

Hyperthermia Treatment Protocol

Literature Review & Departmental Guidelines

Background Info

Harrison's Internal Medicine:

- Fever: temperature $> 99.9^{\circ}\text{F}$
 - Illness and other conditions may reset temperature regulation point to 39°C (102.2°F)
- Hyperpyrexia: temp $> 41.5^{\circ}\text{C}$ (106.7°F)
 - Sometimes seen in infection, sepsis
- Hyperthermia:
 - NOT fever, but temp elevation from other cause
 - Can be rapidly fatal
 - Skin likely to be hot / dry but not cold as in fever

Causes of Hyperthermia Syndromes

- 1. Heat Stroke:** Production of heat is greater than ability to dissipate heat
 - Exertional: Exercise in higher than normal heat and/or humidity
 - Non-exertional: Anticholinergics, including antihistamines; anti-parkinsonian drugs; diuretics; phenothiazines
- 2. Drug-Induced Hyperthermia:** Amphetamines, cocaine, phencyclidine (PCP), methylenedioxymethamphetamine (MDMA; "ecstasy"), lysergic acid diethylamide (LSD), salicylates, lithium, anticholinergics, sympathomimetics
- 3. Neuroleptic Malignant Syndrome:** Phenothiazines; butyrophenones, including haloperidol and bromperidol; fluoxetine; loxapine; tricyclic dibenzodiazepines; metoclopramide; domperidone; thiothixene; molindone; withdrawal of dopaminergic agents
- 4. Serotonin Syndrome:** Selective serotonin reuptake inhibitors (SSRI's), Monoamine oxidase inhibitors (MAOI's), tricyclic antidepressants (TCA's)
- 5. Malignant Hyperthermia:** Inhalational anesthetics, succinylcholine
- 6. Endocrinopathy:** Thyrotoxicosis, pheochromocytoma
- 7. Central Nervous System Damage:** Cerebral hemorrhage, status epilepticus, hypothalamic injury

Basic Hyperthermia Treatment

- Antipyretics may be of little use, but if etiology is uncertain they are likely to decrease temperature of fever or infectious hyperpyrexia
- Surface cooling
- Core cooling with lavage; consider CPB / hemodialysis
- Drug Rx
 - MH: Dantrolene
 - NMS: Bromocriptine, Amantadine, Nifedipine; consider neuromuscular blocker
 - TCA overdose: Physostigmine

Malignant Hyperthermia

- Treatment:
 - **Discontinue trigger** (may be all that's needed if "slow" onset or brief exposure)
- If severe:
 - Dantrolene 2.5 mg/kg and repeat "until symptoms subside" every 5 to 10 minutes
 - Side effects:
 1. Prolong relaxant / need for intubation
 2. Cholestasis if administered for >3 weeks
 3. NO OTHER SERIOUS SIDE EFFECTS
 - Dantrolene likely needed for several days: 50% recrudescence by 6.5 hrs
 - Treat acid base problems (bicarb, etc)
 - ACTIVE COOLING!!!!
 - Surface
 - Bladder / NG iced saline
 - Irrigate wound / body cavities
 - STOP COOLING between 38 – 39° as temp decreases
 - UO: myoglobinuria
 - Hyperkalemia Rx
 - Coag abnormalities

Disorders that can Mimic MH

- Alcohol therapy for limb arteriovenous malformation
- Contrast dye
- Cystinosis
- Diabetic coma
- Drug toxicity or abuse
- Environmental heat gain more than loss
- Equipment malfunction with increased carbon dioxide
- Exercise hyperthermia
- Heat stroke
- Freeman-Sheldon syndrome
- Hyperthyroidism
- Hypokalemic periodic paralysis
- Intracranial free blood
- Osteogenesis imperfecta
- Prader-Willi syndrome
- Wolf-Hirschhorn syndrome
- Muscular dystrophies (Duchenne's, Becker's)
- Myotonias
- Neuroleptic malignant syndrome
- Pheochromocytoma
- Sepsis
- Ventilation problems
- Rhabdomyolysis

Hypothermia

- Hypothermia is much more common during anesthesia than is hyperthermia
- Exception: procedure induced hyperthermia as during HIPEC, induced hyperthermia during free-flap / re-implantation surgery or during warming on CPB

HYPERTHERMIA DURING ANESTHESIA

- Consider cooling measures any time temperature is above “normal”
 - Common setting: small child, minimal skin/surgery site exposure under drapes and with active heating measures
 - Often treatment is to turn off heater and uncover some of patient’s skin

At what temperature
should we consider
active cooling measures?

Goldstein: *Summary, conclusions and recommendations: adverse temperature levels in the human body.* Int J Hyperthermia 2003; 19:373-384

- Heat related illness caused CNS damage when temperature was between 39 and 41.6°C
- “Most healthy people can tolerate core temperature excursions up to 40°C when adequately hydrated”
- However “brain and GI tract are particularly susceptible to heat-induced damage from whole body temperature” with whole body temperature at the time of death between 39 and 41.6°C (unknown duration of hyperthermia in these however)

Sharma: *Hyperthermia induced pathophysiology of the central nervous system.* Int J Hyperthermia 2003; 19:325-354.

- Moderate hyperthermia: temp up to 40°C
- **Heat stroke: temp >40°C**
 - **Heat induced brain injury not uncommon cause of death in young athletes**
 - **Delirium, seizures, coma may result**
- In heat stroke, can NOT auto-regulate temperature / cooling
- BBB leaks and cerebral edema may develop
- **Wide impact in CNS, may occur in few hours:**
- **Some human evidence suggests therapeutic hyperthermia up to 40°C for a few hours may not induce lasting adverse effects**
- Hyperthermia 40.5 to 43°C for 3 – 11 hours “results in fatality and visible organ injury”
- **Death within 24 hours in 70% of heat stroke victims (41.5 – 44°C)**
- **Critical level suggested as 41.6 – 42°C, although animal studies suggest 41°C**

Pediatric TBI guidelines. *Pediatr Crit Care Med* 2003; 4:S53-55

- Post-TBI hyperthermia defined as temperature $>38.5^{\circ}\text{C}$
- No RCT evidence to support Rx at that temperature
- However: avoidance of hyperthermia and consideration of induced hypothermia are therapeutic options

Lugo-Amador: *Heat-related illness.* *Emerg Med Clin N Am* 2004; 22:315-327

- “Temperature above $41.6-42^{\circ}\text{C}$ are considered to be above the critical thermal maximum for humans”
- Heat stroke: temp $>40^{\circ}\text{C}$
- “Morbidity and mortality is directly associated with the duration of elevated core temperature”
- Rapid cooling: cold water immersion, etc

Haveman: *Effects of hyperthermia on the central nervous system: What was learnt from animal studies?* Int. J. Hyperthermia, August 2005; 21(5): 473–487

- Localized temperature of 42-42.5°C may be tolerated up to 60 minutes
- Localized temperature 43°C tolerated only 10 to 30 minutes
- Whole body hyperthermia may be associated with some CNS tolerance as time is needed to heat the brain as the body heats

Wang: *Hyperthermia exacerbates ischaemic brain injury.* International Journal of Stroke 2009; 4: 274-284

- Both prospective and retrospective studies support association of worse outcome with elevated temperature following stroke
- Temperature of 39°C may be threshold for worse outcome
- However, temperature above normal may be bad
- RCT evidence lacking for acute stroke

Thulesius: *Thermal Reactions of Blood Vessels in Vascular Stroke and Heatstroke.* Med Princ Pract 2006; 15: 316-321

- “(Heat stroke) is a complex disorder of thermoregulation with multiple organ dysfunction, arterial hypotension, renal failure, disseminated intravascular coagulation, rhabdomyolysis, acid-base and electrolyte disturbances. It is a medical emergency”
- Heating induces constriction of the carotid artery
- In heat stroke (core $>40^{\circ}\text{C}$), hypermetabolic state develops BUT carotid vasoconstriction occurs: this may contribute to CNS damage seen in heat stroke

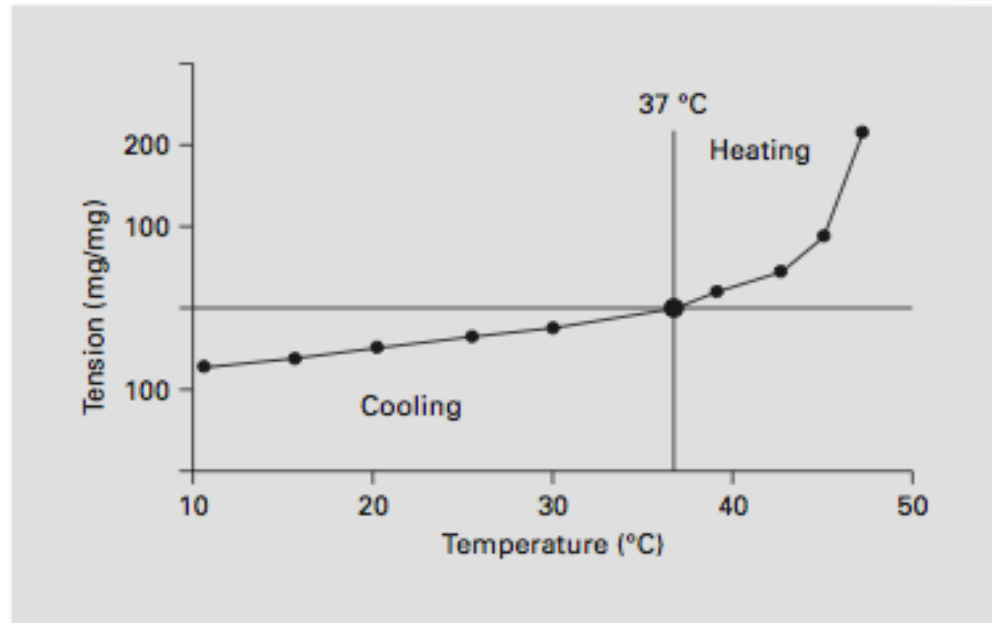


Fig. 3. Effects of cooling and heating on the contractile response of rabbit carotid artery specimens. Note the potentiated response during hyper- and hypothermia.

Thompson: Fever Management Practices of Neuroscience Nurses: National and Regional Perspectives. J Neurosci Nurs 2007; 39:151-162

- Survey of contemporary practice regarding temperature management of patients in ICU for neurologic disorders
- Wide range of core temperature to trigger treatment protocols: from 37 to 39.4°C
- **Regional differences: East and West coast hospitals: lower trigger than Midwest**

Badjatia: *Hyperthermia and fever control in brain injury.* Crit Care Med 2009; 37:S250-7

- Neuro injury: outcomes are worse in patients with fever, even though it is not clear if fever is cause or result of worse injury
- Temperature >38.3°C found in 70% of neurologic injury patients
- Fever unexplained up to 1/3 of cases
- Early fever may be an acute phase response
- Meta-analyses support association with worse outcomes
- Seen after TBI, stroke, SAH and cardiac arrest
- Suggests some protocols but points out limited RCT evidence

Conclusions

- Hyperthermia is clearly associated with adverse neurologic outcomes in the setting of neurologic injury (hypoxia, ischemia, stroke, SAH, TBI)
- Hyperthermia during anesthesia should be treated unless a therapeutic reason for hyperthermia is present (HIPEC, possibly flaps / reimplantation) – EVEN if a certain diagnosis explaining the hyperthermia (infection, sepsis) is known
- Temperature during general anesthesia at which intraoperative cooling should be started is less clear

Hyperthermia Treatment Protocol

- When hyperthermia develops or worsens in previously afebrile patients under general anesthesia in the absence of a therapeutic indication for hyperthermia:
- **Basic steps:**
 - Rule out malfunction of warming equipment, room thermostat, heat lamps, etc.
 - Look for signs of hypermetabolic state: high ETCO_2 (with normally functioning absorber and valves); tachycardia
 - Search for causes including sepsis, drug reaction, MH
 - Consider ABG analysis to establish acid base state
 - DISCUSS with staff anesthesiologist and resident / CRNA: consider differential diagnosis, need for invasive monitors, etc.
 - NOTE: Plan to stop cooling measures when temperature is reduced to 38°C BUT continue monitoring core temperature to detect recrudescence which mandates resumption of active cooling

Interventions based on core temperature (nasopharyngeal, esophageal, bladder, or rectal)

Temperature above 38°C (100.4°F)

- Should be treated with passive cooling at minimum:
 1. Uncover portions of the patient's skin as able
 2. Lower room temperature
 3. Ensure adequate hydration
 4. Consider higher fresh gas flow rate
 5. Remove airway humidifier if present
 6. CONSIDER ACTIVE COOLING IF TEMPERATURE CONTINUES TO INCREASE

Temperature above 39°C (102.2°F)

- Should be treated with active cooling:
 1. Water blanket set to cool
 2. Forced air device set to cool
 3. Administer IV acetaminophen (Ofirmiv) 10 mg/kg
 4. CONSIDER SURFACE COOLING MEASURES
 - Bathe in cold water
 - Iced saline gastric and/or surgical wound lavage
 - Pack ice bags around head, axillae and femoral artery / groin if surgical draping allows
 5. Obtain ABG since hyperthermia is a late sign of MH

Temperature above 40°C (104°F)

1. Continue active cooling measures
2. **DECLARE HYPERTHERMIA EMERGENCY**
 - Mandatory discussion of temperature management between anesthesiology, surgery, and nursing personnel
 - Contact Surgical Intensivist on call for consultative help
 - Consider possibility of other causes for hyperthermia
3. **MUST EXCLUDE MH - or - Initiate MH protocol**
 - Administer Dantrolene 2.5 mg/kg IV every 10 minutes until temperature decreases
 - Be aware of risk for hypotension in presence of calcium channel blockers
4. Consider invasive methods of cooling: **Intravenous Iced Saline 2 liters over one hour** (drops temperature by 1.2°C); urinary lavage, peritoneal lavage, CPB, dialysis, invasive cooling catheters exist (not available at LLUMC as of 8/28/12)