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## Evaluation of Rapid Brain Cooling Methods for Induction of Mild Resuscitative Hypothermia

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**Objectives**: To summarize new data on various methods for lowering brain and total body temperature (T) to 33-35°C within 15 minutes (min) after an insult. To help clinical implementation of rapid, mild cooling, which proved beneficial in animals after cardiac arrest, brain trauma, stroke or shock.
**Dog Studies**: In more than 80 dogs (18–28 kg), various cooling methods were evaluated during no-flow, low-flow (CPR), or high-flow (spontaneous circulation). Core and tympanic membrane (brain) T were monitored, and sometimes also epidural and deep brain T. The rapidity of cooling to brain T 34°C was 2–5 min with cardiopulmonary bypass or carotid cold flush, 10–15 min with head-neck-trunk surface cooling. The latter could be reduced to 15 min by adding nasopharyngeal and gastric, or esophageal cooling and an intravenous (IV) cold fluid load.
**Human Cadavers**: In two human cadavers (no-flow), surface cooling by head immersion in ice water lowered deep brain T to 34°C in ±30 min.
**Phantom**: Calculations of heat transfer from 0°C applied to the "head surface" showed that "deep brain T" of 34°C is achieved after >30 min.
**Conclusions**: Surface cooling alone is too slow. Clinical trials of surface-combination cooling methods are encouraged.

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## Rapid Induction of Mild Cerebral Hypothermia with Peritoneal Cold Lavage in Dogs

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**Introduction:** In dogs, it has been shown that mild resuscitative (post-insult) cerebral hypothermia (34°C) immediately for 1–2 hours (h) after prolonged cardiac arrest reduces brain damage. A 15-minute (min) delay in initiation of cooling almost offsets the beneficial effect. Such rapid cooling could be achieved in dogs by blood cooling or cumbersome combinations of external cooling. This study presents a relatively simple alternative using peritoneal lavage with cold fluid.
**Methods**: Five dogs (23 ±1 kg) under spontaneous circulation, with $N_2O$:$O_2$ 50:50% - halothane 0.5% anaesthesia and paralysis, with intermittent positive pressure ventilation (IPPV) and controlled normotension, had various temperatures (T) monitored. A catheter was inserted just below the umbilicus into the peritoneal cavity. Two liters of Ringer's solution at 10°C (7–15°C) were instilled rapidly into the peritoneal cavity, retained there for five minutes, and then drained by gravity.
**Results**: Pulmonary artery T was controlled at 37.5°C before cooling. Other Ts were observed. By the end of peritoneal cold fluid instillation, all Ts had decreased rapidly. Tympanic membrane T (Tty) reflecting brain T reached 34°C at 7–10 min after peritoneal instillation. With dogs at 25°C room T, Tty remained 32–34°C for 60 min, without the need for further surface cooling. Physiologic variables did not change. The rate of peritoneal cooling was significantly more rapid than that observed in previous studies using either an intravenous (IV) fluid load of 10 ml/kg at 4°C; or esophageal, nasopharyngeal, or head-neck surface cooling.
**Conclusions**: Peritoneal instillation of cold Ringer's solution may be an effective method for rapid induction of mild cerebral hypothermia, and should be tried in comatose patients who could benefit from therapeutic mild hypothermia.

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## A Method for Systematic Evaluation of Novel Cerebral Resuscitation Therapies after Cardiac Arrest (CA)

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**Objective**: Controversies about the evaluation of new cerebral resuscitation potentials after cardiac arrest have been caused by uncoordinated studies in different laboratories on different species with different models, and the use of often unreliable methods of evaluation. Through years of experience, a systematic sequence of such studies has been developed, including specific requirements for animal outcome models.
**Methods**: Novel therapeutic potentials were selected on the basis of rationale and promising bench data. Phase I consisted of one or more brain morphologic outcome studies in a rat forebrain ischemia or rat cardiac arrest (CA) model. Significant mitigation of brain damage had to be demonstrated to progress to the next phase. Phase II used normal dogs, without CA, with and without anesthesia, to study side-effects caused by IV infusion (to overdose) of the experimental therapy (shams). In Phase III, the most reproducible CA dog outcome model (with brief CPB for controlled reperfusion) was used to compare a small series of the experimental treatment with a large series of historic controls (which achieved reproducibly poor outcome). If Phase III results suggest benefit, Phase IV was used with the same dog outcome model for a large randomized, placebo blinded study with concurrent controls. If Phase IV shows benefit, Phase V (with a clinically more realistic external CPR dog outcome model) was used to confirm the results of Phase IV. If Phase V shows benefit, Phase VI will be a randomized clinical trial.
**Results:** Several novel treatment potentials (blood flow promoting measures; calcium entry blocker therapies; mild hypothermia; excitatory amino acid receptor blocker; and other drugs) have been exposed to this process. Data will be summarized.