# Critical Care Management of Acute Ischemic Stroke

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# USC Stroke Center


# Acute Ischemic Stroke-Strategies

- The New Revolution: Reperfusion
- Neuroprotection

# Basic ICU Care

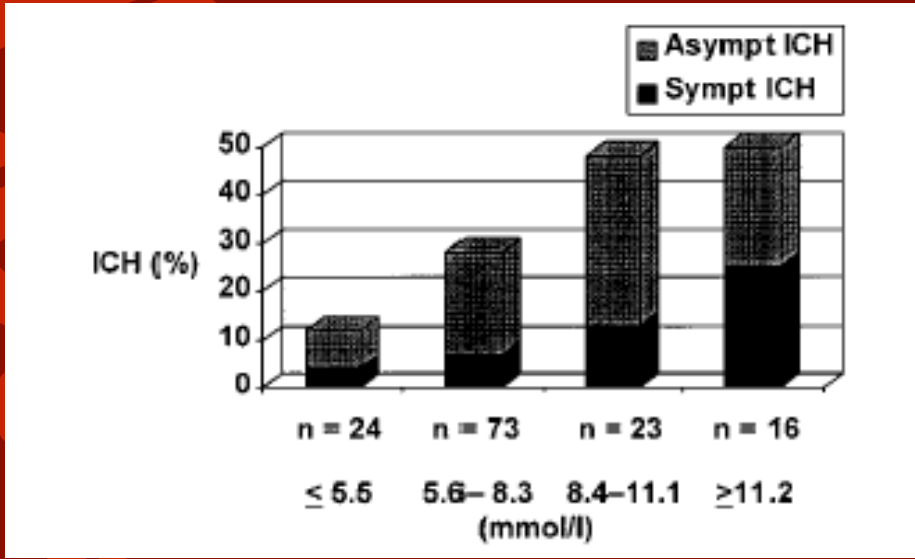
- Glucose
- Fluids
- Temperature
- Blood Pressure

# Glucose

## Serum Glucose Level and Diabetes Predict Tissue Plasminogen Activator–Related Intracerebral Hemorrhage in Acute Ischemic Stroke

Andrew M. Demchuk, MD, FRCPC; Lewis B. Morgenstern, MD; Derk W. Krieger, MD; T. Linda Chi, MD; William Hu, MD; Theodore H. Wein, MD, FRCPC; Robert J. Hardy, PhD; James C. Grotta, MD; Alastair M. Buchan, BM, FRCPC

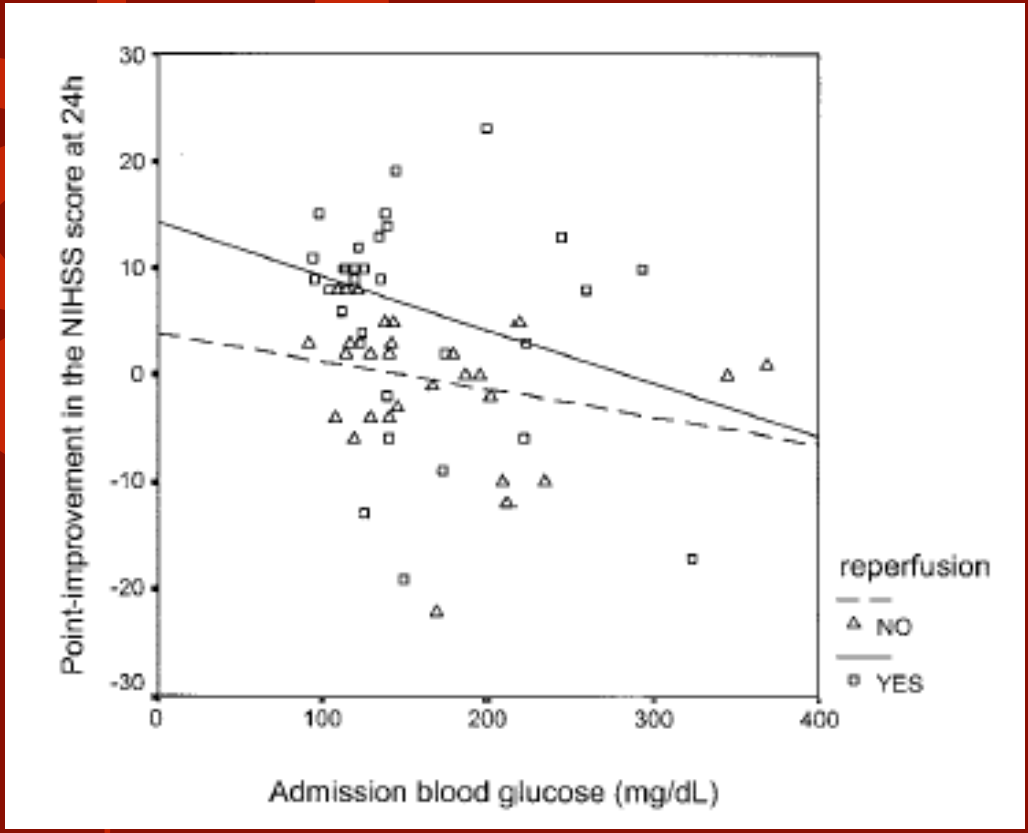
- Serum glucose > 200 mg/dl was associated with a 25% symptomatic hemorrhage rate.



# Effects of Admission Hyperglycemia on Stroke Outcome in Reperfused Tissue Plasminogen Activator–Treated Patients

José Alvarez-Sabín, MD, PhD; Carlos A. Molina, MD, PhD; Joan Montaner, MD, PhD; Juan F. Arenillas, MD; Rafael Huertas, MD; Marc Ribo, MD; Agusti Codina, MD, PhD; Manuel Quintana

- Admission glucose 140 mg/dL was associated with poor outcome among in reperfused patients.



# Hyperglycemia

- RCT of 1,000 patients in a med-surg ICU *(Van Den Berghe NEJM 2001)*
  - Intensive control 80-110 mg/dl vs loose control<150
  - Decreased mortality in intensive glycemia group
- Subgroup analysis of 63 patients (*Van Den Berghe Neurology 2005)*
  - Improved mortality in neurology patients

# GIST Glucose Insulin in Stroke Trial

- 21 centers, 1998-2006
- <24 hrs after onset, ischemic stroke or ICH
- Baseline glc 6-17 mmol/l (108-306 mg/dl)
- Tx GKI - 10% glucose, potassium, insulin
- N=933; 464 GKI 100 cc/hr, 469 control
- DM 16.5%, median tx 13.5 hrs, baseline glc 7.6 mmol/L (137mg/dl)

# GIST

- tx regimen changes 74%
- Low glucose 41% 4 mmol/L (72 mg/dl)
- Mean reduction glc 0.57 mmol/L (10mg/dl)
- BP reduction 9 mm Hg

# GIST

- Mortality: tx 30%, 27.3%
- mRS >3: tx 322, saline 339
- BI<9: tx 309, saline 327
- Subgroups:
  - before/after 12 hrs
  - Higher/lower 11 mmol/L

2007 ISC Gray CG

# THIS

- Treatment of Hyperglycemia in Ischemic Stroke
- AIS & glc 150-499
- Insulin drip & glc goal 70-130 vs sliding scale
- Trend toward benefit (46 pts total)

# GRASP

- Glucose Regulation in Acute Stroke Patients
- Glc goals: 70-110 (24), 70-200 (25), <300 (24)
- AIS within 24 hrs
- Tight control had trend for benefit

# SHINE
# Stroke Hyperglycemia Insulin Network Effort

- Insulin drip glc goal 80-130 vs sliding scale glc goal <185
- AIS within 12 hrs
- N=1400

# SHINE
# Stroke Hyperglycemia Insulin Network Effort

- Begun 2012
- Halted early for lack of effect
- N=1100 (1400)

# ASA Guideline 2018

- Glucose goal 140-180
- Monitor closely
- Treat Hypoglycemia aggressively

# Fluids

# Fluid Management

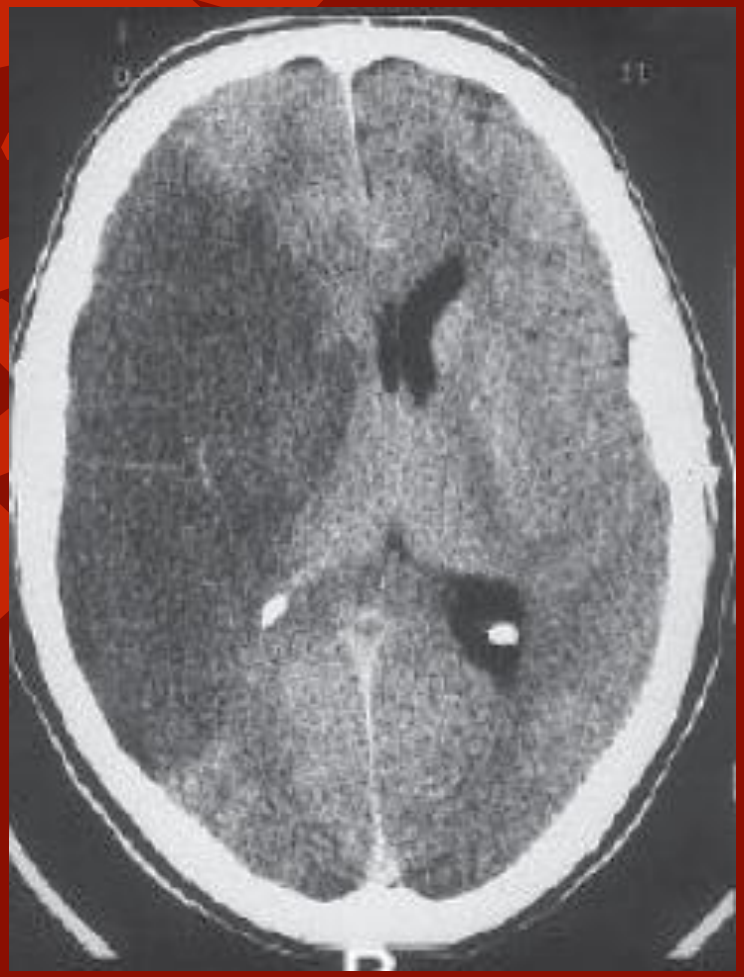
- Two antecubital peripheral IVs
- Use only 0.9NS
- Avoid 0.45 saline solution
- No D5 solution
- Euvolemia

# ALIAS
# Albumin in Acute Ischemic Stroke

- AIS
- NIHSS>5
- within 5 hrs stroke onset
- Albumin 2gm/kg in 2 hrs

# Treatment of Cerebral Edema

- Traditional Treatments include:
  - Hyperventilation
  - Mannitol
  - Sedation
  - Paralysis
  - Hypertonic Saline



# Mannitol or Hypertonic Saline

- Mannitol 0.25- 1 gm/Kg IV bolus for effect
- 2-3% NaCl infusion as maintenance fluid with Na goal 145-155
- 23.4% NaCl: Bolus for effect
- Hypertonic saline may be more effective than mannitol for midline shift (Manno et al 1999)

# 23.4% HS

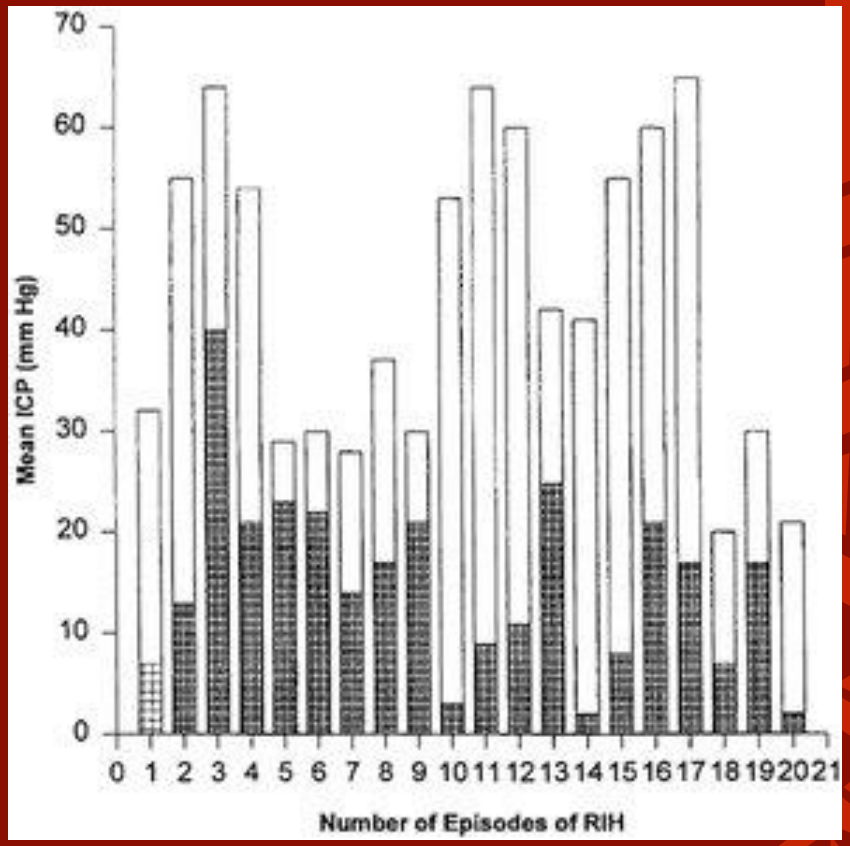
**Treatment of refractory intracranial hypertension with 23.4% saline**

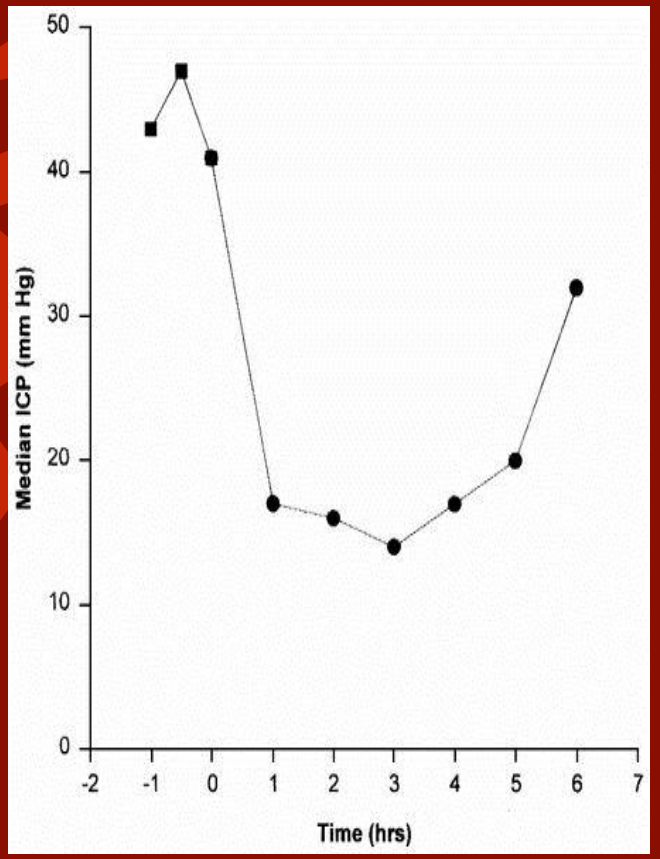
Jose I. Suarez, MD; Adnan I. Qureshi, MD; Anish Bhardwaj, MD; Michael A. Williams, MD; Mark S. Schnitzer, MD; Marek Mirski, MD; Daniel F. Hanley, MD; John A. Ulatowski, MD, PhD

CRITICAL CARE MEDICINE 1998;26:1118-1122

- Refractory Intracranial HTN (RIA)
- Failure to conventional therapies - ICP < 50%
- (HV, Mannitol, Furosemide, Barbiturates)
- 8 Patients ( SAH - 5; TBI - 1; Hemangiopericytoma - 1; ICH -1); 20 episodes; Retrospective Analysis

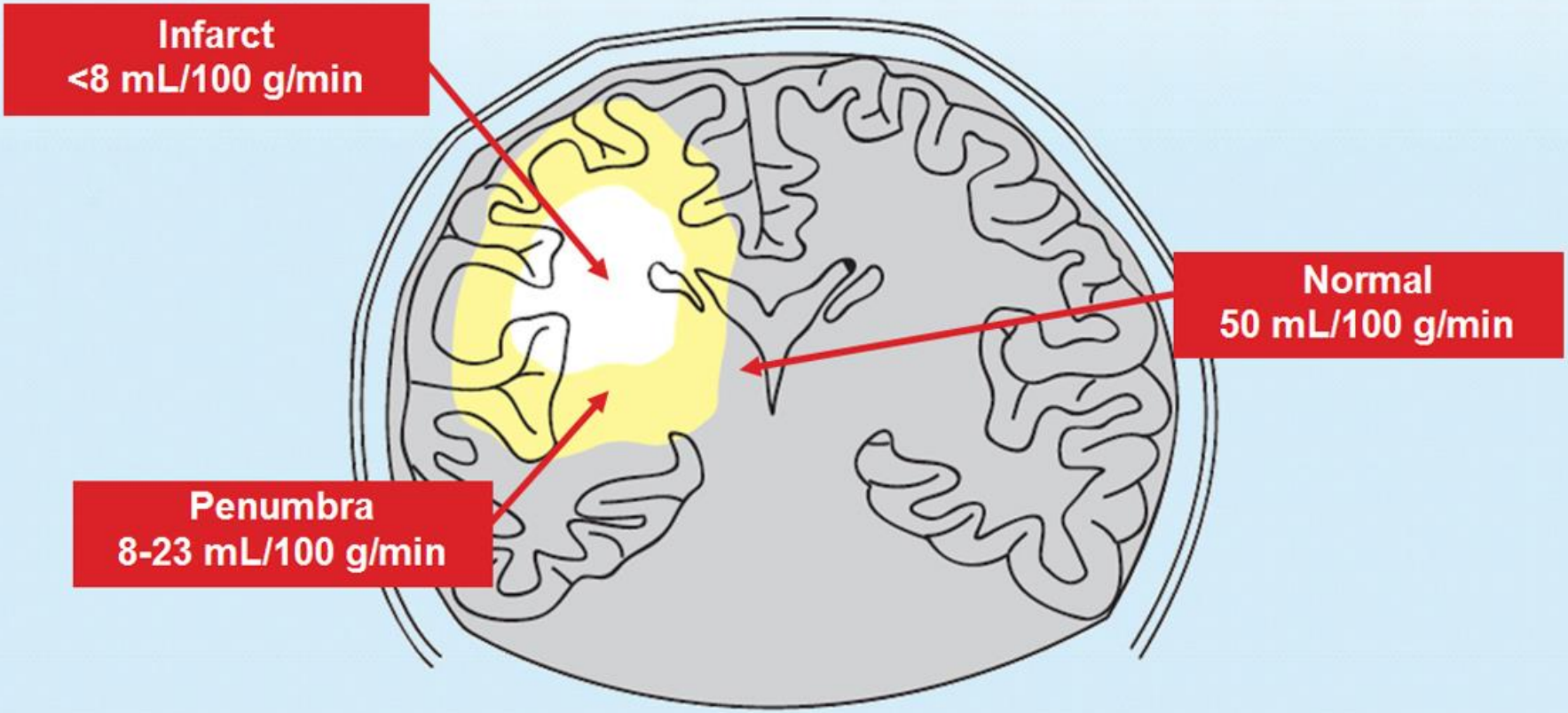
# Effect of 23.4% HS on ICP



# Blood Pressure

# Ischemic Penumbra: Hypoperfused Area of Focal Ischemia That Can Be Salvaged by Timely Intervention




Ahmed SH, et al. In: Fisher M, ed. *Stroke Therapy*. 2nd ed. Woburn, Mass: Butterworth-Heinemann; 2001:25-57. Ullman JS. In: Andrews BT, ed. *Intensive Care in Neurosurgery*. New York, NY: Thieme; 2003:29-46.

# Management of Hypertension in Acute Ischemic Stroke: Patients Not Eligible for Thrombolytic Therapy

(2003)

- **SBP <220 or DBP <120**
  - No antihypertensive therapy
- **SBP >220 or DBP=121-140**
  - Labetalol or nicardipine to 10%-15% reduction
- **DBP >140**
  - Nitroprusside to 10%-15% reduction

- (2007)
- "aforementioned data suggest that the systolic blood pressure level that would prompt treatment would be >180 mm Hg"
- "pending more data, the consensus of the panel is that …antihypertensive agents should be withheld unless the DBP > 120mmHg or SBP > 220 mmHg"

Adams HP, et al. *Stroke*. 2003;34:1056-1083.

# Management of Hypertension in Acute Ischemic Stroke: Patients Not Eligible for Thrombolytic Therapy 2018

- In patients with BP ≥ 220/120 mm Hg who did not receive IV alteplase or EVT and have no comorbid conditions requiring acute antihypertensive treatment, the benefit of initiating or reinitiating treatment of hypertension within the first 48 to 72 hours is uncertain. It might be reasonable to lower BP by 15% during the first 24 hours after onset of stroke.

# Management of Hypertension in Acute Ischemic Stroke: Patients Eligible for Thrombolytic Therapy

- (2003)
- **Prior to initiating teatment with TPA:**
  - SBP >185 or DBP >110
    - Labetalol or nitropaste
- **During and after treatment with TPA:**
  - SBP=180-230 mm Hg or DBP=105-120 mm Hg
    - Labetalol
  - SBP >230 mm Hg or DBP=121-140 mm Hg
    - Labetalol or nicardipine
  - DBP >140 mm Hg
    - Nitroprusside

- (2007)
- **Eligible for tPA or other acute reperfusion tx**
  - SBP >185 or DBP >110
    - Labetolol or nitropaste or nicardipine
- **During or after tx**
  - SBP=180-230 mm Hg or DBP=105-120 mm Hg
    - labetolol
  - SBP > 230 mm Hg or DBP 121-140 mm Hg
    - Labetolol or nicardipine
  - If uncontrolled, consider nitroprusside

Adams HP, et al. *Stroke*. 2003;34:1056-1083.

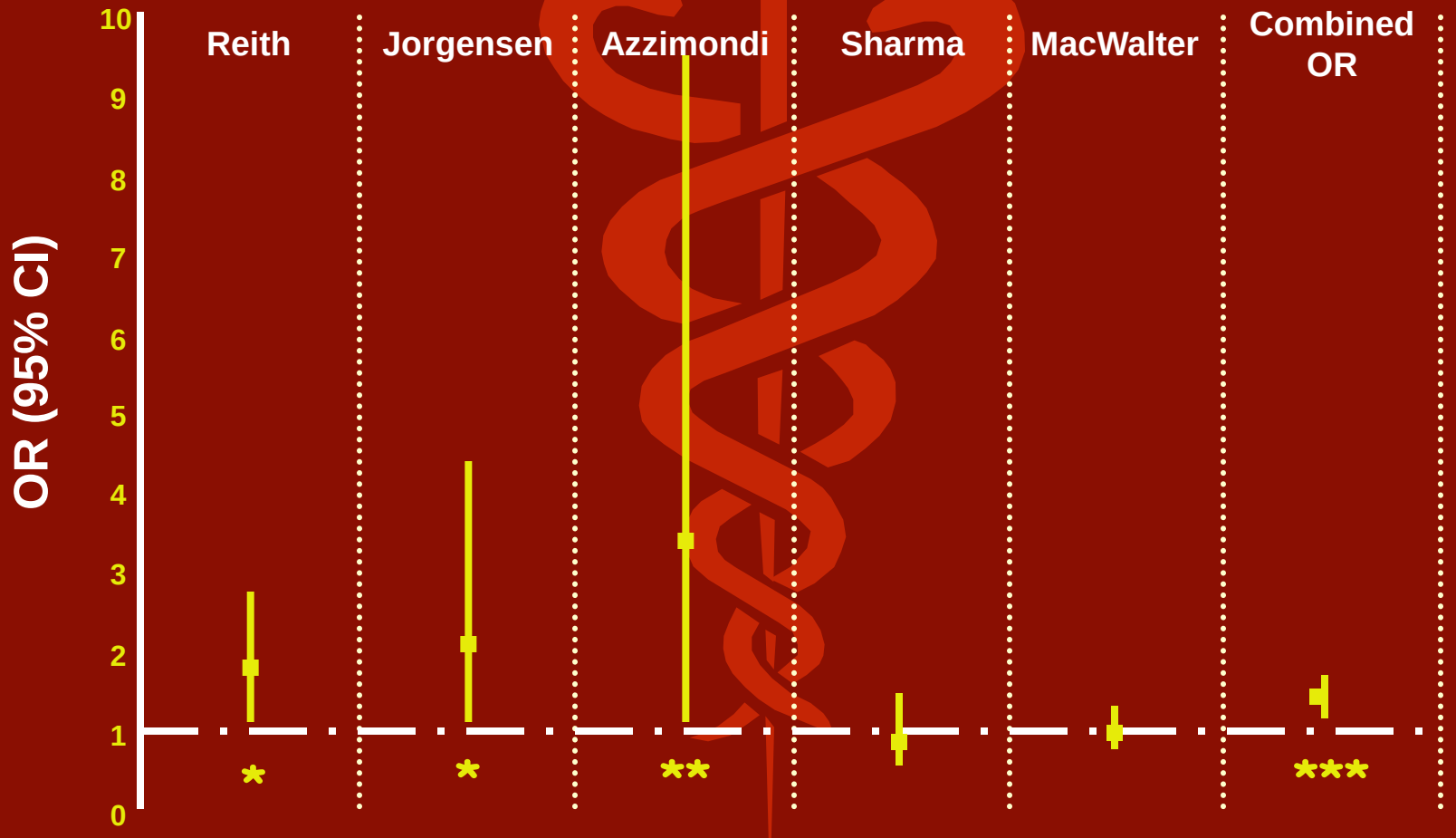
# Management of Hypertension in Acute Ischemic Stroke: Patients Eligible for Thrombolytic Therapy 2018

- Patients who have elevated BP and are otherwise eligible for treatment with IV alteplase should have their BP carefully lowered so that their systolic BP is <185 mm Hg and their diastolic BP is <110 mm Hg before IV fibrinolytic therapy is initiated.

# Temperature

# Fever and Stroke Mortality

**A Meta-Analysis:** Hajat et al. *Stroke*. 2000;31:410



# Fever and Stroke Outcome

| | Infarct Volume | Greater Deficit | Poor Fx |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| **Covariates** | | | |
| Age | 1.02 (0.99–1.05) | 1.04 (1.01–1.07) | 1.08 (1.05–1.12) |
| Infection | 0.72 (0.32–1.62) | 0.92 (0.43–2.01) | 1.49 (0.65–3.39) |
| Highest temp | 2.81 (1.34–5.89) | 1.68 (0.84–3.40) | 1.85 (0.88–3.88) |
| **Time at which hyperthermia was observed:** | | | |
| 0–24 h | 3.23 (1.63–6.43) | 3.06 (1.70–5.53) | 3.41(1.69–6.88) |
| 24–48 h | 1.14 (0.52–2.51) | 1.47 (0.78–2.80) | 1.41(0.66–3.05) |
| 48–72 h | 0.23 (0.05–1.09) | 0.33 (0.10–1.03) | 0.20 (0.04–0.96) |

Castillo et al. *Stroke*. 1998;29:2455-2460.

# Hyperthermia - BAD!
# Hypothermia - Good?

# Use of hypothermia in *ischemic stroke:*

| Authors | No of pts (H/C) | Target temp | Time from injury to start of cooling | Time to target temp | Duration | Re-warming rate |
|---|---|---|---|---|---|---|
| **Severe stroke, mostly sedated patients in ICU setting** | | | | | | |
| Naritomi H et al. 1996 | 4 (4 / 0) | 33°C | < 5 hrs | | 72-96 hrs | |
| Schwab et al. 1998 | 20 (20 / 0) | Patient data included in subsequent study (Schwab et al. 1998, see below). | | | | |
| Schwab et al. 1998 | 25 (25 / 0) | 33°C | 14±7 hrs, range 4-24 | 3.5-6.2 hrs | 48-72 hrs | 7-24 hrs median 18 |
| Steiner T et al. 2001 | 15 (15 / 0) | 32-33°C | 4-84 hrs, median 17 | 2-7 hrs | 72 hrs | 26-88 hrs |
| Schwab et al. 2001 | 50 (50 / 0) | 33°C | 22 ± 9 hrs | 3.5-11 hrs | 48-72 hrs | Passive 17 hrs |
| Jian S et al. 2003 | 50 (50 / 0) | Patient data included in subsequent study (Schwab et al. 2001, see above). | | | | |
| Georgiadis et al. 2001 | 6 (6 / 0) | 33°C | 28 ± 17 hrs | 3±1 hrs, range 2-4.5 | 48-72 hrs | 0.12-0.2°C/hr |
| Georgiadis et al. 2002 | 36 (19 / 17) | 33°C | 24 (range 18-24) | 4 ± 1 hrs, range 2-6 | 48-72 hrs | Not stated |
| De Georgia et al. 2004* | 40 (18 / 22) | 33°C | 8'59'' ± 2'52'' | Variable; | 24 hrs. | 0.2°C/hr |
| **Moderate Stroke (awake patients)** | | | | | | |
| Kammersgaard et al. 2000 | 73 (17 / 56) | 35.5°C | 3.25 ± 4.5 hrs | 6 hrs | 6 hrs | 4 hrs |
| Krieger et al. 2001* | 19 (10 / 9) | 32±1°C | 6.2 ± 1.3 hrs | 3.5 ± 1.5 | 48 (range 24-96) hrs | 0.25-0.5°Ch |
| Knoll et al. 2002 | 18 (18 / 0) | 36-37°C | | 3.3 hrs | 24 hrs | N/A |
| Els et al. 2006 | 25 (12 / 13) | 35°C | 15 ± 6 hrs | 2±1 (range 1.5-3.5) hrs | 48 hrs | Not stated |
| Lyden et al. 2006* | 18 (18 / 0) | 33°C | 7.7 ± 3.1 hrs | 7 hrs | 12-24 hrs | 12 hrs |
| Guluma et al. 2006 | 10 (10 / 0) | 33°C | <6 hrs | 1.7±0.7 hrs | 24 hrs | 0.3°C/hr |
| Hemmen et al. 2010 ICTuS-L* | 58 (28 / 30) | 33°C | <6 hrs | 1.1 hrs (median) | 24 hrs | 0.33°C/hr |

*Cooling combined with thrombolytics/reperfusion.

270.

157.

113.

# Ventilated patients

| | N= | Goal temperature ° C | Time to Treatment (hours± SD) | Duration of hypothermia |
|---|---|---|---|---|
| **Schwab,1998** | 25 | 33° C | 14±7 | 2-3 days |
| **Schwab, 2001** | 50 | 33° C | 22±9 | 1-3 days |
| **Georgiadis, 2001** | 6 | 33° C | 28±17 | 2-3 days |
| **Georgiadis, 2002** | 19 | 33° C | 24 (18-14) | 2-3 days |

Kollmar, Schwab, 2010

# Awake patients

| | $N_{hypothermia}$= | Goal temperature in ° C | Time to Treatment (hours+/-SD) | Hypothermie -duration |
|---|---|---|---|---|
| **Kammersgaard, 2000** | 17 | 35,5° C | 3±4 | 6 n |
| **Krieger, 2001** | 10 | 32±1° C | 6±1 | 1-4 days |
| **DeGeorgia,2004** | 18 | 33° C | 9±3 | 24h |
| **Lyden, 2005** | 18 | 33° C | 8±3 | 24h |
| **Guluma, 2006** | 10 | 33° C | 6±1 | 24h |
| **Kollmar, 2009** | 10 | 35,5° C | 1,5 | - |
| **Hemmen, 2010** | 28 | 33° C | | 24h |

Kollmar, Schwab, 2010

# CHILI - Controlled Hypothermia in Large Infarction

- U.S.C.
- Columbia University
- U.M.D.N.J.
- Case Western
- Lehigh Valley
- Wayne State University
- Via Christi Regional Medical Center

# CHILI

- Large hemispheric stroke
- Within 72 hours of onset
  - no herniation
- Immmediate cooling to 35.0 for 3 days
- 0.5 C q12 hr rewarming
- Uniform shivering prophylaxis
- Measure: GCS, NIHSS, CT, Rankin, Barthel, Mortality, discharge location, LOS/costs

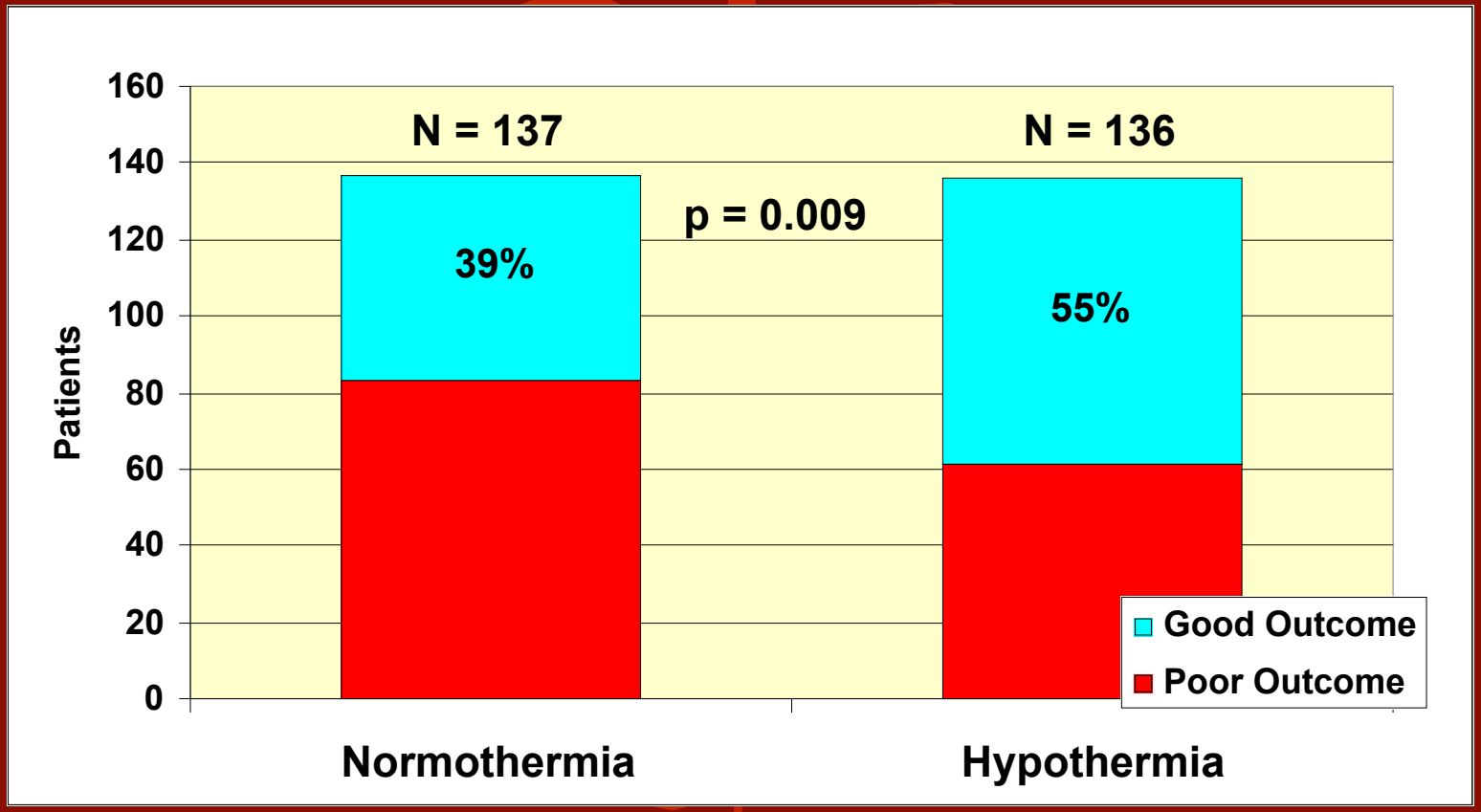
# Hypothermia after Cardiac Arrest

*Two studies reported in NEJM 21 Feb 02*

- **European Study: 24-hours @ 32-34˚ C**
- **Australian Study: 12-hours @ 33˚ C**
- **1˚ endpoint: neurological function, 5-point scale**
- **2˚ endpoint: mortality & complications**

# Cardiac Arrest
## European Study

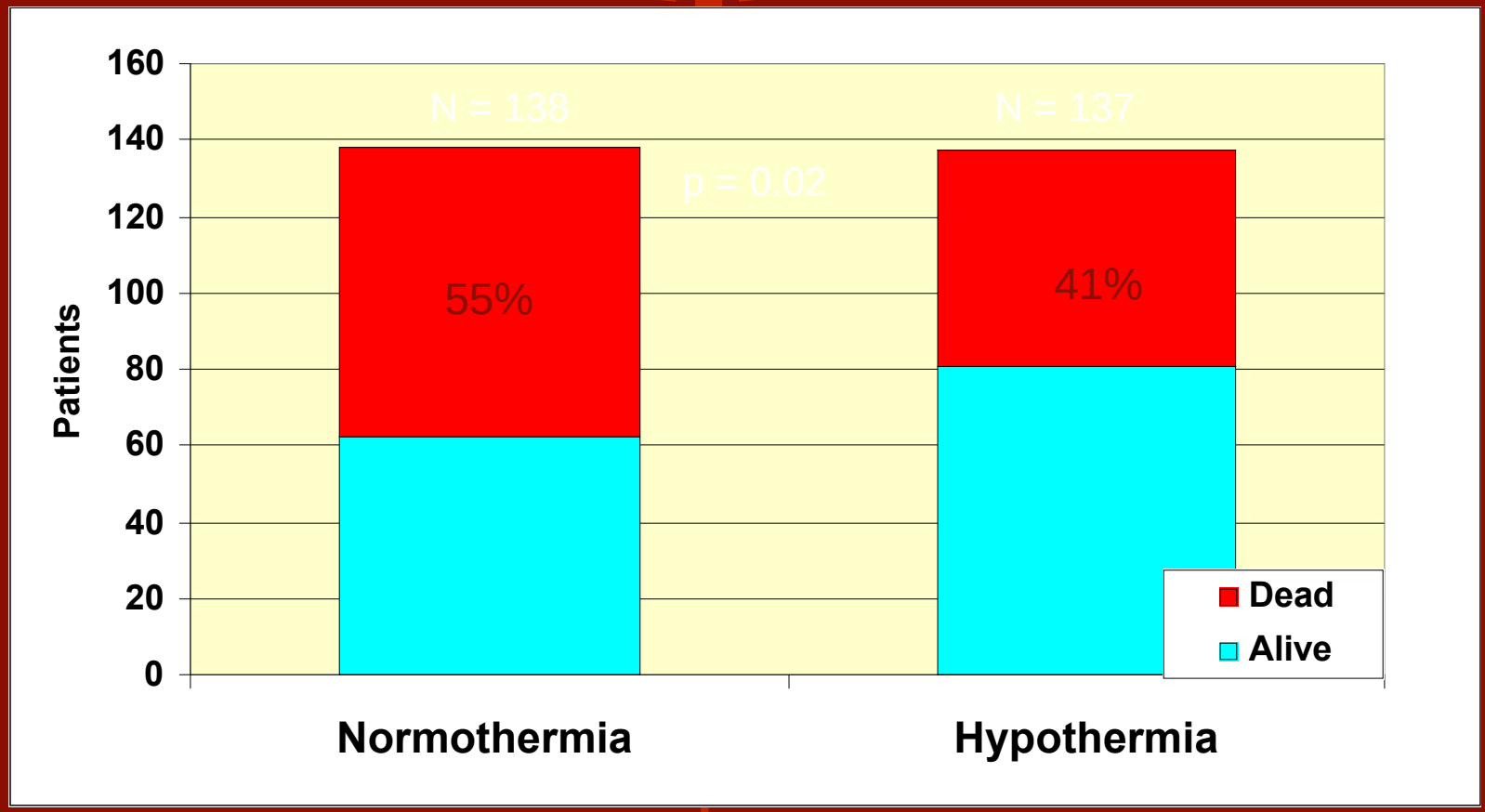
6-mo neurological outcome: 41% relative improvement




Holzer M, Sterz F, et. al. NEJM 346(8):549-56.

# Cardiac Arrest
## European Study

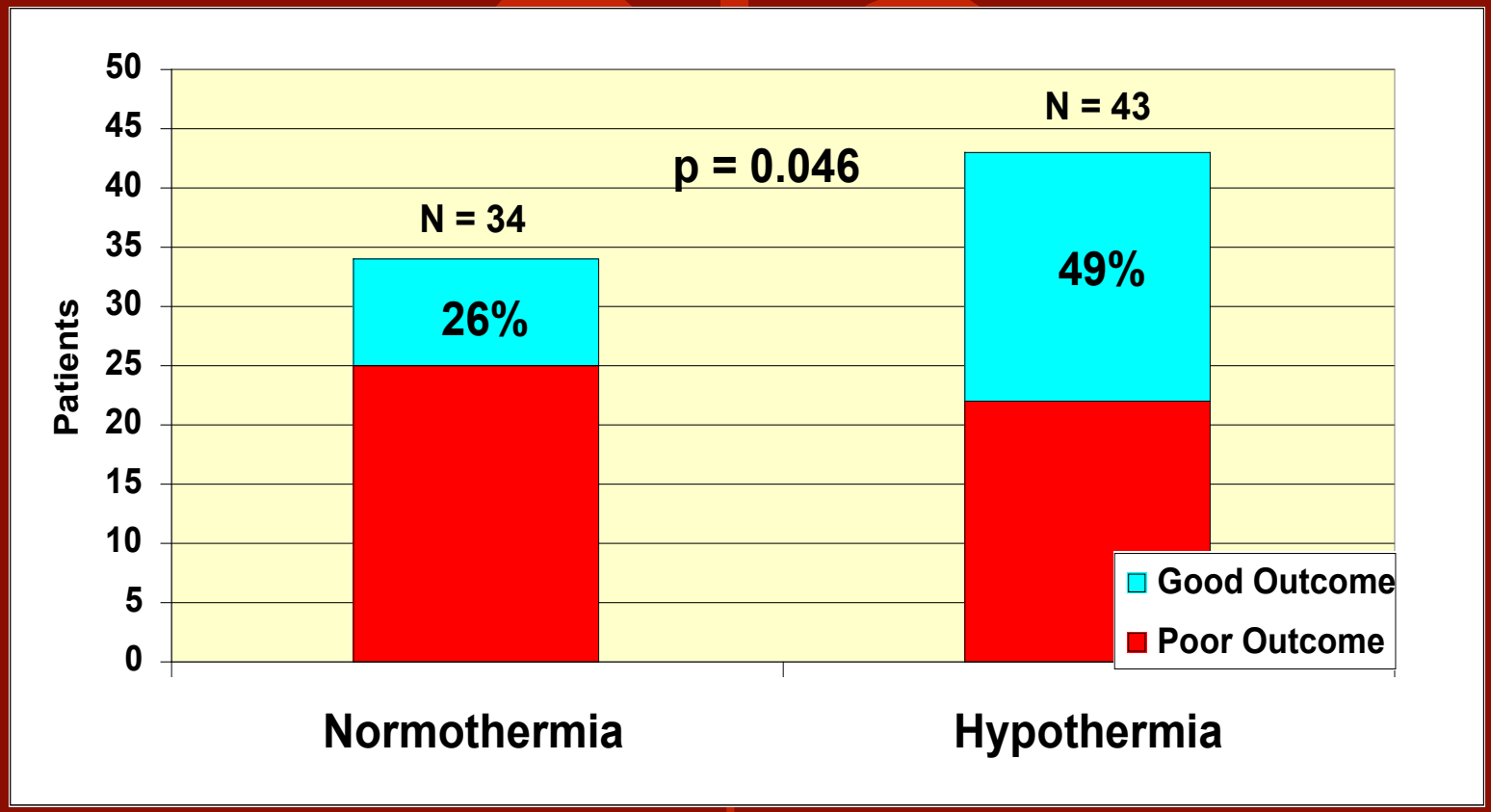
**6-mo mortality: 26% relative reduction**




Holzer M, Sterz F, et. al. NEJM 346(8):549-56.

# Cardiac Arrest
## Australian Study

**30-day neurological outcome: 88% relative improvement**




Bernard SA, et. al. NEJM 346(8):557-63.

# Hypothermia: Side effects

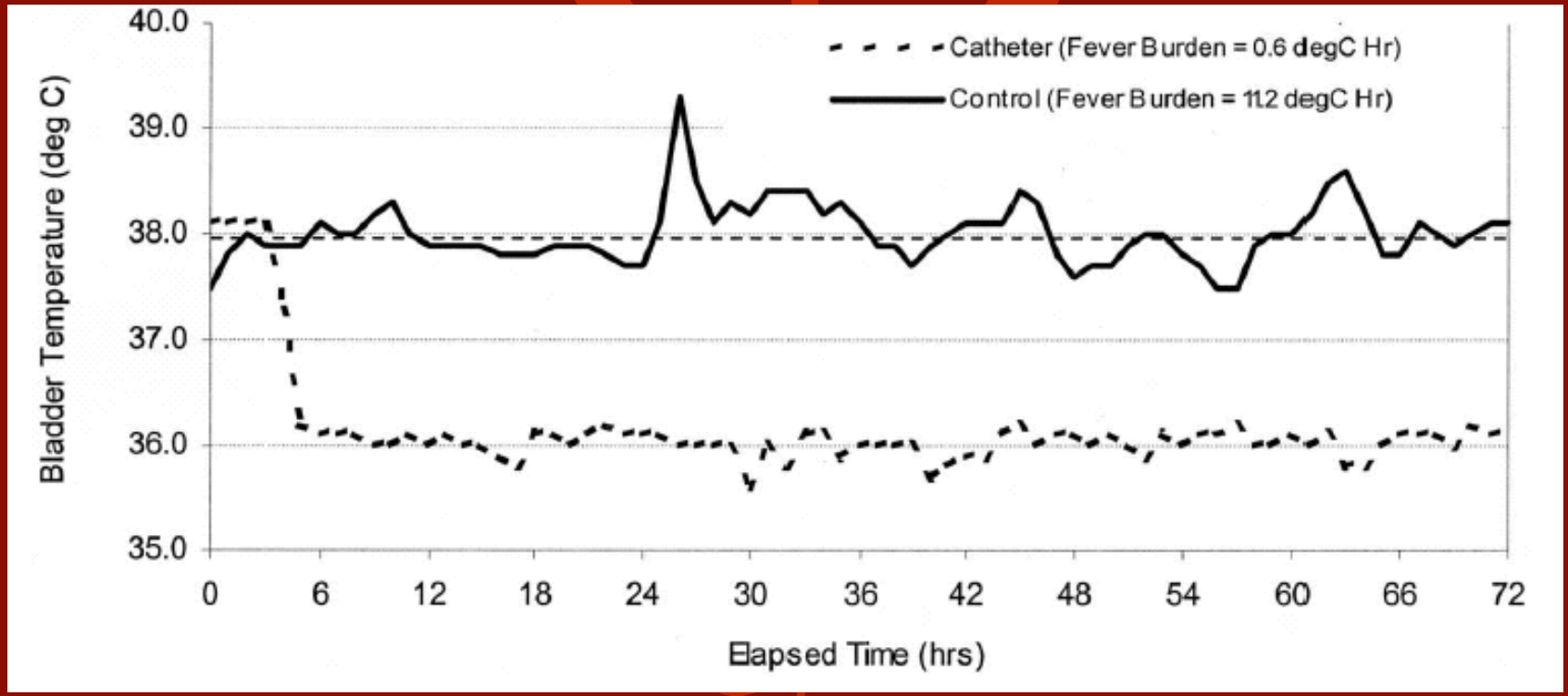
- Decreased cardiac output
- Increased systemic vascular resistance
- Thrombocytopenia
- Bradycardia
- Pneumonia

# Hypothermia: Cooling Techniques

- Traditional Surface cooling
  - Rate of core temperature decrease of 0.3-0.9 $^{o}$C/hr
  - Inconvenient for medical and nursing staff
- Intravascular
  - Rapid infusion of large volume (30 ml/kg), ice-cold (4$^{o}$C) LR decrease core temp by 1.6$^{o}$C over 25 min
  - Intravascular catheter devices

# Treatment of fever in the neurologic intensive care unit with a catheter-based heat exchange system

Michael N. Diringer, MD; for the Neurocritical Care Fever Reduction Trial Group

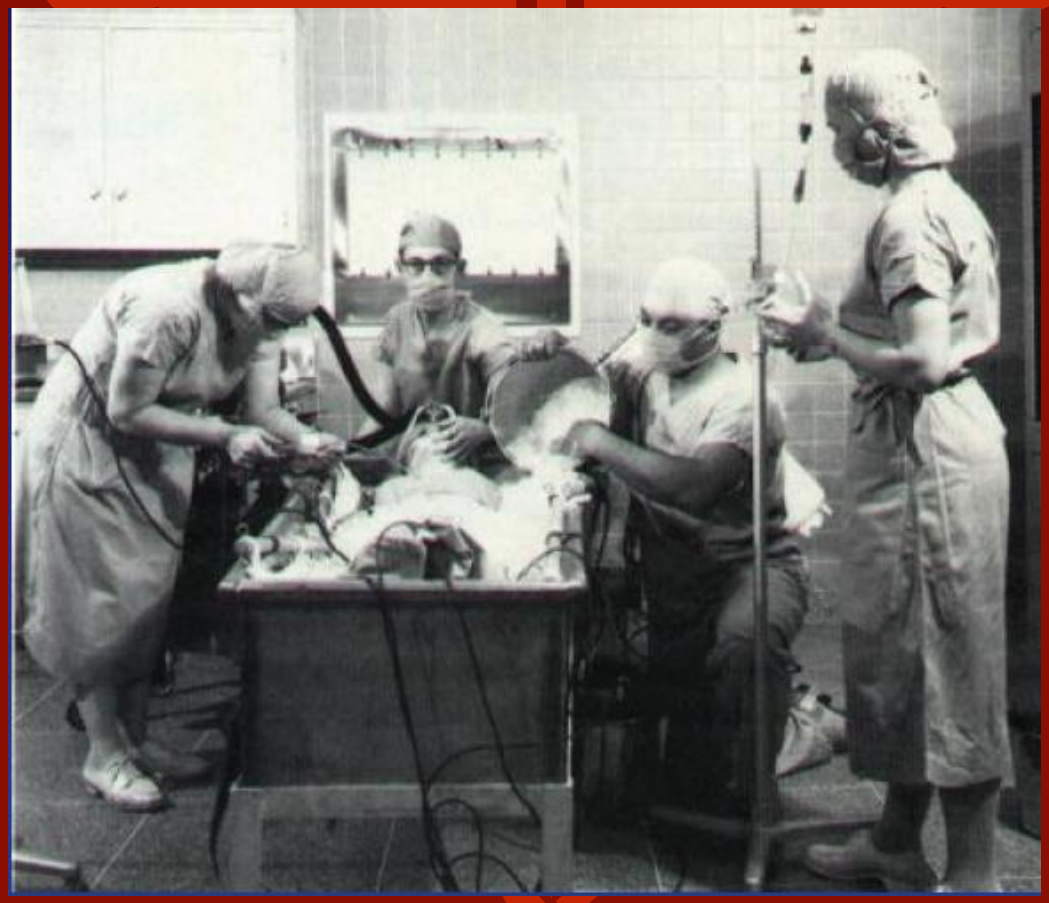


Treatment of fever in the neurologic intensive care unit with a catheter-based heat exchange system

Michael N. Diringer, MD; for the Neurocritical Care Fever Reduction Trial Group

- 64% reduction in fever burden using catheter
- No need for heavy sedation or paralysis
- Minimal Shivering response

# Past



Dr Temple Fay 1941

# Zoll Intravascular Temperature Management


# MEDIVANCE

# INTREPID

Impact of Fever Prevention in Brain Injured Patients

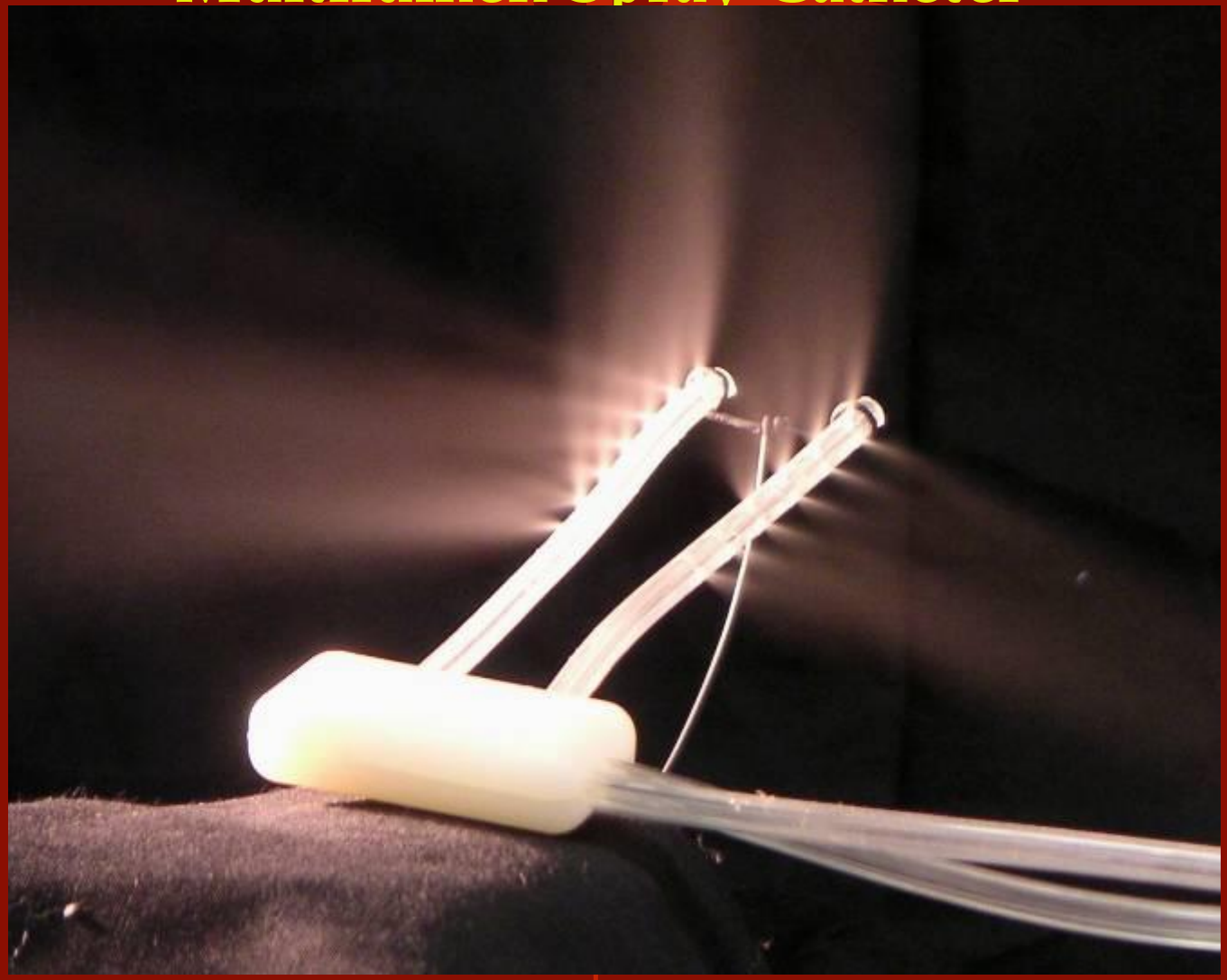
# INTREPID

- International Randomized Controlled Trial of aggressive fever prevention
- AIS, ICH and SAH
- N=1200

# INTREPID

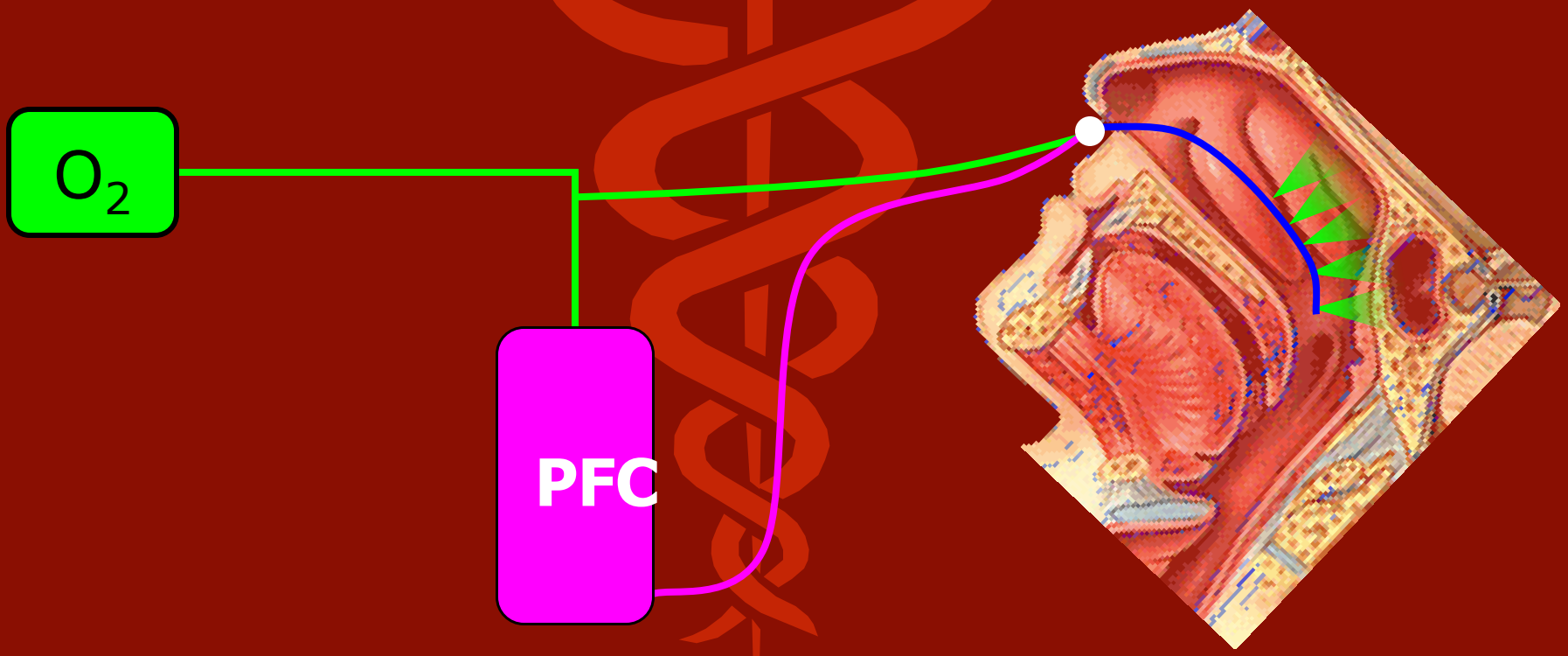
- Fever burden (°C-hour; defined as the area under the temperature curve above 37.9°C)
- 3- , 6- , and 12-month follow-up neurologic assessment
- Mortality rates [7-day (or hospital discharge), 3-month, 6-month, 12-month]
- ICU and hospital lengths of stay

# Multilumen Spray Catheter



BENECHILL

# PFC Intranasal Cooling Schematic

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# Basic ICU Care

- Glucose
- Fluid Management
- Hemodynamics
- Temperature