The Future of the Treatment of Acute Brain Injury

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Some thoughts on the future of acute brain injury......

- Diagnosis
- Protection
- Treatment
- Regeneration
- Outside the Box!
• Critical Care, especially NeuroCritical Care starts in the field!
• Earlier treatment leads to better results
Early Treatment!

- Trauma – ‘Golden Hour’ / MASH
- Stroke – reperfusion
- Infection – meningitis
- Seizures – status epilepticus
Trauma – Golden Hour
Stroke - Reperfusion Therapy

The graph shows the odds ratio for favorable outcome at 3 months as a function of minutes from stroke onset to start of treatment. The x-axis represents minutes from stroke onset to start of treatment, ranging from 60 to 180 minutes. The y-axis represents the odds ratio for favorable outcome at 3 months, ranging from 0 to 8.

The graph includes two lines, one solid and one dashed, indicating the relationship between treatment timing and outcome. The solid line shows a steeper decline, suggesting that earlier treatment is associated with a higher odds ratio for a favorable outcome. The dashed line indicates a less steep decline, suggesting a more gradual improvement with later treatment.

The graph also includes a horizontal line labeled with the symbol μ, which represents a baseline or reference point for comparison with the treatment outcomes.
Stroke - Reperfusion Therapy
Status Epilepticus

Figure 1A. Discrete seizures (Pattern 1)(Patient #1)
But early treatment depends on early DIAGNOSIS

- Education
  - Stroke Scale (LAPSS, FAST..)
  - Emergency Neurologic Life Support
- Technology
NeuroCritical Care Units
Brain Monitors

Catheter

- Pre-calibrated, stable
- Single, double, or triple lumen bolt
- Tunneled
Cerebral Microdialysis

- Glucose
- Lactate
- Pyruvate
- Glycerol
- Glutamate
- Urea

Blood capillary → Microdialysis catheter → Extracellular fluid

Glucose metabolism
Fat metabolism
Nitrogen Metabolism
Membrane damage
Drilling holes in his head isn't the answer.
The Future: Diagnosis

- Pressure
- Perfusion
- Oxygenation
- Metabolism
- Electrical Activity
- Function
Neuroprotection

- How to protect the brain from injury
- How to protect the brain after injury
Temple Fay, pioneered ‘human refrigeration’. In November 28, 1938, he first introduced whole body hypothermia as a treatment for malignancies and head injuries.
History of Hypothermia
History of Hypothermia
### EXPERIENCES WITH REFRIGERATION OF HUMAN BRAIN

#### TABLE 1

Survey of refrigeration material (126 cases)  
July 9, 1936 to October 1, 1940

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>112</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4</td>
</tr>
<tr>
<td>Brain tumor (glioblastoma)</td>
<td>5</td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>3</td>
</tr>
<tr>
<td>Filariasis</td>
<td>1</td>
</tr>
<tr>
<td>Syphilis</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>126</td>
</tr>
</tbody>
</table>

- **Patients receiving local refrigeration**: 88
- **Total period of applied local refrigeration**: 2807 days
- **Patients receiving general refrigeration**: 66
- **Episodes of general refrigeration**: 169
- **Biopsies**: 189
- **Autopsies**: 72 (57.1%)
History of Hypothermia

EARLY EXPERIENCES WITH LOCAL AND GENERALIZED REFRIGERATION OF THE HUMAN BRAIN*

TEMPLE FAY, M.D.+  
Philadelphia, Pennsylvania

(Received for publication April 25, 1958†)

The clinical benefits from the use of local cold applications to the cutaneous surfaces of the body and head have been known to the profession for many centuries.

As far as I am aware, capsules housing refrigerated solutions were first introduced into the tissues of the human skull and brain in 1938 at Temple University Hospital in Philadelphia, on the author’s Neurosurgical Service.

The original apparatus devised for local refrigeration of an area was crude (Fig. 1). Ice water was circulated by the method of gravity. An old

Fig. 1. Closed irrigation unit with constant thermal control used with metal capsules for clinical observations of the effect of local refrigeration. (Reproduced from Surgery, Gynecology and Obstetrics.)
History of Hypothermia
History of Hypothermia
History of Hypothermia
History of Hypothermia

- **Rosomoff & Safar**: Comatose patients
- **Safar**: Hypothermia as part of the first CPR ABCs
- **Conn**: Hypothermia for pediatric drowning
- **Busto et al.**: Mild hypothermia in rat global brain ischemia
- **Tisherman et al.**: Early work on emergency preservation for exsanguination cardiac arrest
- **Leonov et al.**: Mild hypothermia improves outcome after VF cardiac arrest in dogs

Graph showing the number of articles on cardiac arrest and hypothermia over the years from 1960 to 2000.
Hypothermia Past

Dr Temple Fay 1941
Multilumen Spray Catheter
Ischemic Brain Injury

- EAA release
- Opening of EAA-coupled ion channels
  - Massive ionic fluxes
  - Activation of energy-dependent ion pumps
- Increase in energy demand
  - Activation of glycolysis
  - Metabolic Depression
The Future: Neuroprotection

- Targeted Neuroprotection
Drilling holes in his head isn't the answer.
Hemicraniectionomy
The Future: Treatment

- ICU based Minimally Invasive therapy
The Future: Diagnosis

- Pressure
- Perfusion
- Oxygenation
- Metabolism
- Electrical Activity
- Function
The Future: Treatment

- Targeted Therapy based on Monitoring
NeuroRestoration

- New strategies for the restoration of an injured or diseased nervous system by developing new technologies that harness advances in basic neuroscience and neural engineering
Regenerative Medicine

- replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function
Results III – CT examples
Outside the Box
Who should get Neurocritical Care and Where?

- Prognostication
- Limiting Critical Care
- TeleCritical Care
- Home Critical Care
But really, I would be happy with......

- Improve patient care
- Practice variance
- Evidence-based medicine
- Raising the bar with standardized training
Neurocritical Care

- Specialized Care
- Better patient outcomes
- Better financial outcomes
- Newer and better tools and treatments
Neurocritical Care
NeuroIntensive Care
NeuroSciences Critical Care