Induced Hypothermia

**Rationale**
Use of hypothermia treatment decreases the severity of ischemic brain damage and leads to improved neurological outcomes at 6 months after cardiac arrest and has also been shown to be effective for refractory intracranial pressure (ICP) elevations.

**Ethical Considerations**
- **Prognostication:** Allow a minimum of 72 hours from time of rewarming cardiac arrest before considering withdrawal of treatment.
- **Consider Neurology consult**
- **Consider Palliative Care / Ethics Consult** to assist in establishing goals of care and for family support.

**Indications, Goals and Duration of Cooling**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Preferential time until initiation</th>
<th>Duration of cooling</th>
<th>Rewarming Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Arrest*</td>
<td>Within 6 hours</td>
<td>24 hours from initiation of cooling</td>
<td>0.2-0.5°C per hour</td>
</tr>
<tr>
<td>Refractory Intracranial Pressure (ICP) Elevation**</td>
<td>When standard measures fail to control ICP/cerebral edema</td>
<td>Disease specific</td>
<td>&lt;0.5°C per hour</td>
</tr>
</tbody>
</table>

**Criteria**
All of the following criteria must be met:
- Intubated with mechanical ventilation
- No purposeful movement to verbal command
  - Brainstem reflexes and pathological posturing movements permissible.
  - Patients with Glasgow Coma Scale (GCS) of <5 are eligible.

**Cautions**
- Temperature < 30°C (86°F) after cardiac arrest.
- Pregnancy
- Systemic infection / sepsis.
- Major surgery within 14 days.
- Active ongoing bleeding or known bleeding predisposition

**Preparation**
1. **Begin treatment early**
   - Initiate therapy in the ED when possible (continue if already started in field).
   - If already started at outlying facility, continue treatment upon receipt.
   - Do not actively warm patients who are spontaneously hypothermic following cardiac arrest.

2. **Determine method to initiate and sustain cooling**

   **Internal Cooling Catheter (Preferred)**
   - **Selection Considerations**
     - **Cannot use in suspected/confirmed heparin-induced thrombocytopenia (HIT) – catheter is heparin bonded**
     - Femoral placement
       - Zoll Quattro catheter (9.3 F/ 45 cm)
       - Zoll Icy catheter (9.3 F/ 38 cm)
   - FAQ/Pearls
     - If standard catheter infusion lumens unavailable, cooling catheter may be used to administer IV fluids, medications or blood products.
     - Always use a 500 ml bag of saline and NEVER replace an empty bag of saline. (An empty bag is a sign of a broken or pierced balloon.)
     - System is not cooling or warming when in STANDBY MODE.
     - Roller Pump and pinwheel may stop for 15 minutes when switching from cooling to rewarming.

   **External Surface Cooling System**
   - **Selection Considerations**
     - Alternative method for therapeutic hypothermia if intravascular cooling contraindicated or unable to be placed
   - FAQ/Pearls
     - May note larger oscillations/fluctuation in temperature control

3. **Establish continuous core temperature monitoring**
   - Sites of monitoring in order of preference are bladder (if making adequate urine), esophageal, pulmonary artery catheter (if available) or rectal. Intermittent oral temperatures can be considered only if no other alternatives.
   - Temperature should be monitored continuously and documented every 30 minutes during active cooling and rewarming, and every hour during maintenance phase.
   - Secondary temperature monitoring should be considered if core body temperature < 30°C (86°F).

4. **Place an arterial line** for pressure monitoring. Place early to avoid placement difficulties, but do not delay cooling if unable to place line.

5. **Place nasogastric or orogastric tube.**

6. **Continue other therapies as indicated.**

*Evidence indicates that best neurological outcomes occur if initial rhythm at time of cardiac arrest was ventricular tachycardia (VT) or ventricular fibrillation (VF)*

**Often associated with hepatic failure, intracerebral hemorrhage (ICH), ischemic stroke, or traumatic brain injury (TBI) where patients may be cooled for as long as 5 days.**
Goal: Sustain Cooling for at least 24 Hours

- See Appendix A for “Physiologic Effects of Mild to Moderate Hypothermia”
- See Appendix B for “Induced Hypothermia Flowsheet”

### Phase I: Cooling

#### Goal of achieving target cooling temperature within 3-hours (or less) of initiation:
- Cooling to core body temperature of 32-34º C (89.6-93.2º F)
- Notify House Officer if unable to achieve cooling goal within 3 hours

#### Provide Immediate Means of Cooling
- Give cold saline infusion (30 mL/kg) via a peripheral line or central venous catheter to assist in achieving goal temp. (Cold saline is stored in the emergency department or call pharmacy.)
- Infuse cold normal saline (4º C / 39.2º F) over 30 minutes or less – every liter of cold saline decreases core temperature by ~ 0.8 to 1 º C
- Use caution in administering fluids if there is clinical evidence of CHF or CVP greater than 20.
- Avoid “overcooling”

#### Provide Cooling via Device
- Decrease heated-wire circuit temperature on ventilator to 32º C if able
  - This may prevent unintended core temperature warming
- If patient is supported with ECMO, utilize ECLS to modulate temperature changes per protocol goals. Otherwise, proceed as indicated below:

<table>
<thead>
<tr>
<th>Internal Cooling Catheter (Preferred)</th>
<th>External Surface Cooling System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Packing in Ice NOT necessary</td>
<td>Pack patient in ice (groin, chest, axillae, side of neck) to bring temperature between 32-34º C (89.6-93.2º F).</td>
</tr>
<tr>
<td>Follow OSUWMC Intravascular Access Devices Policy for insertion and maintenance</td>
<td>o Avoid packing ice on top of the chest, as this may impair chest-wall motion.</td>
</tr>
<tr>
<td>Once catheter placed, turn unit on and work through system set-up per instruction card on device</td>
<td>Obtain two cooling blankets, cables, and one external surface cooling system device to “sandwich” the patient.</td>
</tr>
<tr>
<td>Document temperatures every 30 minutes until at within goal temperature range</td>
<td>Select “MANUAL” mode and adjust set point temperature to 4º C (39.2º F) or the lowest temp for the system.</td>
</tr>
<tr>
<td></td>
<td>Once temperature is &lt; 34º C (93.2º F) see instructions in “Phase II: Maintenance”</td>
</tr>
</tbody>
</table>

#### Prevent and Treat Shivering
- Acetaminophen 650 mg PO/NG/PR Q6H x 4
- Buspirone 30 mg NG Q8H x 3
- Magnesium 4 g IVBP Q8H (hold if Mg >4 mg/dL) x3
- See algorithm, page 3

#### Provide Sedation/Anesthesia
- Record Pain and RASS at least every 4 hours (more frequently if also shivering)
- See algorithm, page 3

#### Electroencephalogram (EEG) Monitoring
- Continuous EEG monitoring is highly recommended during cooling after cardiac arrest for seizure detection and assistance with prognostication
  - 10-30% of patients will have seizures after cardiac arrest, many of which are non-convulsive
- Do not delay cooling while awaiting for placement

#### Labs / Blood Gases
- At time 0, obtain Chem 7 with Mg, troponin (if post-cardiac arrest), CBC, PT/PTT, INR, blood gas if not already checked
- Check Neuron Specific Enolase (NSE) at initiation of cooling (to be repeated 24 hours after initiation)
- NSE may be helpful as a surrogate marker in prognostication
- Accu-Chek q1h x4. (ICU glycemic target 120-150 mg/dL)
### Induced Hypothermia: Overcoming Natural Thermoregulatory Processes

**Normal Process:** Temperature < 37°C = arteriovenous vasoconstriction → Temperature 33-35.5°C = shivering response

#### Induction of Hypothermia

- Acetaminophen 650 mg PO/NG/PR Q6H x 4
- Buspirone 30 mg NG Q8H x 3
- Magnesium 4 g IVPB Q8H (hold if Mg >4 mg/dL) x3
- Continuous EEG Monitoring

**Advisory Statements:**
- Shivering typically SLOWS or STOPS at temperatures < 33°C
- Pharmacodynamics / pharmacokinetics of most sedatives, narcotic analgesics, and NMBs are SIGNIFICANTLY affected during induced hypothermia (See page 7)

**Goal RASS -3 to -4**

- If Temperature at goal:
  - Increase level of sedation to Goal RASS -4 to -5 – use boluses
  - Apply warm cloths to hands and feet (peripheral application of warmth can alter shivering response)
  - Consider manually decreasing device goal to 35.5°C

- If Temperature is NOT at goal:
  - Manually decrease device goal temperature to 32.5°C
  - Apply warm cloths to hands and feet (peripheral application of warmth can alter shivering response)
  - Consider 500 ml of COLD Saline if >2 hr after initiation bolus

**Level 1 shivering**

- **(Mild to Moderate and localized)**

**Level 2 shivering**

- **(Severe whole body)**

- Increase level of sedation to Goal RASS -4 to -5 – use boluses
  - Manually decrease device goal to 32.5°C
  - Apply warm cloths to hands and feet (peripheral application of warmth can alter shivering response)
  - Consider 500 ml of COLD Saline
  - Consider surface counter-warming (bair-hugger blanket) only if using cooling catheter

**Suspected or Confirmed Seizures**

- **STAT Neurology consult**
- **Consider midazolam or lorazepam bolus**
- **Do NOT use NMBs**

**Level 3 shivering**

- **(Severe whole body)**

**If above is unsuccessful AND NO SEIZURE SUSPICION**

- Consider Single bolus vecuronium IVP (0.1 mg/kg) ONCE followed by (0.05 to 0.1 mg/kg) Q4H prn shivering
- If shivering persists after > 3 boluses of vecuronium, administer additional vecuronium bolus and initiate infusion at 1 mcg/kg/min

(Physician must be present for first NMB dose per policy)

**Suspected or Confirmed Seizures**

- **STAT Neurology consult**
- **Consider midazolam or lorazepam bolus**
- **Do NOT use NMBs**

**NO intention to be able to fully assess neurologic status until ≥ 72 hr after rewarming**

Monitor for changes to temperature control and address by starting at previous steps in algorithm

**Shivering?**

- **YES**
  - Level 1 shivering
  - **(Mild to Moderate and localized)**

- **NO**
  - Initiate scheduled or continuous IV sedative using one the following:
    - Midazolam
    - Lorazepam

- If Temperature is NOT at goal:
  - Increase level of sedation (Goal RASS -4 to -5) – use boluses
  - Apply warm cloths to hands and feet (peripheral application of warmth can alter shivering response)
  - Consider manually decreasing device goal to 32.5°C

- If Temperature at goal:
  - Increase level of sedation (Goal RASS -4 to -5) – use boluses
  - Apply warm cloths to hands and feet (peripheral application of warmth can alter shivering response)
  - Consider manually decreasing device goal to 32.5°C

**Advisory Statements:**
- Close monitoring is required for early suspicion and detection of seizures
- Meperidine should be used cautiously due to the following:
  - Hypothermia by definition decreases GFR
  - Meperidine increases risk of inducing seizures in patients with low GFRs

Because of pharmacokinetic changes in induced hypothermia:
- Train of Four (TOF) should NOT be used as it is NOT reliable in patients undergoing induced hypothermia for monitoring/titrated of neuromuscular blockers (NMBs)
- Vecuronium is preferred for intermittent boluses (half-life is 2-3 X longer)

- Upon initiation of controlled re-warming phase (PHASE III), NMB use should be minimized/discontinued.
- If patient has received NMB, sedatives/analgesics should be decreased with caution until 8 hrs after last dose of NMB.
- If no NMB has been used, sedation and analgesia may be decreased during rewarming unless evidence of shivering is seen.
Phase II: Maintenance

Maintain Goal Temperature

<table>
<thead>
<tr>
<th>Internal Cooling Catheter (Preferred)</th>
<th>External Surface Cooling System</th>
</tr>
</thead>
<tbody>
<tr>
<td>• This is Automatic – There are no settings to maintain or change</td>
<td>• Once temperature is &lt; 34º C (93.2º F):</td>
</tr>
<tr>
<td>• Document core temperature from device Q1H during maintenance phase</td>
<td>• Remove ice bags to prevent excessive drop in patient’s core temp.</td>
</tr>
<tr>
<td>• Watch for bleeding at catheter insertion site</td>
<td>• Switch to “AUTO mode” and the target temp to 33º C (92.3º F)</td>
</tr>
<tr>
<td>• Assess skin integrity beneath cooling catheter every 4 hours</td>
<td>• Document core temperature from device hourly during maintenance phase</td>
</tr>
<tr>
<td></td>
<td>• Check skin every 2 hours for injury caused by ice or cold blankets.</td>
</tr>
</tbody>
</table>

Blood Pressure

• Mean arterial pressure (MAP) goal should be at least >65 mmHg.
  • Because of peripheral vasoconstriction, BP may remain elevated during hypothermia.

Arrhythmias

• Monitor patient for arrhythmias associated with hypothermia.
  • If persistent, life-threatening dysrhythmias, hemodynamic instability, or bleeding develops, discontinue cooling, and ensure that the patient is actively re-warmed.
  • Heart rates < 40 BPM are frequent and are not alone a cause for concern in the absence of other evidence of hemodynamic instability.

Continue Shivering Prevention and Maintain Sedation/Anesthesia

Labs / Blood Gases

• At hours 8, 16, and 24, obtain Chem 7, Mg and blood gas.

• Potassium Goal: 4.0 – 4.5 mEq/L
  Treat potassium values < 4.0 mEq/L with IV administration of K+ while the patient is being cooled.

• Glucose should be kept at target range of 120-150 mg/dl and treated with insulin if elevated.
  (For IV Insulin Infusion guideline, refer to OneSource/Clinical Practice Guidelines/Diabetes)

• Maintain PaCO₂ in the normal range (35-45 mm Hg)

Nutrition

• May provide trophic enteral nutrition during the initiation, maintenance, or re-warming phases of therapy.
**Phase III: Transition to Rewarming and Controlled Rewarming**

### Provide Controlled Rewarming

<table>
<thead>
<tr>
<th>Internal Cooling Catheter (Preferred)</th>
<th>External Surface Cooling System</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Modify device settings per orders relative to indication for hypothermia listed as “A” or “B” below</td>
<td></td>
</tr>
<tr>
<td>• Document temperatures every 30 minutes until at goal</td>
<td></td>
</tr>
<tr>
<td>• Most patients require about 8 hours to rewarm unless ordered otherwise</td>
<td></td>
</tr>
<tr>
<td>• The goal after rewarming is normothermia.</td>
<td></td>
</tr>
<tr>
<td>• It is preferred to keep catheter in place for ~48 hours. Notify MD for order to remove if still in place by day 4</td>
<td></td>
</tr>
<tr>
<td>• Rewarm at ordered rate/hour relative to indication for hypothermia listed as “A” or “B” below</td>
<td></td>
</tr>
<tr>
<td>• Document temperatures every 30 minutes until at goal</td>
<td></td>
</tr>
<tr>
<td>• Most patients require about 8 hours to rewarm unless ordered otherwise</td>
<td></td>
</tr>
<tr>
<td>• The goal after rewarming is normothermia.</td>
<td></td>
</tr>
</tbody>
</table>

**Rate of rewarming is dependent on indication for induced hypothermia (See “A” or “B”)**

### A. Post Cardiac Arrest:

**Controlled Rewarming within an 8-Hour Goal:**
- Begin rewarming 24 hours after initiation of cooling.
  - Time 0 is at initiation of cooling
- Rewarm at a rate of 0.3°C (0.5°F) every hour up to a target of 37°C (98.6°F) unless directed otherwise.
- Most patients require 8 hours to rewarm.
- The goal after rewarming is normothermia.

**Medications During Rewarming**
- Maintain sedation until a temperature of 35°C (95°F) is reached.
  - If patient has received a neuromuscular blocker (NMB), discontinue the NMB before the sedative/analgesic agents.
  - Do not decrease sedatives/analgesics until 8 hours after last dose of NMB.
  - If no NMB has been used, sedation and analgesia may be minimized/discontinued upon rewarming.
- Monitor patient for hypotension (secondary to vasodilatation) induced by rewarming.

**Labs and Electrolytes**
- Do not aggressively replace potassium as hyperkalemia can commonly occur during controlled rewarming.
- At hours 32, obtain Chem 7, Mg (if using the most common 24 duration of hypothermia).
- Repeat neuron specific enolase 24 hours after initiation of hypothermia.

**Temperature Control After Rewarming**
- Once patient at 37°C, may change heated-wire circuit temperature on ventilator to 37°C
- Fevers should be treated actively during and after rewarming
- Use acetaminophen and consider keeping cooling device in place in order to keep temperature < 37°C (98.6°F) for 48 hours after rewarming.

### B. Refractory ICP Elevation:

**Controlled Rewarming per physician order:**
- Begin rewarming at physician ordered time (these patients may be cooled for 2-5 days or more)
  - Time 0 is at initiation of cooling
- Rewarm at physician ordered rate
- The goal after rewarming is normothermia.

### References


**Order Sets**
- MIC: Induced Hypothermia [2197]

**Quality Measures**
- Usage rate for comatose out-of-hospital and in-hospital survivors
- Sustain hypothermia for 24 hours
- Incidence of cooling
- Neurological status at discharge (CPC score)
- Rewarming rates
- Incidence of hyperkalemia within 24 hours of rewarming
- Relationship of BMI and cooling goal of < 3 hours

**Guideline Authors**
Erik Abel, PharmD, BCPS
Chad Miller, MD
Eric Adkins, MD
Ravi Tripathi, MD
Marcia Belcher, MSN, RN, CNS
Brenda Vermillion, DNP, RN, CNS

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**Disclaimer**

*Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.*

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Appendix A
Physiologic Effects of Mild to Moderate Hypothermia (30 - 34° C)

Hypothermia decreases the cerebral metabolic rate and oxygen requirements to suppress inflammatory cellular responses associated with reperfusion injury (free radical production, release of neuroexcitatory and inflammatory cytokines and calcium shifts) which mediate apoptosis.

### Table 1. Summary of Physiologic Effects of Induced Hypothermia

<table>
<thead>
<tr>
<th>Potential / Expected Effects</th>
<th>Clinical Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurologic</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased consciousness, lethargy, coma</td>
<td>Increased risk of seizures (9-20%) due to neuroexcitatory cytokine release mediated by the ischemic event</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Risk of ectopy increases as temperatures go below 32° C.</td>
</tr>
<tr>
<td>Vasocostriction</td>
<td>Heart rates of 40 BPM are not uncommon, but attentiveness should be given to the MAP.</td>
</tr>
<tr>
<td>Moderate to Severe arrhythmias</td>
<td>Repolarization abnormalities may contribute to the EKG changes exhibited in hypothermia.</td>
</tr>
<tr>
<td>o Atrial fibrillation/flutter</td>
<td></td>
</tr>
<tr>
<td>o Ventricular tachycardia</td>
<td></td>
</tr>
<tr>
<td>o Ventricular fibrillation</td>
<td></td>
</tr>
<tr>
<td>EKG changes:</td>
<td></td>
</tr>
<tr>
<td>o Prolonged PR, QRS and QT intervals, Osborn waves</td>
<td></td>
</tr>
<tr>
<td>Decreased cardiac output → increased CVP</td>
<td></td>
</tr>
<tr>
<td><strong>Renal/Electrolytes</strong></td>
<td></td>
</tr>
<tr>
<td>Increased urine output (does not reflect true GFR)</td>
<td>Do not mistake increased urine output for improving renal function while cooling a patient. Glomerular filtration is reduced during hypothermia (cold diuresis).</td>
</tr>
<tr>
<td>Decreased creatinine clearance (decreased GFR)</td>
<td>Conservatively replace potassium, particularly as the rewarming phase approaches.</td>
</tr>
<tr>
<td>Renal tubular dysfunction</td>
<td>Cooling affects slows enzyme-dependent processes including the Na⁺-K⁺-ATPase pump. As rewarming ensues this ion pump will gain more activity and serum K⁺ will increase.</td>
</tr>
<tr>
<td>Increased electrolyte loss (K⁺, Na⁺, PO₄³⁻)</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
</tr>
<tr>
<td>Impaired motility</td>
<td>Decreased gastrointestinal absorption can be expected.</td>
</tr>
<tr>
<td>Elevated amylase and lipase</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatobiliary</strong></td>
<td></td>
</tr>
<tr>
<td>Transaminitis</td>
<td>Drugs metabolized or eliminated by the liver will have considerably increased half-lives, duration of action, and increased risks of toxicity.</td>
</tr>
<tr>
<td>Reduced activity of cytochrome P450 mediated metabolism</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic/Endocrine</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased activity of most/all enzyme mediated processes (P450 metabolism, coagulation cascade, etc.)</td>
<td>Emphasize glycemic control due to common hyperglycemia and insulin resistance.</td>
</tr>
<tr>
<td>Decreased oxygen consumption and carbon dioxide production</td>
<td>Maintain glucoses &lt; 200 mg/dL.</td>
</tr>
<tr>
<td>Increased gluconeogenesis and glycogenolysis → hyperglycemia</td>
<td></td>
</tr>
<tr>
<td>Decreased insulin production and sensitivity</td>
<td></td>
</tr>
<tr>
<td>Increased catecholamine and cortisol secretion</td>
<td></td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td></td>
</tr>
<tr>
<td>Shivering</td>
<td>Shivering usually ceases &lt; 33.5° C.</td>
</tr>
<tr>
<td><strong>Hematologic</strong></td>
<td></td>
</tr>
<tr>
<td>Elevated aPTT</td>
<td>Current bleeding diatheses will be further aggravated by hypothermia.</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Unless patients are normothermic or near normothermic, FFP or recombinant factor products will not work effectively to stop bleeding.</td>
</tr>
<tr>
<td>Impaired clotting ability and activity of the coagulation cascade</td>
<td></td>
</tr>
<tr>
<td>Impaired platelet function due to decreased production of thromboxane A₂</td>
<td></td>
</tr>
<tr>
<td><strong>Immunologic</strong></td>
<td></td>
</tr>
<tr>
<td>Impaired macrophage and neutrophil function</td>
<td>Theoretical increased risk of infection</td>
</tr>
<tr>
<td><strong>Pharmacologic/pharmacodynamic</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased metabolism and elimination of many drugs</td>
<td>Give careful attention to both drug toxicity and efficacy during hypothermia due to changes in drug disposition and response.</td>
</tr>
<tr>
<td>Altered receptor affinity and altered effects of some drugs</td>
<td>See Table 2</td>
</tr>
<tr>
<td>Drug</td>
<td>Pharmacokinetic / Pharmacodynamic Change</td>
</tr>
<tr>
<td>------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td><strong>Sedatives / Analgesics</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Midazolam | • Nearly 100-fold decrease in systemic elimination at core temp < 35°C.  
• Clearance decreases by ~11% per °C decrease below 36.5°C. | • Cooling for ~12 hours will cause some buildup of both parent and active metabolites. Allow adequate time for clearance once normothermic. |
| Morphine | • Affinity for the µ-receptor decreased as temperature decreases. Potency at 30°C is 1/5th of that at 37°C. | • Consider alternative agents since there is evidence that, despite likely decreased hepatic clearance, relative potency also decreases with hypothermia. |
| Fentanyl | • Up to ~2-fold increases in plasma concentrations and ~3.7 fold decreases in clearance have been observed and many persisted for up to 6 hours after rewarming. | • Accumulation of the parent drug can be expected during cooling with potential for increases in effect and duration of action. |
| Propofol | • Plasma concentrations increase by up to ~30% during hypothermia. |  |
| Remifentanil | • Clearance decreases by ~6% with each degree of decrease in Celsius below 37°C. |  |
| **Neuromuscular Blockers (NMB)** |  |  |
| Atracurium | • Bolus dosing during mild hypothermia showed a decrease clearance by ~1.5 fold. | • Hypothermia appears to prolong duration of action NMB; however, TOF is not a reliable method to monitor NMB during hypothermia.  
• Hypothermia appears to prolong duration of action NMB; however, TOF is not a reliable method to monitor NMB during hypothermia.  
• When used for shivering, attempt to minimize NMB use and depress temperatures below the shivering threshold if tolerated. |
| Cisatracurium | • Cleared by Hofmann elimination which is a temperature dependent reaction |  |
| Rocuronium | • There is up to a 2-fold decrease in clearance during hypothermia. |  |
| Vecuronium | • There is ~3 fold increase in duration of action during hypothermia with ~11% decrease in plasma clearance per degree Celsius. |  |
| **Anticonvulsants** |  |  |
| Phenytoin | • Hepatic clearance is decreased during hypothermia. Plasma concentration may increase by up to 180% at 34°C, while \( K_e \) and clearance have been shown to decrease by 50% or more. | • Treat seizures aggressively during hypothermia; however, when using phenytoin or fosphenytoin, increased monitoring for toxicities is recommended |
| **Cardiac Drugs** |  |  |
| Nitroprusside | • Enzyme mediated conversion of the metabolite cyanide to thiocyanate is slowed during hypothermia. | • Consider alternative antihypertensives to avoid potential toxicity. |
| Aspirin | • Minimal to no increases in effect in platelet dysfunction via thromboxane A2 are seen.  
• Inhibition/slowing of thromboxane synthetase and subsequent platelet dysfunction is caused by hypothermia. | • Continue aspirin as indicated. |
| Glycoprotein IIb/IIIa inhibitors | • Eptifibatide and tirofiban have exhibited increases in platelet dysfunction at less subclinical dosing. Abciximab did not demonstrate this finding. | • Increased monitoring for bleeding is recommended. |
Appendix B: Induced Hypothermia Flowsheet

(Timeline may be extended when used for refractory ICP elevation)

Corresponding Lab Draw Schedule

<table>
<thead>
<tr>
<th>Lab Draw Schedule</th>
<th>Base-line</th>
</tr>
</thead>
<tbody>
<tr>
<td>aPTT/PT/INR</td>
<td>X</td>
</tr>
<tr>
<td>ABG</td>
<td>X</td>
</tr>
<tr>
<td>Accuchek (if no insulin gtt)</td>
<td>X x x x</td>
</tr>
<tr>
<td>CBC</td>
<td>X</td>
</tr>
<tr>
<td>Chem 7, Mg</td>
<td>X</td>
</tr>
<tr>
<td>Troponin</td>
<td>X</td>
</tr>
<tr>
<td>Neuron Sp. Enolase</td>
<td>X</td>
</tr>
</tbody>
</table>

The following are the minimum labs that are to be drawn during Induced Hypothermia

- aPTT/PT/INR
- ABG
- Accuchek (if no insulin gtt)
- CBC
- Chem 7, Mg
- Troponin
- Neuron Sp. Enolase

Time/Date Initiated

Time/Date first at <34°C

Time/Date to begin transition

Normothermia

- Target Temperature Range 32 – 34°C
- MAP Goal greater than 65 mmHg

Phase I: Cooling

- Attempt arterial line placement early

Phase II: Maintenance

- Shivering response likely between 33.5 and 35°C

Phase III: Controlled Rewarming

- Two to three hours prior to Phase III: minimize potassium replacement and discontinuation of muscle blockade

Increasing physiologic abnormalities as temperature approaches 30°C. See Appendix A “Physiologic Effects of Mild to Moderate Hypothermia”