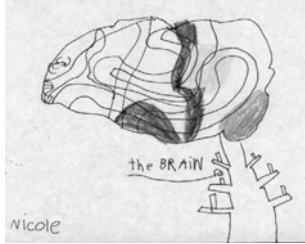


Neurologic Resuscitation and the Role of Therapeutic Hypothermia

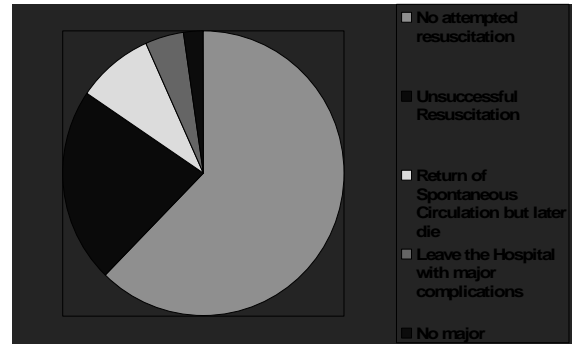
Ralph K. Losey MD, FACEP

Neurologic Resuscitation and the Role of Therapeutic Hypothermia



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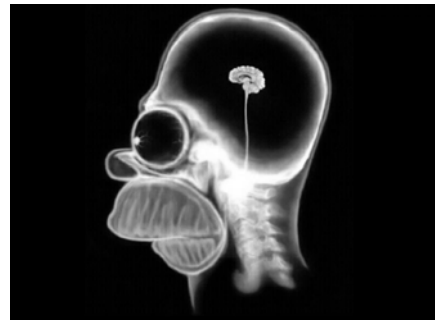
Surviving out of hospital cardiac arrest



The excitement of early successes in cardiac resuscitation



Reality is many patients with functional organs but non-functional brains



"All organs serve the brain." - - - a somewhat egotistical neurosurgeon

TRUE

"All physicians serve the neurosurgeon." - - - what same surgeon really meant

FALSE

COLD FACT

The success rate of resuscitation with an endpoint of full neurologic recovery is very low. . . . yet consider . . .

Then

1967: sudden cardiac arrest was considered nearly untreatable and full recovery seemed more related to chance than anything else

Now

2007: successful cardiac resuscitation is not rare;

- almost the expected norm for patients experiencing cardiac arrest in the emergency department, operating suite or other highly staffed and closely monitored areas of the hospital.

Brain resuscitation in 2007 is probably where cardiac resuscitation was in 1967

Current State of the Art for Cerebral Resuscitation

We are

- detecting patterns of success;
- refining the treatment protocols and
- conducting basic research into how the brain can be functionally salvaged.

The brain's problem with cardiac arrest.

Sudden global ischemia,
Energy supply ends,
Cellular metabolism ceases,

The brain's problems don't end there.

Without metabolism,
Cells begin to deteriorate
the point of no return is the fragmentation of nuclear DNA (apoptosis)

Problems are just beginning!

The cerebral microcirculation is disrupted by cell breakdown products,

The return of circulation should help, right?

Sorry.

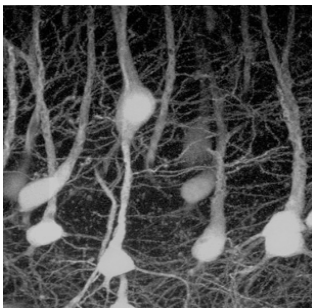
The return of circulation initially brings cytotoxic substances released from cells elsewhere in the body resulting in a further cycle of destruction.



Areas of the brain most sensitive to ischemic injury

- the hippocampus,
- caudate nucleus,
- putamen,
- thalamus and
- the large cell layers of the neocortex.

Approaches to salvaging function



- Identify markers of injury
- Identify opportunities for intervention
- Evaluate interventions by clinical trials

Identify markers for severity of injury

- elevated glucose
- elevated lactate
- elevated S-100, an astroglial protein
- presence of Neuron-Specific Enolase, a glycolytic enzyme found almost exclusively in neuronal tissue

Elevated glucose

- Associated with both neurologic injury and future poor neurologic outcome.
- Very close glucose monitoring and control is necessary

Elevated lactate

- No absolute level has been established
- The most consistent ominous indicator is the failure of lactate to decrease over time (days).

Brain specific markers

- elevated S-100, an astroglial protein correlates with cerebral injury
- Neuron-Specific Enolase, is the most substantiated marker of neuronal injury – the correlation with good neurologic outcome is with a decreasing level of NSE rather than an absolute level.

Potential areas of intervention

- Slowing or interrupting apoptosis
- Stopping or repairing the destruction of the microvasculature.

Apoptosis

- A rat line was developed with neuronally expressed antiapoptotic proteins.
- In a controlled study a significantly higher number of these rats had full recovery after 6 minutes of induced cardiac arrest.

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Microvascular destruction

- Endothelial cell swelling
- Increased leukocyte adhesion
- Disseminated intravascular coagulation
- European clinical trial utilizing prehospital thrombolysis for cardiac arrest was discontinued after two years due to lack of improvement compared to placebo.

Areas of known successful intervention

- **Hypothermia** is the only therapy for neurologic resuscitation proven to be successful by randomized controlled clinical trials.

Therapeutic Hypothermia

Initial reports of its effectiveness for preserving brain function were in the 1950s!
Only scattered reports were published until 2 landmark studies appeared in NEJM in 2002.



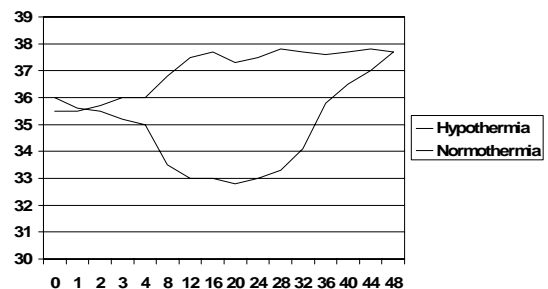
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- Australian study had 77 v. fib survivors; the experimental group was cooled to 32-34 degrees C for 12 hours
- European study had 275 v. fib survivors; the experimental group was cooled to 32-34 degrees C for 24 hours

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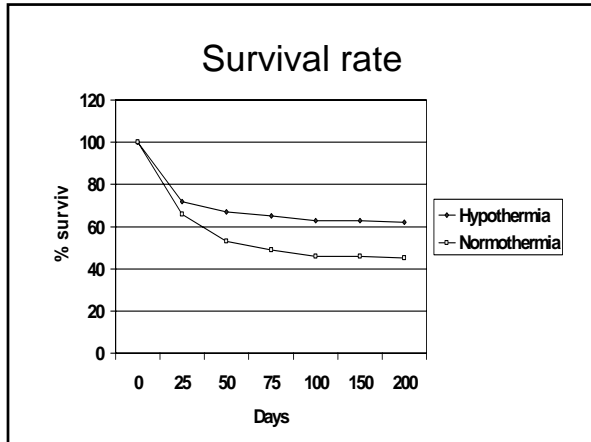
- Australian study had an endpoint of discharge to rehab or home; the hypothermia group had 88% more patients reach the endpoint
- European study had an endpoint of "good recovery or moderate disability" at 6 months; the hypothermia group had 41% more patients reach the endpoint

Bladder temp v time(hours)



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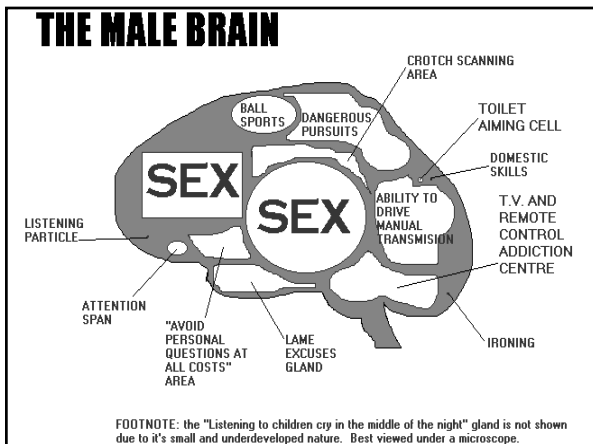
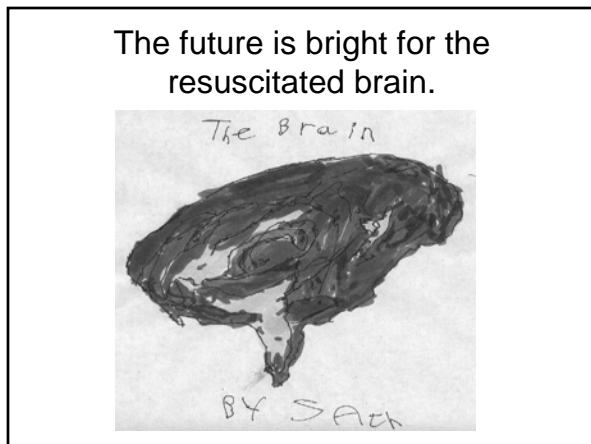
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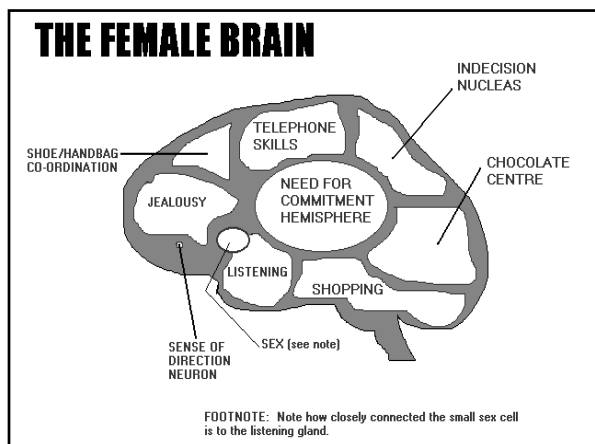
- ### Why does hypothermia work?
- Mild hypothermia(32-34 degrees C)
- Decreases heart rate
 - Increases systemic vascular resistance
 - Decreases intracranial pressure
 - Exerts an anti-inflammatory effect on the biochemical cascade of “reperfusion injury”

- ### Complications of Therapeutic Hypothermia
- Need for paralysis to control shivering
 - Glucose increases
 - Potassium, magnesium and phosphate all decrease
 - Increased infections

- ### Current frequency of use
- Therapeutic hypothermia is not currently commonly used
 - A survey of ER MDs, intensivists and cardiologists indicated 87% had not used therapeutic hypothermia because
 - unconvinced of data, not part of ACLS protocols and technical difficulties with cooling methods.



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Thank you.