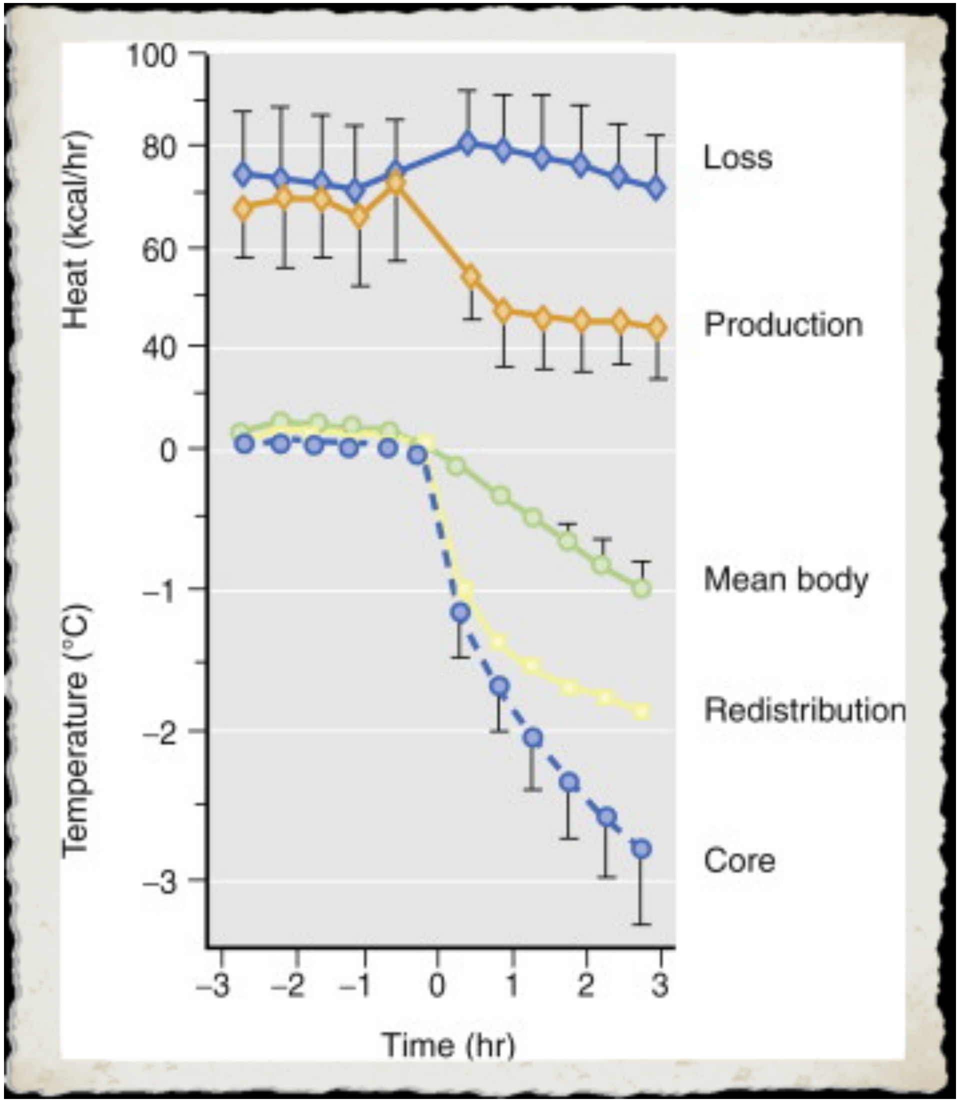
The Thermoregulation Story

Daniel I. Sessler, M.D.*

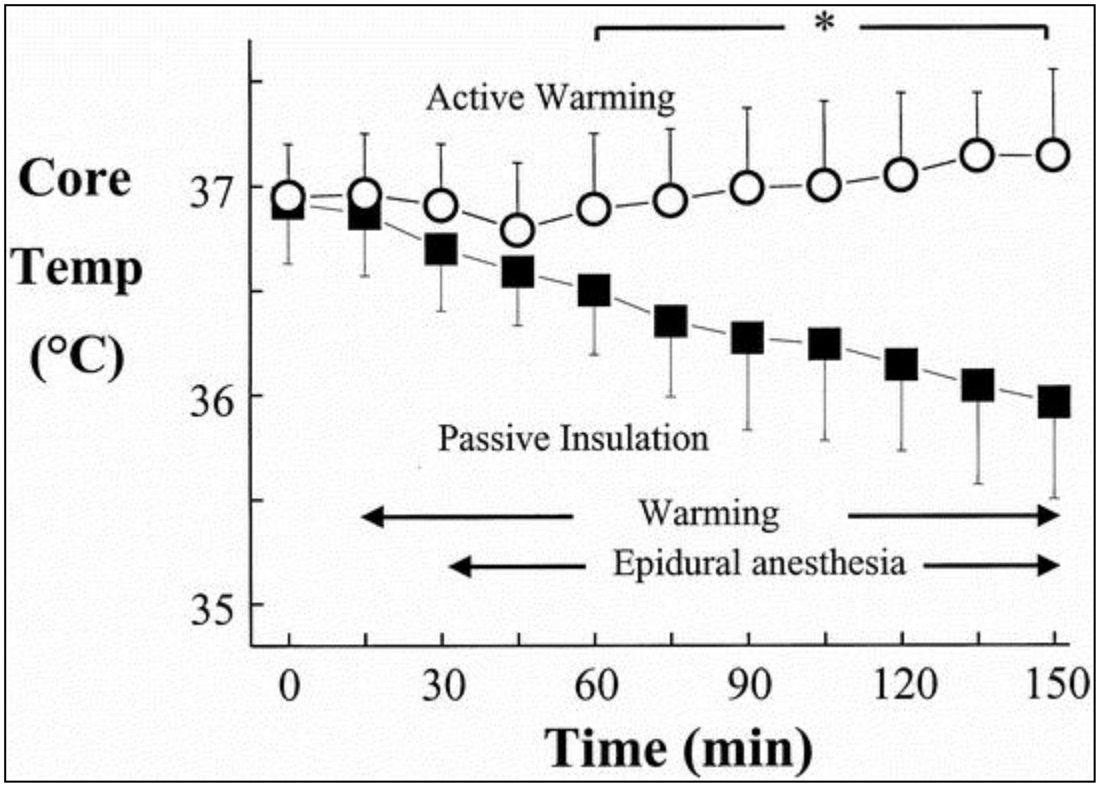
CORE HEAT LOSS: REDISTRIBUTION



CHANGE IN HEAT CONTENT AND TEMPERATURE



CAESARIAN SECTION



Active Warming During Cesarean Delivery.
Horn, Ernst-Peter; Schroeder, Frank; Gottschalk, Andre; Sessler, Daniel; Hiltmeyer, Natascha; Standl, Thomas; Schulte Esch, Jochen

Anesthesia & Analgesia. 94(2):409-414, February 2002.
DOI: 10.1213/00000539-200202000-00034

Figure 1 . Core temperature in patients assigned to passive insulation or active warming. Data are expressed as means +/- sd. All values after 60 elapsed minutes differed significantly in the two treatment groups (*). Core temperatures at the end of surgery were significantly greater in the actively warmed patients (37.1[degrees]C +/- 0.4[degrees]C) than in those assigned to passive insulation (36.0[degrees]C +/- 0.5[degrees]C;P < 0.05).

Wolters Kluwer Health | OvidSP

CONSEQUENCES of Hypothermia

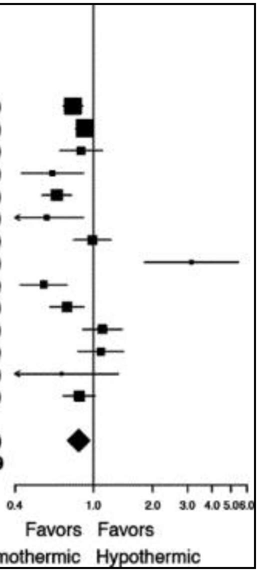
- Coagulopathy
- Surgical site infection
- Alteration in enzyme function
- Postoperative shivering
- Contribution to postop myocardia stress
- Thermal discomfort

COAGULOPATHY

- Reversible impairment of platelet aggregation via reduced release of thromboxane A^2 which reduces formation of an initial platelet plug
- also impairs the function of enzymes in the coagulation cascade which reduces clot formation

COAGULOPATHY / TRANSFUSION

Study	Sample Size (N) N : H	Normothermic (N) mean (sd)	Hypothermic (H) mean (sd)	Outcome (N/H) mean (95%CI)
Schmied	30 : 30	1670 (320)	2150 (550)	0.79 (0.70 , 0.88)
Winkler	75 : 75	1531(1055,1746)	1678(1366,1965)	0.90 (0.82 , 1.00)
Widman	22 : 24	923 (410)	1068 (482)	0.87 (0.68 , 1.11)
Persson	29 : 30	186 (145)	308 (257)	0.62 (0.43 , 0.89)
Hofer	29 : 29	1497 (497)	2300 (788)	0.65 (0.55 , 0.77)
Bock	20 : 20	635 (507)	1070 (803)	0.58 (0.38 , 0.89)
Johansson	25 : 25	1047 (413)	1066 (441)	0.99 (0.80 , 1.23)
Smith	31 : 30	423 (562)	159 (268)	3.14 (1.82 , 5.42)
Frank	142 : 158	390 (834)	520 (754)	0.56 (0.43 , 0.73)
Mason	32 : 32	111 (40)	157 (73)	0.73 (0.60 , 0.89)
Casati	25 : 25	470 (170)	442 (216)	1.11 (0.89 , 1.40)
Murat	26 : 25	160 (61)	161 (100)	1.09 (0.84 , 1.43)
Hohn	43 : 73	660(230,1870)	956(340,5480)	0.69 (0.36 , 1.34)
Nathan	73 : 71	569 (356)	666 (405)	0.85 (0.70 , 1.02)
Summary				0.84 (0.74, 0.96) Treatment effect P = 0.009



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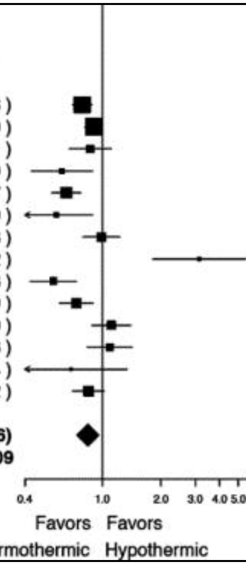
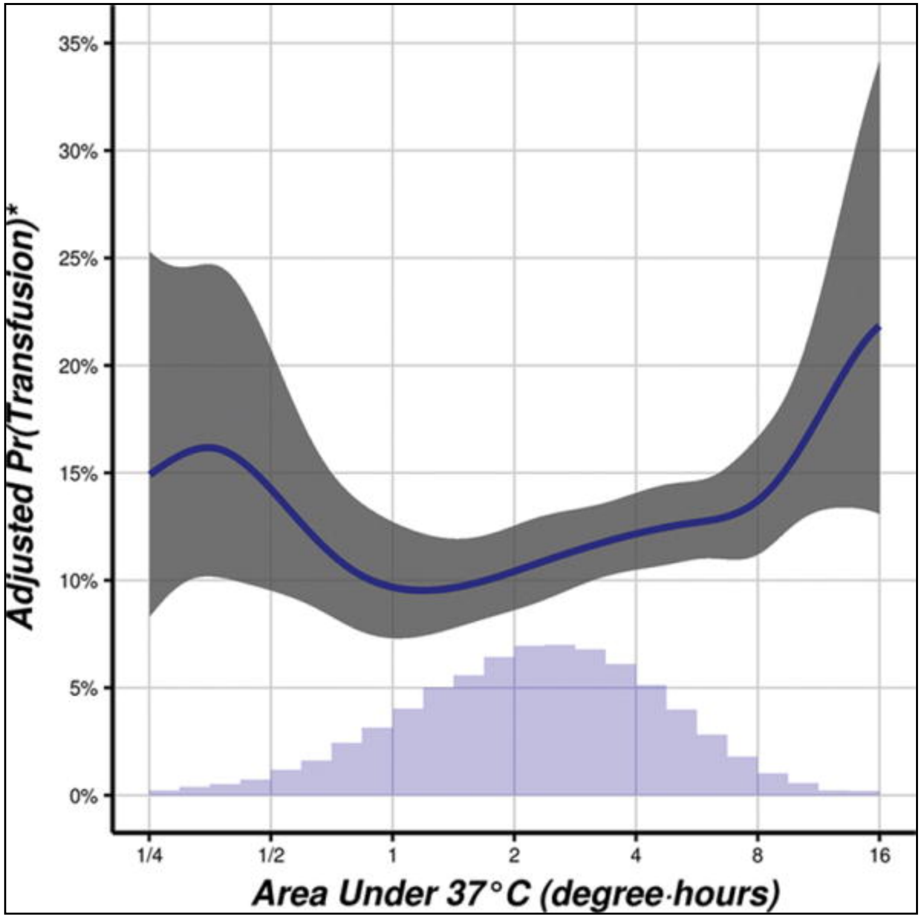


Anesthesiology 2008; 108:71–7

The Effects of Mild Perioperative Hypothermia on Blood Loss and Transfusion Requirement

Suman Rajagopalan, M.D., Edward Mascha, Ph.D.,† Jie Na, M.S.,‡ Daniel I. Sessler, M.D.§*

COAGULOPATHY / TRANSFUSION



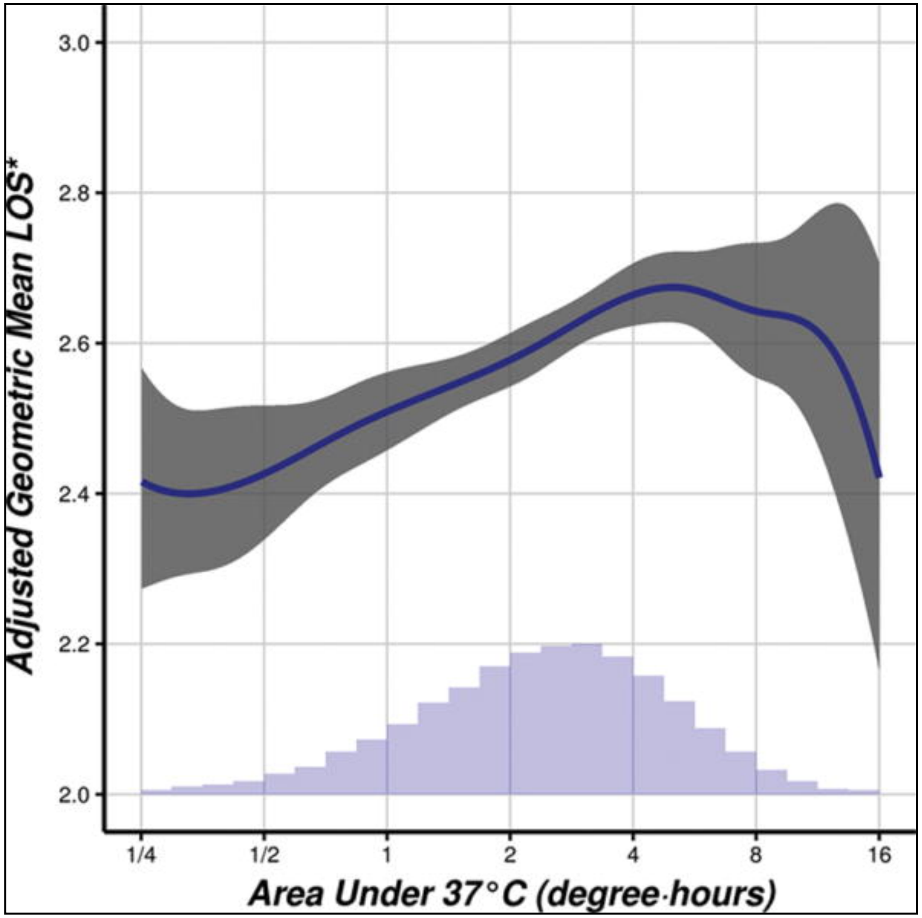
Intraoperative Core Temperature Patterns, Transfusion Requirement, and Hospital Duration in Patients Warmed with Forced Air.

Sun, Zhuo; Honar, Hooman; Sessler, Daniel; Dalton, Jarrod; Yang, Dongsheng; Panjasawtwong, Krit; Deroee, Armin; Salmasi, Vafi; Saager, Leif; Kurz, Andrea

Anesthesiology. 122;2:276-285, February 2015

Fig. 6 . Adjusted probability of transfusion estimates versus integrated area above the core temperature versus time curve and below a threshold of 37[degrees]C, Estimates adjusted to an "at-risk" reference population defined by age > 55 yr, body mass index 2, preoperative hemoglobin 4 h. Shaded regions represent pointwise, Bonferroni-adjusted (for simultaneous analysis on two outcomes) 95% confidence intervals. The regression model was based on 45,866 patients who were admitted on the day of surgery and who had esophageal temperature monitoring. *Adjusted for year, type, and duration of surgery, body mass index, age, preoperative platelet count, preoperative hemoglobin, estimated blood loss, and individual anesthesiologist, as well as the Elixhauser comorbidities 16 (see table 2 for a listing of these comorbidities).Pr = probability.

COAGULOPATHY / TRANSFUSION



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Anesthesiology. 122;2:276-285, February 2015

Fig. 7 . Adjusted estimates of geometric mean duration of hospitalization in days versus integrated area above the core temperature versus time curve and below a threshold of 37[degrees]C, for 39,180 hospital in-patients who were admitted on the day of surgery and who had intraoperative esophageal temperature monitoring. Shaded regions represent pointwise, Bonferroni-adjusted (for simultaneous analysis on two outcomes) 95% confidence intervals. *Adjusted for year, type, and duration of surgery, body mass index, age, preoperative platelet count, preoperative hemoglobin, estimated blood loss, and individual anesthesiologist, as well as the Elixhauser comorbidities 16 (see table 2 for a listing of these comorbidities). LOS = length of stay.

SSI

- All surgical wounds become contaminated. Whether contamination progresses to infection is mostly determined by host defence.

SSI - NEJM

The New England
Journal of Medicine

Volume 334 MAY 9, 1996

PERIOPERATIVE NORMOTHERMIA TO REDUCE THE INCIDENCE O
INFECTION AND SHORTEN HOSPITALIZATION

ANDREA KURZ, M.D., DANIEL I. SESSLER, M.D., AND RAINER LENH
FOR THE STUDY OF WOUND INFECTION AND TEMPERATURE G

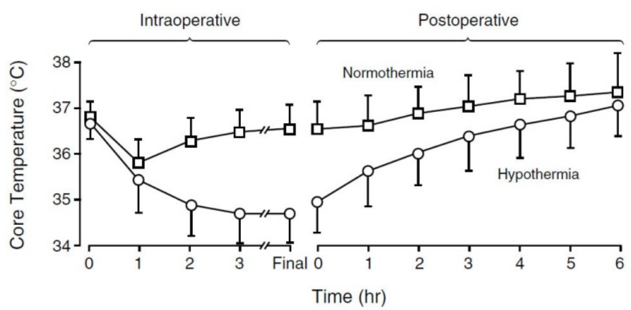


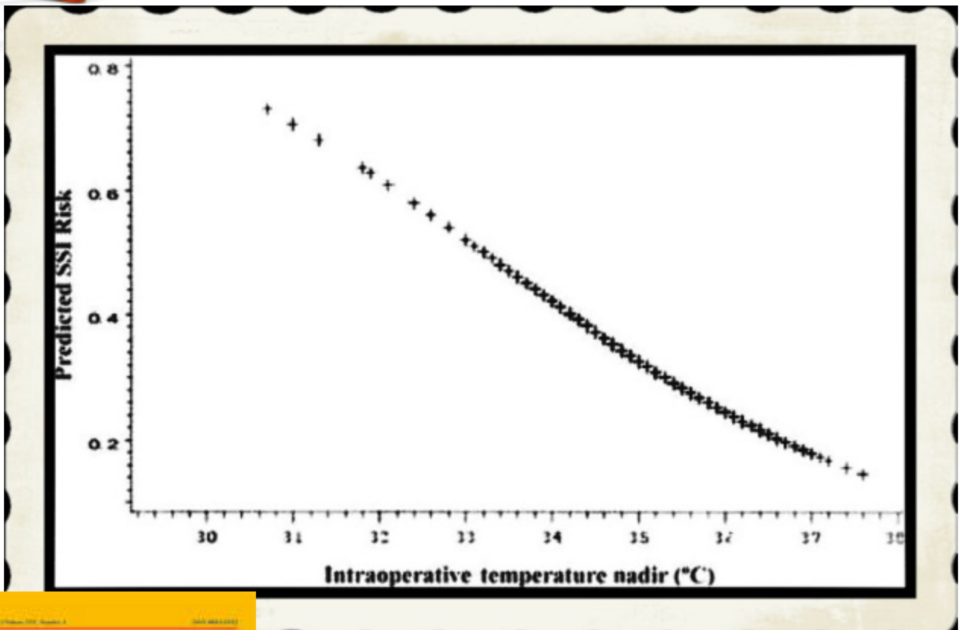
Figure 1. Core Temperatures during and after Colorectal Surgery in the Study Patients.

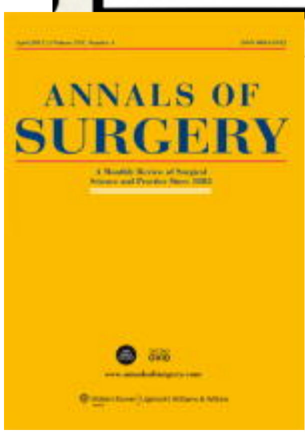
Table 3. Multivariate Analysis of Risk Factors for Surgical-Wound Infection.

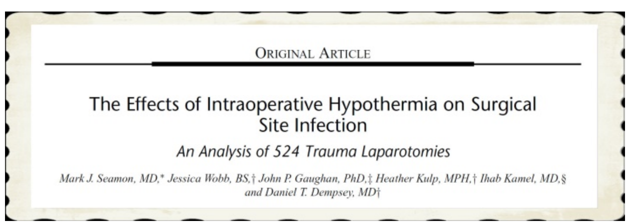
RISK FACTOR	ODDS RATIO (95% CONFIDENCE INTERVAL)
Tobacco use (yes vs. no)	10.5 (3.2–34.1)
Group assignment (hypothermia vs. normothermia)	4.9 (1.7–14.5)
Surgical site (rectum vs. colon)	2.7 (0.9–7.6)
NNISS score (per unit increase)*	2.5 (1.2–5.3)
Age (per decade)	1.6 (1.0–2.4)

*NNISS denotes National Nosocomial Infection Surveillance System.

SSI2 – TRAUMA LAPAROTOMY





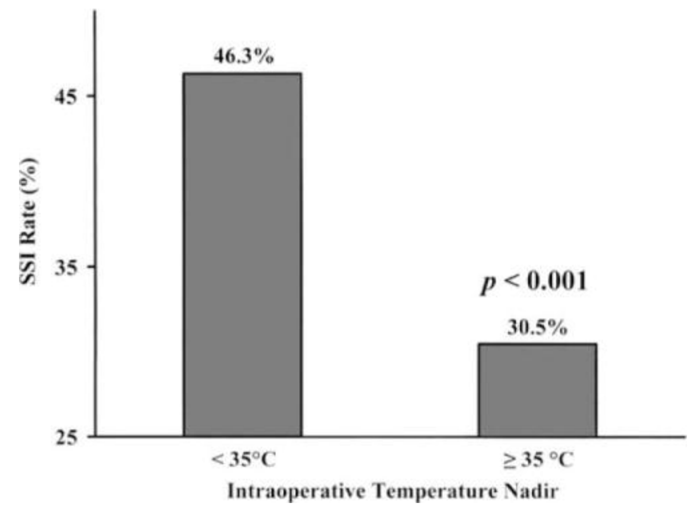


ORIGINAL ARTICLE

The Effects of Intraoperative Hypothermia on Surgical Site Infection

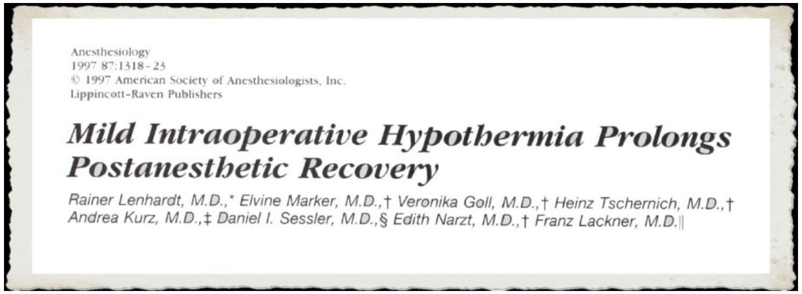
An Analysis of 524 Trauma Laparotomies

Mark J. Seamon, MD, Jessica Wobb, BS,† John P. Gaughan, PhD,‡ Heather Kulp, MPH,† Ihab Kamel, MD,§ and Daniel T. Dempsey, MD†*



Enzyme dysfunction

- Given the thermal sensitivity of enzymes, it is unsurprising that even mild hypothermia prolongs the action of various drugs.
- Muscle relaxants, propofol, …
- A predictable consequence of delayed drug disposition is that postanaesthetic recovery is prolonged in hypothermic patients



Anesthesiology
1997 87:1318-23

Lippincott-Raven Publishers

Mild Intraoperative Hypothermia Prolongs Postanesthetic Recovery

Rainer Lenhardt, M.D., Elvine Marker, M.D.,† Veronika Goll, M.D.,† Heinz Tschernich, M.D.,† Andrea Kurz, M.D.,‡ Daniel I. Sessler, M.D.,§ Edith Narzt, M.D.,† Franz Lackner, M.D.‖*

SHIVERING AND MYOCARDIA STRESS

- Three hundred patients undergoing abdominal, thoracic, or vascular surgical procedures who either had documented coronary artery disease or were at high risk for coronary disease.
- Mean core temperature after surgery was lower in the hypothermic group (35.4±0.1°C) than in the normothermic group (36.7±0.1°C)
- Perioperative morbid cardiac events occurred less frequently in the normothermic group than in the hypothermic group (1.4% vs 6.3%; *P*=.02)
- Hypothermia was an independent predictor of morbid cardiac events by multivariate analysis (relative risk, 2.2; 95% confidence interval, 1.1-4.7; *P*=.04), indicating a 55% reduction in risk when normothermia was maintained

JAMA 1997: Morbid Cardiac Events

Original Contributions

Perioperative Maintenance of Normothermia Reduces the Incidence of Morbid Cardiac Events

A Randomized Clinical Trial

Steven M. Frank, MD; Lee A. Fleisher, MD; Michael J. Breslow, MD; Michael S. Higgins, MD; Krista F. Olson; Susan Kelly, BSN; Charles Beattie, MD

JAMA. 1997;277:1127-1134

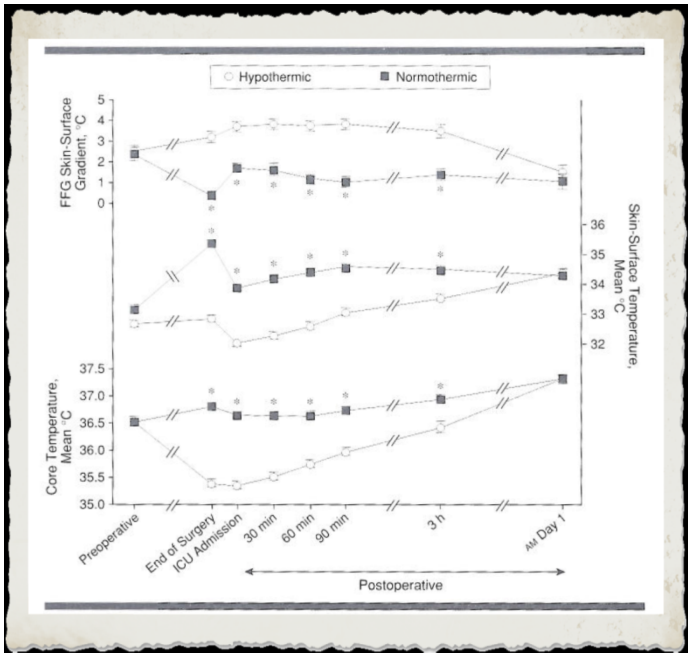


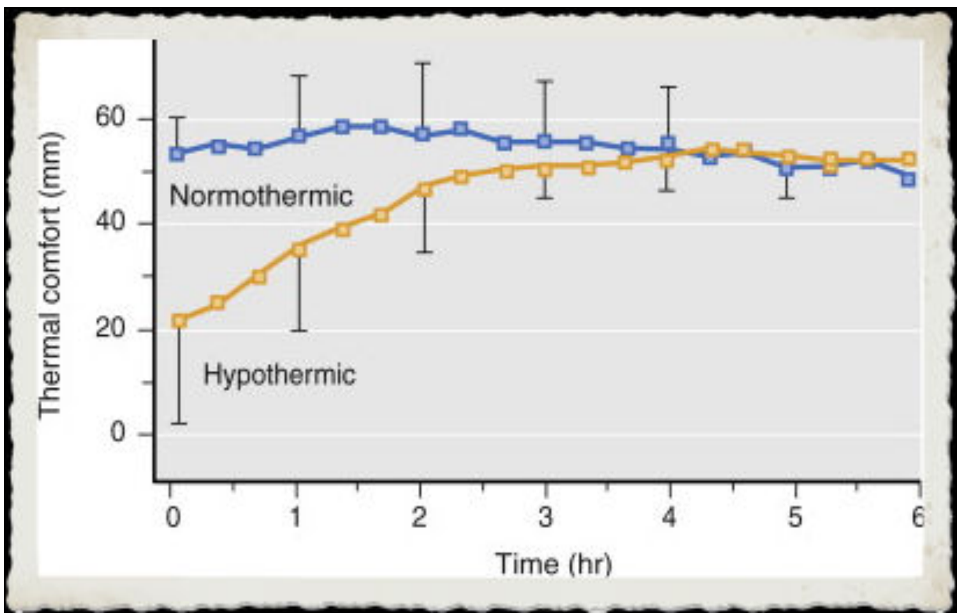
Table 3.—Intraoperative and Postoperative Cardiac Outcomes

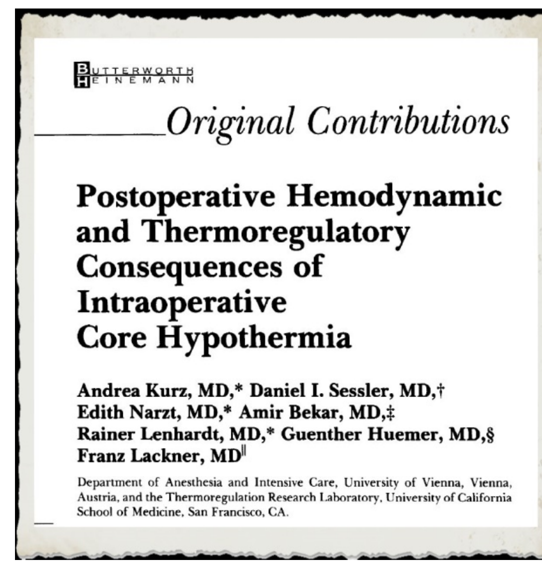
	No. (%) Hypothermic (n=158)	No. (%) Normothermic (n=142)	*P*
Intraoperative Cardiac Outcomes			
Electrocardiographic event*	15 (10)	13 (9)	.76
Myocardial ischemia	8 (6)	7 (6)	.99
Ventricular tachycardia	7 (5)	6 (5)	.95
Postoperative Cardiac Outcomes†			
Electrocardiographic event*	23 (16)	9 (7)	.02
Myocardial ischemia‡	12 (9)	6 (5)	.17
Ventricular tachycardia§	11 (8)	3 (2)	.04
Morbid cardiac event‖	10 (6)	2 (1)	.02
Unstable angina/ischemia	7 (4)	2 (1)	
Cardiac arrest	2 (1)	0 (0)	
Myocardial infarction	1 (1)	0 (0)	
Electrocardiographic or morbid cardiac event	33 (21)	11 (8)	.001

*Myocardial ischemia or ventricular tachycardia.
†Postoperative outcomes include those events that occurred in the first 24 postoperative hours.
‡Includes 140 patients in the hypothermic group and 123 patients in the normothermic group with interpretable Holter monitor data.
§Includes 143 patients in the hypothermic group and 127 patients in the normothermic group with interpretable Holter monitor data.
‖Unstable angina/ischemia, cardiac arrest, or myocardial infarction.

THERMAL COMFORT

- Hypothermic patients felt uncomfortably cold during recovery, and their postoperative core temperatures remained significantly less than in the normothermic patients for more than four hours. Peripheral vasoconstriction and shivering were common in the hypothermic patients but rare in those kept normothermic.





BUTTERWORTH HEINEMANN

Original Contributions

Postoperative Hemodynamic and Thermoregulatory Consequences of Intraoperative Core Hypothermia

Andrea Kurz, MD,* Daniel I. Sessler, MD,† Edith Narzt, MD,* Amir Bekar, MD,‡ Rainer Lenhardt, MD,* Guenther Huemer, MD,§ Franz Lackner, MD‖

Department of Anesthesia and Intensive Care, University of Vienna, Vienna, Austria, and the Thermoregulation Research Laboratory, University of California School of Medicine, San Francisco, CA.

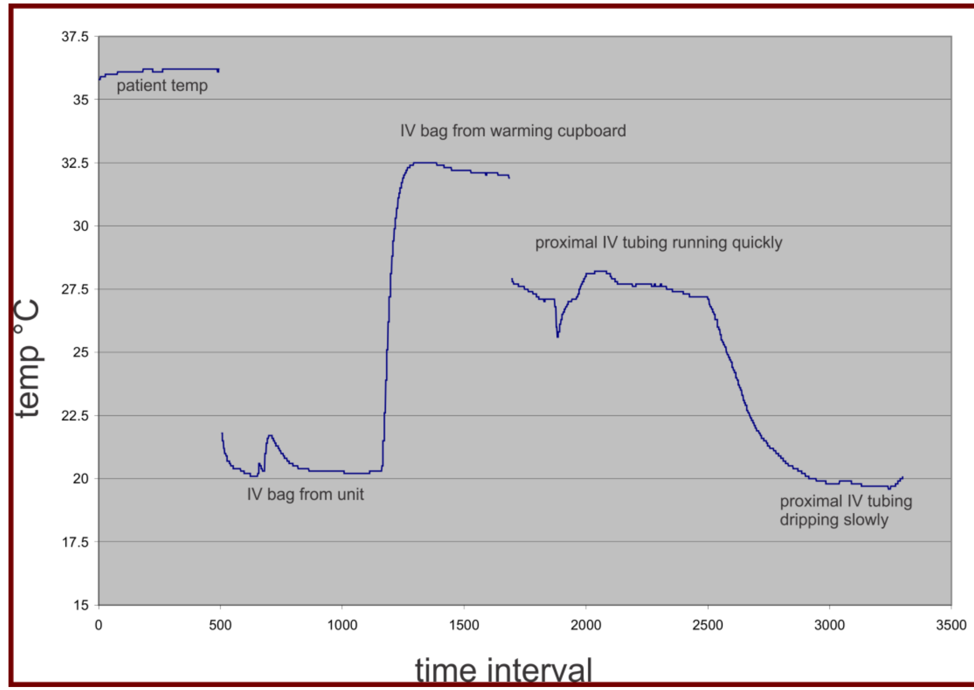
HOW TO AVOID HYPOTHERMIA

- **Avoid active cooling** (warming intravenous fluids, HME exchangers)
- Keep OR warm
- Keep patient covered
- Actively warm patient
  - … **Forced Air warming devices**
  - … **Warm water circulators**
  - … **electric heated mattresses and pads**
  - … **conductive warming systems (such as resistive conductive polymer blankets)**
  - … **infrared lights, anaesthetic air warming and warm CO in laparoscopic surgery**

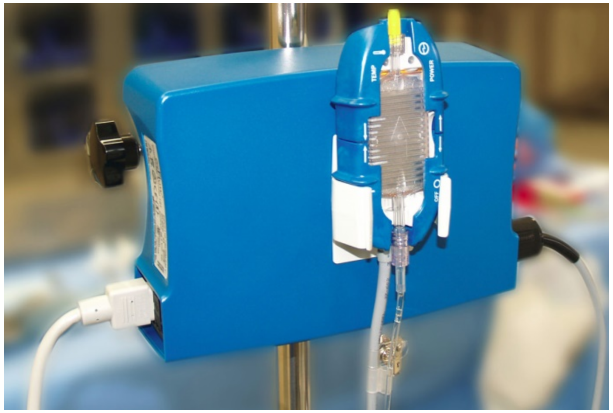
AVOID ACTIVE COOLING

- 1000 cc IV fluid at 20^{o} ↓ core temp $.25^{o}$

Warming fluids in cabinets?



Fluid warming devices



NICE FLUID GUIDELINE

Clinical practice guideline

The management of inadvertent perioperative hypothermia in adults

National Collaborating Centre for Nursing and Supportive Care
commissioned by
National Institute for Health and Clinical Excellence

April 2008

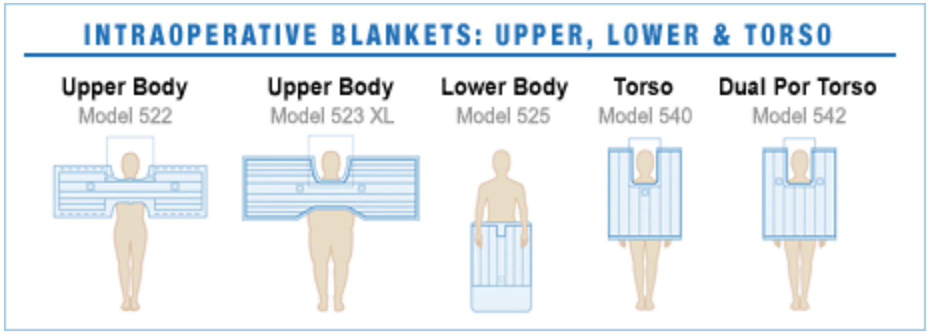
Full guideline

- Intravenous fluids (500 ml or more) and blood products should be warmed to 37°C using a fluid warming device. **1.3.5**

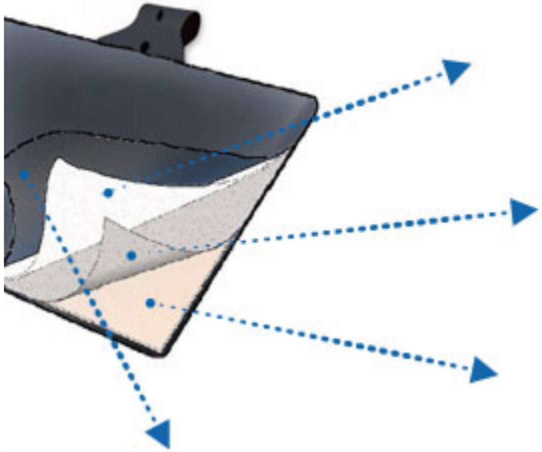
ACTIVE WARMING

- Keep OR warm
- Keep patient covered
- Actively warm patient
  - … **Forced Air warming devices**
  - … **Warm water circulators**
  - … **electric heated mattresses and pads**
  - … **conductive warming systems (such as resistive conductive polymer blankets)**
  - … **infrared lights, anaesthetic air warming and warm CO_2 in laparoscopic surgery**

Forced air warming devices



CONDUCTIVE HEATING



IS ACTIVE WARMING EFFECTIVE?

Cochrane Library

Cochrane Database of Systematic Reviews

Active body surface warming systems for preventing complications caused by inadvertent perioperative hypothermia in adults (Review)

Madrid E, Urrútia G, Roqué i Figuls M, Pardo-Hernandez H, Campos JM, Paniagua P, Maestre L, Alonso-Coello P

IS ACTIVE WARMING EFFECTIVE?

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Active warming systems			
Infection and complications of the surgical wound	157 per 1000	57 per 1000 (31 to 104)	RR 0.36 (0.20 to 0.66)	589 (3 studies)	⊕⊕○○ low[1]
Major cardiovascular complications (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, and non-fatal cardiac arrest)	63 per 1000	14 per 1000 (3 to 63)	RR 0.22 (0.05 to 1)	300 (1 study)	⊕⊕○○ low[1]
All-cause mortality	16 per 1000	16 per 1000 (4 to 63)	RR 1.01 (0.26 to 4)	500 (2 studies)	⊕⊕○○ low[1]
Participants transfused	291 per 1000	259 per 1000 (163 to 413)	RR 0.79 (0.50 to 1.23)	621 (8 studies)	⊕⊕○○ moderate[2]
Chills/shivering	212 per 1000	83 per 1000 (59 to 115)	RR 0,39 (0,28 to 0,54)	1922 (29 studies)	⊕⊕○○ high[3]

NICE 2008

- Patients who are at higher risk of inadvertent perioperative hypothermia (see section 1.2.1) and who are having anaesthesia for less than 30 minutes should be warmed intraoperatively from induction of anaesthesia using a forced air warming device. **1.3.6**

- All patients who are having anaesthesia for longer than 30 minutes should be warmed intraoperatively from induction of anaesthesia using a forced air warming device. **1.3.7**

AT RISK PATIENTS

- neonates
- low ambient OR temperature
- burn patients
- general anesthesia combined with neuraxial anesthesia
- geriatric patients
- low patient temperature before induction
- thin body type
- large blood loss (in that order)

MEASURING TEMPERATURE

- **Pulmonary artery catheter:** considered the gold standard for measuring core body temperature.
- **Esophageal temperature:** accurately reflects core body temperature.
- **Nasopharyngeal temperature**: This is reasonably close to brain and core temperature.
- **Tympanic membrane temperature:** This is a reliable measure of core temperature but requires the transducer to be placed in contact with the tympanic membrane. Infrared tympanic thermometers are difficult to handle and might not reflect tympanic temperature.
- **Bladder Temperature:** although a close approximation of core temperature, the accuracy of this site decreases with low urine output and during abdominal surgery. Reliable choices during regional anes.
- **Skin temperature monitors**: These can be confounded….

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available online at http://www.sciencedirect.com

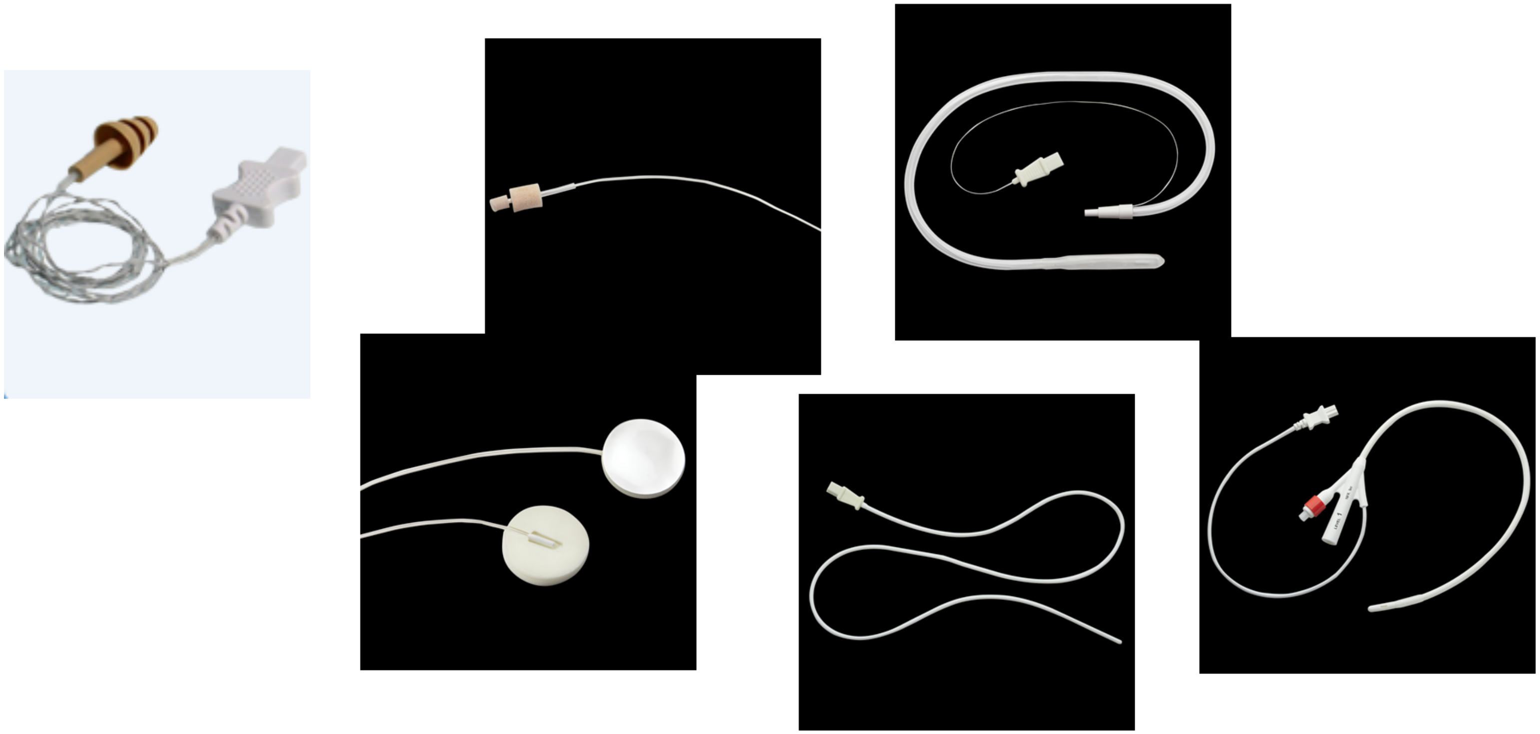
BEST PRACTICE & RESEARCH

3

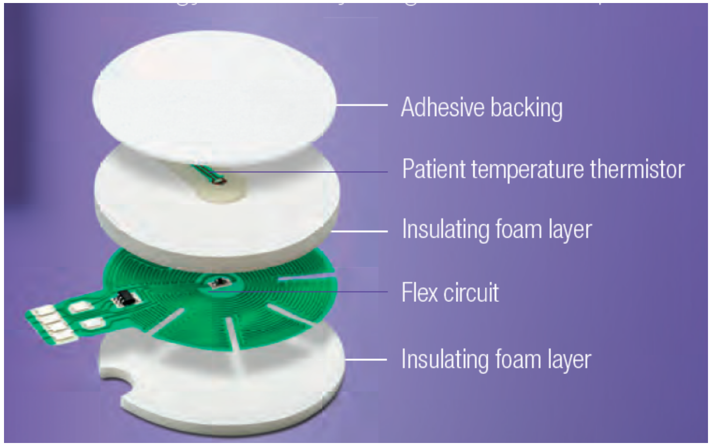
Thermal care in the perioperative period

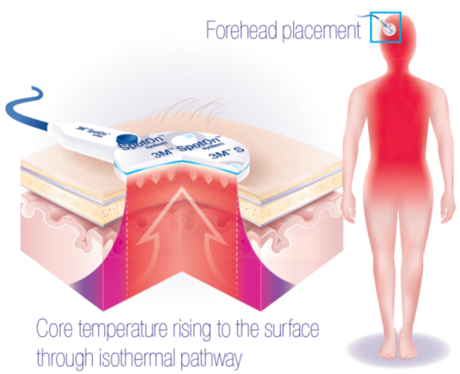
Andrea Kurz* MD
Vice Chair
Department of Outcomes Research, The Cleveland Clinic, 9500 Euclid Avenue — P77, Cleveland, OH 44195, USA

SENSORS



- Zero-Heat-Flux Thermometry

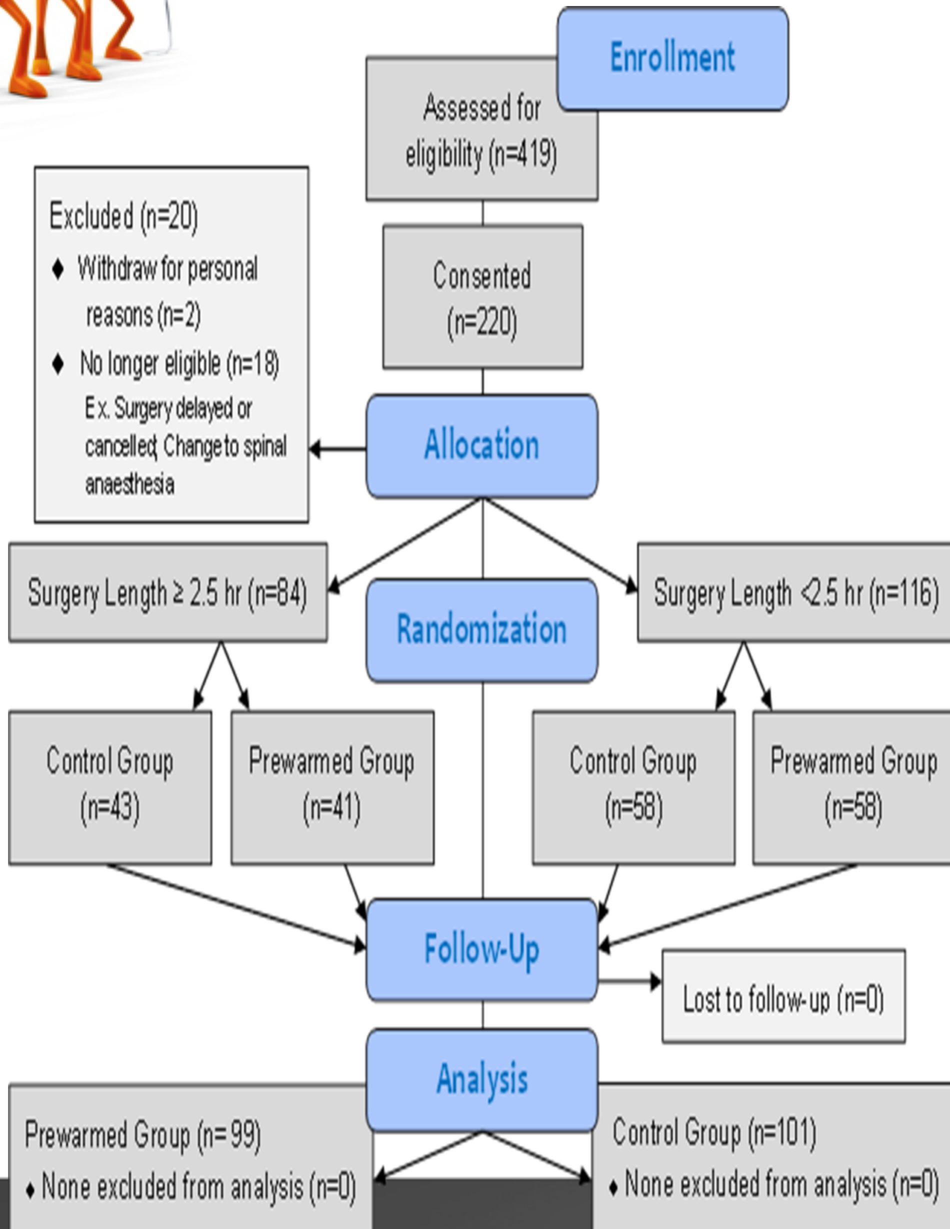




Treatment of Shivering

- Post-anesthetic shivering can be treated by skin-surface warming because the regulatory system tolerates more core hypothermia when cutaneous warm input is augmented.[32]
- a variety of drugs, including
  - **clonidine (75 µg iv),**
  - **ketanserin (10 mg, iv),**
  - **physostigmine (0.04 mg/kg),**
  - **tramadol (1 mg/kg),**
  - **magnesium sulfate (30 mg/kg).**
- meperidine is reportedly far more effective in treating shivering than equi-analgesic doses of other µ agonists.

- Thanks
  - … **For your attention**
  - … **3M for their sponsorship**

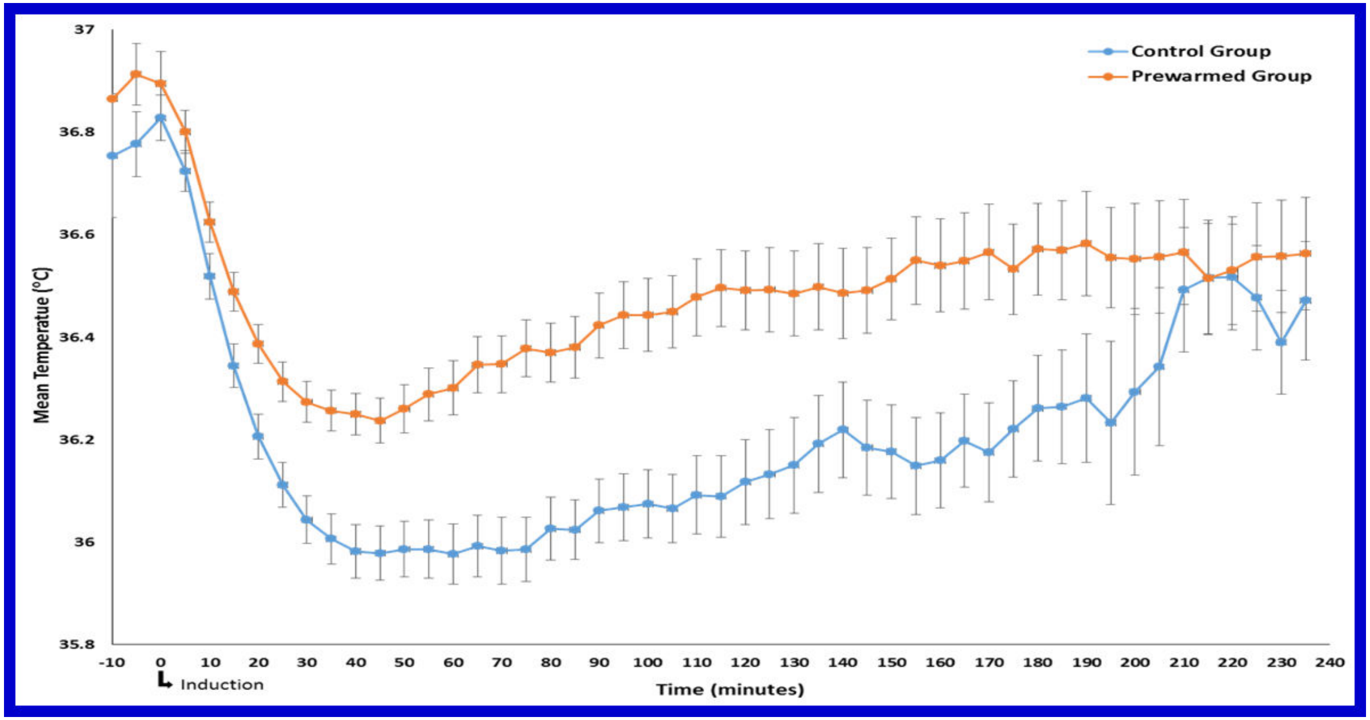


RCH Prewarming study

- Standard of care passive warming via flannel blankets or control group
- prewarmed via BairPaws^{TM} forced air warming gowns starting at least 30 min before entering the operating room (OR).

BAIR PAWS

POWS



Control Group
Prewarmed Group
Mean Temperatue (°C)
37
36.8
36.6
36.4
36.2
36
35.8
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
240
Induction
Time (minutes)

POWS RESULTS3

Table 2. Secondary Outcome Variables for subjects in the control and prewarmed groups. P-values have been adjusted for multiple comparisons ($p \leq 0.0055$ is considered significant). Values are presented as mean (SD) or n (%).

Secondary Outcomes	Control (n=101)	Prewarmed (n=99)	Adjusted critical p-value
Thermal Comfort*	2.4 (2.2)	1.6 (1.7)	0.006
Anxiety* OR	4.6 (2.8)	4.3 (3.2)	0.010
Anxiety* PACU Discharge	1.4 (2.3)	1.8 (2.4)	0.008
Pain* PACU Discharge	3.0 (2.2)	3.0 (2.2)	0.050
EBL (mL)	221.3 (309.4)	254.6 (409.6)	0.017
Flannel Blankets	3.9 (2.3)	2.5 (1.3)	0.0055
PACU LOS (hours)	3.0 (2.6)	2.6 (2.2)	0.007
Hospital LOS (days)	3.6 (3.9)	4.3 (6.6)	0.025
SSI	11 (11%)	14 (14.6%)	0.0125

OR = operating room; PACU = post anesthetic care unit; EBL = estimated blood loss; SSI = surgical site infections
* 0 = comfortable/ not anxious/ no pain, 10 = uncomfortable/ very anxious/ most pain ever

COMPARING TEMPERATURE MEASUREMENT

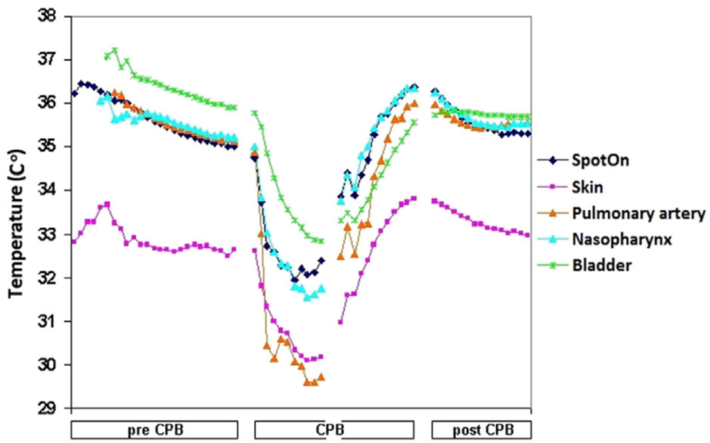


Fig 3. SpotOn, pulmonary artery, nasopharynx, urinary bladder, and forehead skin (skin) mean temperatures of cardiac surgical patients before (pre-CPB), during (CPB), and after CPB (post-CPB) at 5-minute intervals. Each temperature point was included in the illustration when 10 or more measurements were complete at that time.

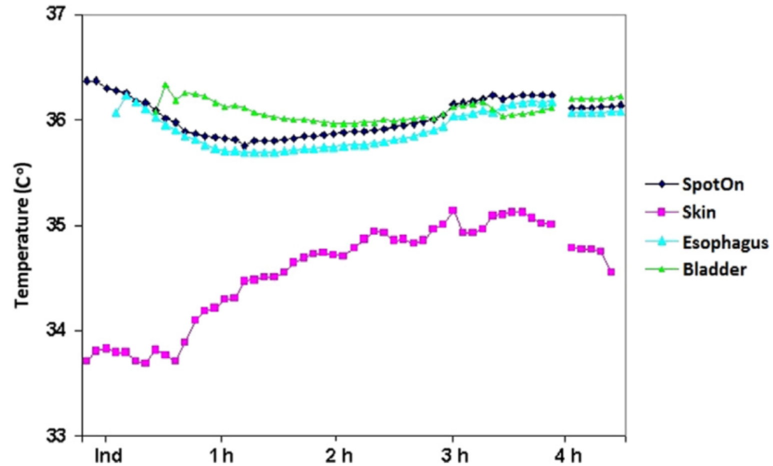


Fig 1. SpotOn, distal esophageal, urinary bladder, and forehead skin (skin) mean temperatures of the vascular surgery patients at 5-minute intervals. Each temperature point was included in the illustration when 10 or more measurements were complete at that time. Ind, induction of anesthesia; 1 h, 2 h, 3 h, and 4 h, hours after induction.

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Original Article

Novel Zero-Heat-Flux Deep Body Temperature Measurement in Lower Extremity Vascular and Cardiac Surgery

Marja-Tellervo Mäkinen, MD, PhD*, Anne Pesonen, MD, PhD*, Irma Jousela, MD, PhD*, Janne Päivärinta, RN*, Satu Poikajärvi, RN, MNSc*, Anders Albäck, MD, PhD†, Ulla-Stina Salminen, MD, PhD‡, Eero Pesonen, MD*

* Division of Anaesthesiology, Department of Anaesthesiology, Intensive Care and Pain Medicine
† Abdominal Center, Department of Vascular Surgery, Meilahti Hospital, Helsinki, Finland
‡ Heart and Lung Center, Department of Cardiac Surgery, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

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