
# CrackCast Episode 8 – Brain Resuscitation

## Episode Overview:

1) Describe 6 therapeutic interventions for the post-arrest brain
2) List 5 techniques for initiating therapeutic hypothermia
3) List 4 mechanisms of therapeutic hypothermia in improving neurologic outcome

**Wisecracks:**
1) What components make up cerebral blood flow and CPP?
2) (shownotes only) Essential Evidence: Target Temperature Management at $33^0$C vs $36^0$C after Cardiac Arrest (Nielsen *et al.*, 2013)

## Rosen's in Perspective – Why Cerebral Resuscitation?

We frequently see post-cardiac arrest patients in the ED

- prognostic significance of immediate post-ROSC period is limited
- no laboratory or clinical predictors exist (yet) for the ED physician to make accurate predictions on who will survive and who will not
    - each patient should be given a chance of recovery

In any shock state (see episode 6) we know that cerebral blood flow is often compromised

- cerebral resuscitation is just as important as cardiac resuscitation
- post-ischemic encephalopathy is a huge contributor to poor outcomes after ROSC
- deprivation of blood flow leads to neuronal cell death in minutes of ischemia
- re-perfusion injury also contributor to negative sequelae

Rosen's thinks this topic is important enough to include complex figures in the textbook:

- decreased cerebral blood flow (CBF) -- > cellular hypoxia -- > inability to produce ATP --> (impairment of the ATPase pump leads to) excess intracellular Na+ ---> cytotoxic edema --> excess Ca+ and GABA release --> metabolic failure --> oxygen radical formation --> DNA damage/apoptosis/membrane degradation/cytoskeleton destruction --> membrane attack complexes --> demargination / proteases --> increased cerebrovascular resistance which leads to more decreases in cerebral blood flow

Let's bring it back to the clinically relevant points.

## 1) Describe 6 therapeutic interventions for the post-arrest brain

Goal of therapeutic interventions are two-fold:


1) restore cerebral blood flow
2) prevent secondary injury

**Standard Strategies:**

For anyone still in cardiac arrest our first goal is ROSC

- good quality CPR is vital to ROSC (good depth, speed, and **minimize interuptions**) – inverse correlation between brain survival and CPR time

After we have achieved ROSC, a nice way to think about the post arrest brain is "**"keep their vitals and ABG in the normal range and keep their brain asleep"**

General Goals:

1) avoid hypotension: MAP > 65 mmHg
2) avoid hypertension: diastolic < 120 mmHg
3) avoid hypoxia or **hyperoxia**
4) avoid hyper/hypocarbia
5) maintain euthermia **(avoid fever/spikes in temperature)**
6) maintain euglycemia
7) consider therapeutic hypothermia
8) aggressively treat seizures
9) supportive and IMPORTANT care
    a) head in neutral position
    b) collar LOOSELY applied if C spine injured (avoid impeding head's venous drainage)
    c) prevent Valsalva (coughing/gagging)
    d) avoid unnecessary stimulation and noisy environment
    e) sedate and paralyze (consider EEG for subclinical SE)

**Specific Management Strategies:**

<u>Treatment of hypotension, hypoperfusion, and hypoxia</u>

- the injured brain loses its ability to auto-regulate
    - Keep MAP > 65 and diastolic BP < 120
- avoid inadvertent hyperventilation unless patient is **imminently** herniating
    - $PaCO_2$ = 35-45
- avoid hypoxia and hyperoxia
    - $PaO_2$: 80-120 (18% higher mortality when $PaO_2$ =300 for long periods)

<u>Maintenance of body temperature</u>

- fever is damaging to the brain (increases metabolic demand 10% per degree C)
- monitor core body temp: rectal, esophageal, bladder or vaginal
- temp managed with antipyretics, cooling with fans +/- misting, commercial cooling devices

What about resuscitative mild hypothermia?

- stay tuned for question 3 but no clear mechanism

Treatment of HYPERglycemia

- profound hyperglycemia leads to increased cellular pH, increased brain lactate, and increased neuronal loss
- cautiously use insulin for high sugars

Seizure management

- seizures increase brain metabolism by 400%
    - increases oxygen delivery / demand mismatch
- no evidence to support seizure prophylaxis, but if they occur need rapid treatment
- treatment
    - benzos, phenytoin, barbiturates

Immobilization/Sedation/Head position

- appropriate sedation and paralysis can prevent brain stimulation
- ensure quiet environment
- preventing coughing, unnecessary suctioning, neck compression
- ensure neck in neutral position

It all comes back to keeping the patient's values NORMAL!

## 2) List 5 techniques for initiating therapeutic hypothermia

1) Cold saline infusion
2) Misting and fans
3) Ice packs in the groin and axilla
4) Cooling blankets (commercial cooling devices)
5) Internal cooling (bladder irrigation, chest tubes, ECMO)

Why care? The reported NNT for a good neurologic outcome is 7 (from Rosen's)

The most recent edition of Rosen's quotes the 2010 American and European guidelines **for out of hospital cardiac arrest (VF)**

- target temperature was $33^0$C for 12-24 hrs
- ideally begun in the ED after ROSC achieved
    - insert esophageal probe
    - 2 L of cold saline
    - expose patient
- avoid hypotension or hypoxia / do NOT delay PCI if needed


- pharmacologic prevention of shivering:
    - paralytic, sedation, fentanyl

The new 2015 AHA guidelines suggest targeted therapy management between 32-36$^0$C for 24 hours with prognostication at 72 hours post arrest or post cooling.

This does not apply to other types of brain injury. Cooling for adults/children with TBI and acute ischemic stroke have shown **NO** benefits from therapeutic hypothermia

## 3) List 4 mechanisms of therapeutic hypothermia in improving neurologic outcome

No clear mechanism known; however, Rosen's suggests 4:

1) decreases metabolic demand
2) decreases free radical formation
3) decreases production of inflammatory cytokines
4) prevents programmed neuronal cell death

## Summary: key take home points

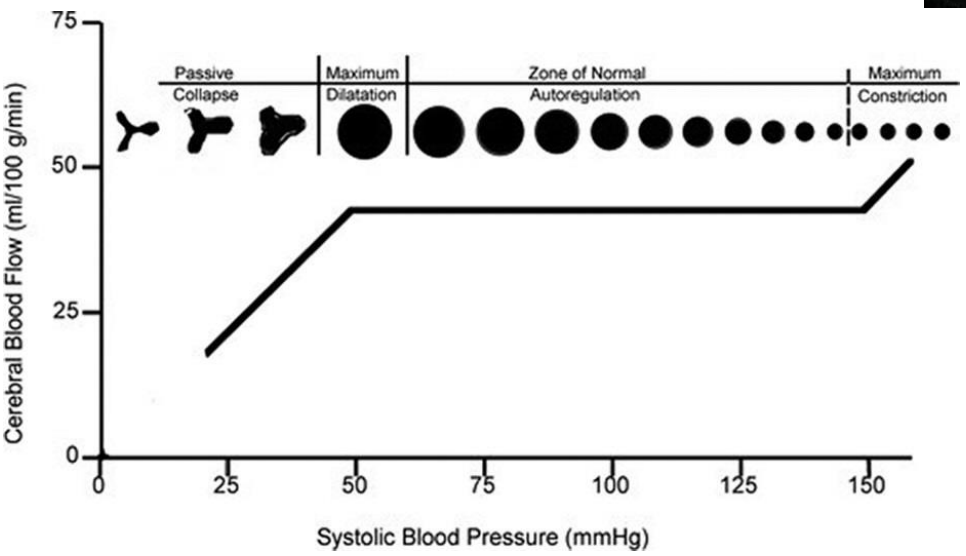
Bottom line:

- initially comatose state in ER does not always mean bad long term outcome! Give everyone the best chance of recovery
- **Prevent**:
    - hypotension, hypoperfusion, hypoxia
    - hyperthermia, hyperglycemia
    - seizures/coughing/vasalva
    - body/head/neck positions that increase ICP

## Wisecracks:

## 1) What components make up cerebral blood flow and CPP?

The graph below should be burned into your cerebral cortex!!




Taken from http://journals.lww.com/anesthesia-analgesia/Fulltext/2008/09000/Cerebral_Perfusion_Pressure_in_Neurotrauma__A.45.aspx

- any change in BP between 50-150 mmHg doesn't increase the cerebral blood flow because your brain is able to AUTOREGULATE the size of the cerebral blood vessels.
- after 150 mmHg the brain is maximally vasoconstricted and the cerebral blood flow spikes upwards again
- ideally we should keep the injured brain in 50-150mmHg sweet spot – ideally more than 100mmHg and less than 150mmHg

Some equations:

Cerebral Perfusion Pressure (CPP) = MAP – ICP or CVP (whichever is highest)

Cerebral Blood Flow (CBF) = CPP/CVR (Cerebral Vascular Resistance)

Brain Trauma Foundation support a CPP of 50-70mmHg in patients with severe traumatic brain injury (this is usually calculated for patients once in the neuro-ICU)

Note: this is a gross oversimplification of a complicated fellowship topic. The key take home point is that we need to do whatever we can to protect the injured brain because it does a finite ability to auto-regulate!

## 2) Wisecracks Essential Evidence: Target Temperature Management at $33^0$C versus $36^0$C after Cardiac Arrest (Nielsen *et al.* 2013)

Worldwide, Nielsen *et al.*'s TTM study has been a practice changing multi-center randomized controlled trial comparing **targeted** $33^0$C vs $36^0$C temperature management for post-cardiac arrest patients. See original paper below:


Crack Cast Show Notes – Brain Resuscitation – Feb 2016
**www.crackcast.org**

http://www.nejm.org/doi/full/10.1056/NEJMoa1310519

Quick overview:

- Very well executed/designed multi-center randomized controlled trial based out of Europe and Australia
- n = 939 (see original paper for full inclusion/exclusion criteria) **BUT** patients with an unwitnessed arrest with initial rhythm of asystole were **excluded.** Thus, this study looked mainly at post-VF arrest patients and thus the generalizability to other initial rhythms can be debated.
- modified intention-to-treat analysis
- **No difference** in primary outcome of **mortality** at 180 days
    - 50% for $33^0$C
    - 48% for $36^0$C
    - hazard ratio for T33°C, 1.06; 95%CI 0.89-1.28; P=0.51
- **No difference** in secondary outcome of **neurological performance** (cerebral performance score and modified rankin scale)
- Differences in:
    - duration of mechanical ventilation shorter in $36^0$C
    - serious events marginally higher in $33^0$C group
    - higher rates of hypokalemia in the $33^0$C group

**Bottom line**: No difference in primary or secondary outcomes between $36^0$C and $33^0$C groups.

- It is important to note that **both** arms of the trial had **active** monitoring and regulation of temperature (temperature was not left to fluctuate naturally)
- **Thus, the target ($33^0$C vs $36^0$C) might not be as important as actively maintaining euthermia/mild hypothermia and preventing fever and spikes in temperature (previously shown to result in poor outcomes)