Hot Topics in Hyperthermia

A Midday Symposium and Live Webinar conducted at the 52nd ASHP Midyear Clinical Meeting and Exhibition

Monday, December 4, 2017
11:30 a.m. – 1:00 p.m.
Orlando, Florida

Agenda

11:30 a.m. – 11:40 a.m.
Welcome and Introduction
Daniel P. Hays, Pharm.D., BCPS, FASHP

11:40 a.m. – 12:50 p.m.
Hot Topics in Hyperthermia: Managing this Life-threatening Condition
Daniel P. Hays, Pharm.D., BCPS, FASHP, and Frank LoVecchio, D.O., M.P.H., ABMT, FACEP

12:50 p.m. – 1:00 p.m.
Faculty Discussion and Audience Questions

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Hot Topics in Hyperthermia

Learning Objectives

After participating in this application-based educational activity, participants should be able to

• Review factors that predispose people to developing hyperthermic conditions
• Explain the morbidity and mortality of hyperthermia
• Review current strategies for preventing, recognizing, and treating hyperthermic conditions
• Using patient cases, illustrate best practices in the management of hyperthermic conditions

DH

The best treatment for hyperthermia is _____.

a. Dantrolene sodium
b. Rapid cooling
c. Antibiotics for presumed sepsis
d. Acetaminophen
e. Succinylcholine

DH

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Hot Topics in Hyperthermia

Hyperthermia: Definition

• Elevation of core body temperature above the normal range of 36-37.5°C (96.8-99.5°F) due to failure of thermoregulation
• Hyperthermia DOES NOT equal fever!

Hyperthermia

• The most common causes of severe hyperthermia (>40°C or 104°F) are
  – Heat stroke
  – Neuroleptic malignant syndrome
  – Malignant hyperthermia

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Physiology

• Body temperature is maintained within a narrow range by balancing heat load with dissipation
• Body heat load results from both metabolic processes and the environment
• As core temperature rises, the anterior hypothalamus stimulates sweating and cutaneous vasodilation

Physiology

• Evaporation is the principal mechanism of heat loss, but this becomes ineffective when humidity is >75%
• Other methods of heat dissipation
  – Radiation
  – Conduction
  – Convection

  Ineffective when environmental temperature exceeds skin temperature

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**Physiology**

- Core temperature elevation $\rightarrow$ $\uparrow$ O$_2$ consumption and metabolic rate $\rightarrow$ hyperpnea and tachycardia
- $>42^\circ$C (108°F), oxidative phosphorylation becomes uncoupled, and a variety of enzymes cease to function
- Hepatocytes, vascular endothelium, and neural tissue are most sensitive to these effects, but all organs may be affected
- As a result, patients are at risk of multiorgan system failure

**Thermoregulatory Effectors**

- Sweating and peripheral vasodilation are the major mechanisms by which heat loss can be accelerated
- In a warm environment, evaporation of sweat from the skin is the most important
- Heat loss from skin by convection and radiation is maximized to facilitate sweating

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Sweat

- Most glands producing “thermal sweat” are eccrine glands
- Individuals exercising in hot environments commonly lose 1 to 2 L/hr of sweat
  - Loss of 4 L/hr for short periods is possible

Sweat

- Cooling is best achieved by evaporation from the body surface
  - Sweat dripping from skin does not cool body
  - Sweat evaporated from clothing is less efficient
- Each liter of completely evaporated sweat consumes 580 kcal of heat
- As humidity increases, evaporative cooling decreases
Which of the following drug classes decreases sweating?

a. Selective serotonin-reuptake inhibitors
b. Antihistamines
c. Carbonic anhydrase inhibitors
d. Opioids

Minor Heat Illness

- Heat cramps
- Heat syncope
- Heat exhaustion
Heat Cramps

- Brief, intermittent, and often severe muscular cramps occurring typically in muscles that are fatigued by heavy work
- Occur most commonly during the first days of work in a hot environment and develop in persons who produce large amounts of thermal sweat and subsequently drink copious amounts of hypotonic fluid
- Appear to be related to salt deficiency

Warning Signs of Heat Syncope

- Fainting – in effort to cool itself, blood vessels dilate such that blood flow to brain is reduced
- Warning signs
  - Tunnel vision
  - Vertigo
  - Nausea
  - Diaphoresis
  - Weakness
- Adequate education prevents many serious injuries
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Heat Exhaustion

- Volume depletion that occurs under conditions of heat stress
- Types: water depletion and salt depletion
- *Water depletion* heat exhaustion results from inadequate fluid replacement by individuals working in a hot environment
  - “Voluntary dehydration” results in progressive hypovolemia

Not Enough Salt

- *Salt depletion* heat exhaustion takes longer to develop than the water depletion form
  - Occurs when large volumes of thermal sweat are replaced by water with too little salt
  - Differs from heat cramps in that systemic symptoms occur
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Heat Exhaustion: Clinical Features

- Weakness
- Fatigue
- Frontal headache
- Impaired judgment
- Vertigo
- Nausea and vomiting
- Muscle cramps
- Orthostatic dizziness and syncope

Heat Exhaustion Diagnosis

- Vague malaise, fatigue, headache
- Core temperature often normal; if elevated, usually <40°C (104°F)
- Mental function essentially intact; no coma or seizures
- Tachycardia, orthostatic hypotension, clinical dehydration (may occur)
- Other major illness ruled out
- If in doubt, treat as heat stroke
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The Liver Knows All...

- Elevations of hepatic transaminases to several thousand units can be seen in patients with heat exhaustion or healthy runners after a marathon
  - In patients with heat stroke, such levels are usually in the tens of thousands after 24 hours

Management

- Heat exhaustion is primarily a volume depletion problem
  - Rapid recovery generally follows fluid administration
- Decisions regarding the type of fluid and electrolyte replacements should be based on serum electrolyte measurements and the estimation of hydration status based on clinical and laboratory parameters
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Management

• In mild cases, recommend rest in a cool environment and consumption of oral electrolyte solution
• Patients with significant volume depletion or electrolyte abnormalities require IV fluids
• If the patient is orthostatic, normal saline should be administered until hemodynamically stable

Management

• Free water deficits should be replaced slowly over 48 hours
• DO NOT decrease serum osmolality more than 2 mOsm/L/hr
• Rapid correction of hypernatremia is associated with seizures caused by cerebral edema
Case 1 and Case 1a

- A 52-year-old woman with confusion and lethargy is brought to the emergency department (ED) by her spouse. They were running a marathon.
  - Exam: Sweating, HR 140 bpm, BP 98/64 mmHg
  - She is slow to answer questions and confused.
- What is your diagnosis and treatment plan?

Upon discharge the husband

- Asked about his rash x 2 weeks, worse today
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Major Heat Illness

- Heat stroke
  - Classic
  - Exertional

Heat Stroke

- Body temperature rises due to failure of homeostatic thermoregulatory mechanisms
- This failure results in elevation of body temperature to extreme levels, usually >40.5°C (105°F), producing multisystem tissue damage and organ dysfunction
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Heat Stroke

- Core body temperature >40.5°C (105°F) with associated CNS dysfunction in the setting of a large environmental heat load that cannot be dissipated
- Complications
  - Acute respiratory distress syndrome (ARDS)
  - Disseminated intravascular coagulation (DIC)
  - Renal failure
  - Hepatic failure
  - Hypoglycemia
  - Rhabdomyolysis
  - Seizures

Tissue Damage Depends on

- Exposure time
- Body temperature
- Work load
- Tissue perfusion
- Individual factors

DH CNS = central nervous system

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Heat Stroke Diagnosis

- Exposure to heat stress, endogenous or exogenous
- Signs of severe CNS dysfunction (coma, seizures, delirium)
- Core temperature usually >40.5°C (105°F), but may be lower
- Dry, hot skin common, but sweating may persist
- Marked elevation of hepatic transaminases

Classic (Nonexertional) Heat Stroke (CHS)

- Affects individuals with underlying chronic medical conditions that either impair thermoregulation or prevent removal from a hot environment
- Conditions include
  - Cardiovascular disease
  - Neurologic or psychiatric disorders
  - Obesity
  - Anhidrosis
  - Extremes of age
  - Use of anticholinergic agents or diuretics
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Comorbidities Can Worsen...

• Victims of CHS commonly suffer from chronic diseases, alcoholism, or schizophrenia, which predispose to heat-related illness
  – Often are taking medications that impair ability to tolerate heat
• Sweating is completely absent in the majority of patients with CHS

Poor Outcomes Associated With

• Advanced age
• Hypotension
• Altered coagulation status
• Endotracheal intubation on arrival at ED

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Exertional Heat Stroke (EHS)

Occurs in young, otherwise healthy individuals engaged in heavy exercise during periods of high ambient temperature and humidity

- Findings
  - Cutaneous vasodilation
  - Tachypnea
  - Rales due to noncardiogenic pulmonary edema
  - Excessive bleeding due to DIC
  - Altered mentation or seizures

- Labs
  - Coagulopathy
  - Acute renal failure (ARF)
  - Elevated LFTs due to acute hepatic necrosis
  - Respiratory alkalosis
  - Leukocytosis with WBC counts as high as 30,000-40,000/mm³

LFT = liver function test
WBC = white blood cell


Exertional Heat Stroke

- Rhabdomyolysis and ARF, rarely seen in patients with CHS, are common in patients with EHS
- Sweating is present in half the cases of EHS
- Hypoglycemia
- Coagulopathy
- Hyponatremia with serum sodium levels <130 mmol/L (neurologic symptoms or seizures)
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Exertional Heat Stroke

• Heavy physical exertion in hot climates produces acidic and maximally concentrated urine, which can result in acute oliguric renal failure when combined with hypotension and myoglobinuria
• Cocaine use is also associated with rhabdomyolysis and hyperthermia

Exertional Heat Stroke

• Diarrhea, probably caused by intense splanchnic vasoconstriction, is commonly seen
• Cooling aggravates the diarrhea, creating an unpleasant treatment problem
• Pancreatitis has been suspected
Diagnosis

• Temperature
  – Oral temperature is affected by mouth breathing and is a poor approximation of the core temperature
  – Rectal temperature is less variable but responds to changes in core temperature slowly

Get The Right Temp

• Temperature probes inserted 15 cm into the rectum offer continuous monitoring of temperature and less variability compared with periodic oral readings
• Although slower to respond to changes in core temperature than tympanic temperature readings, rectal measurements are not biased by head skin temperature
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Cooling

- Immediate cooling is the cornerstone of treatment
  - Must be initiated as soon as possible, in conjunction with initiation of stabilizing treatment
- Mortality increases significantly when cooling is delayed

Evaporative Cooling

- Evaporative cooling is the most widely used cooling method
- Combination of atomized tepid water at 40°C from a spray bottle and standing fans cool at rates comparable to both body cooling unit and immersion in ice water

**Cooling: Water Immersion**

- Immersion in ice water results in a rapid reduction of core temperature to <39°C within 10-40 minutes.
- When the body temperature reaches 39°C, cooling measures should be discontinued to avoid hypothermic overshoot.
- Continuous monitoring is necessary to maintain the core temperature at 37-38°C.


**Cooling: Alternative Modalities**

- Cardiopulmonary bypass with a heat exchanger has been successfully used in the treatment of malignant hyperthermia.
- Peritoneal dialysis with cold fluids is untested in humans.
- Cold-irrigant gastric or rectal lavage will not provide significant heat exchange when used as primary cooling modality.
**Hot Topics in Hyperthermia**

### Fluid Resuscitation

- Parenteral fluid requirements are modest in some cases, averaging 1200 mL of isotonic crystalloid solution in first 4 hours.
- Pulmonary edema occurs in patients with heat stroke and can be exacerbated by overzealous fluid administration.
- Use of a CVP catheter to monitor fluid resuscitation may be deceptive.

_Walls R et al. Rosen’s emergency medicine: concepts and clinical practice. 9th ed.; 2018._

### Blood Pressure in Heat Stroke

- Hypotension is common in patients with heat stroke.
  - Peripheral vasodilation can result in high-output cardiac failure.
- Blood pressure usually rises with cooling.

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Blood Pressure

• Patients can exhibit hypodynamic responses with low cardiac index, elevated CVP, hypotension, and cyanosis
• Skin color of patients with hyperdynamic circulation is initially pink
• Skin color can help in identifying patients who may respond to catecholamines

Dysrhythmias

• A variety of tachyarrhythmias commonly occur during heat stroke
  – Usually resolve with cooling
  – Avoid electrical cardioversion until myocardium is cooled
• Use of α-adrenergic agents, such as norepinephrine, is contraindicated
  – Cause vasoconstriction without improving cardiac output or perfusion
  – Decrease cutaneous heat exchange
  – May enhance ischemic renal and hepatic damage
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Things to Consider...

- Avoid anticholinergic agents
- Avoid large doses of acetaminophen, which can result in further hepatic damage
- Avoid antipyretic agents
  - Salicylates cause uncoupling of oxidative phosphorylation and worsen coagulopathies
- Efficacy of dantrolene not established for treating heat stroke

DH


Dantrolene and Heat Stroke

- Several published case reports and studies comparing dantrolene with conventional cooling methods
  - EHS, n = 20: cooling rate higher with dantrolene
  - CHS, n = 53: no difference in cooling rate or length of stay
  - Limitations: Small studies, confounding variables, possibly inadequate doses
- In July 2017, FDA declined to approve Ryanodex (dantrolene sodium for injectable suspension) for indication to treat exertional heat stroke in conjunction with external cooling methods
  - Requested additional clinical trial


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Adjuncts with Caveats

- Cooling modalities that drastically lower skin temperature may induce violent shivering
  - Increase metabolic heat production and may impede cooling
- Chlorpromazine (25 mg IV) can be efficacious
  - Has anticholinergic properties that can interfere with sweating and cause hypotension

Keep Them Calm and Cool

- Many patients with heat stroke are agitated during the initial cooling period
  - Short-acting benzodiazepines can be used for sedation and to control seizures
- Barbiturates are less desirable for treatment of seizures during cooling because metabolism is altered by hepatic dysfunction
Medication-induced Heat Illness

- Drug-induced heat illness is an important consideration, particularly anticholinergic poisoning
- Differentiating between heat stroke and anticholinergic poisoning may be difficult because both produce hyperpyrexia, hot and dry skin, tachycardia, and abnormal mental status


Differentiating Between Heat Stroke and Anticholinergic Toxidromes

- Constricted pupils are present in many patients with heat stroke
- Mydriasis should be present in patients with anticholinergic poisoning, and its absence argues strongly against this diagnosis
- Typhoid fever, typhus, delirium tremens, and hypothalamic hemorrhage are to be considered in differential diagnosis
Hot Topics in Hyperthermia

Case 2

- A 45-year-old man presents in a coma. He has mumbling speech. Nurses report he has a “psych” and “drug” history.
- What further history is important?
- What exam findings would be important?

Case 2

- Rectal temperature 104.5°F
- Pupils dilated
- Sweating at hands, otherwise none
- Mild muscle rigidity and clonus throughout
- No signs of infection
# Hot Topics in Hyperthermia

## The Differential Is On

<table>
<thead>
<tr>
<th>Clinical Findings</th>
<th>Malignant Hyperthermia</th>
<th>Neuroleptic Malignant Syndrome</th>
<th>Psychomotor Overdose</th>
<th>Anticholinergic Toxicity</th>
<th>Serotonin Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increased CO₂ production</td>
<td>Bradykinesia/akinesia</td>
<td>Agitation, seizures</td>
<td>“Hot as a hare, red as</td>
<td>Diaphoresis</td>
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<td></td>
<td>Muscle rigidity (rigor mortis-like)</td>
<td>Muscle rigidity (“lead pipe”)</td>
<td>Rhabdomyolysis</td>
<td>a beet, dry as a bone,</td>
<td>Mydriasis</td>
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<td></td>
<td>Hyporeflexia</td>
<td>Autonomic instability</td>
<td>Tachycardia</td>
<td>blind as a bat, mad as</td>
<td>Hyperkinesia</td>
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<td></td>
<td>Tachycardia</td>
<td></td>
<td>Heightened “fight or flight” response</td>
<td>a hatter”</td>
<td>Hyperreflexia</td>
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<td>Mydriasis</td>
<td>Urinary retention</td>
<td>Hyperactive bowel sounds</td>
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<td>Hypoactive bowel sounds</td>
<td>Tachycardia</td>
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<tr>
<td>Onset Time</td>
<td>Immediate</td>
<td>Slow onset - ~7 days</td>
<td>Immediate</td>
<td>Immediate</td>
<td>Within 24 hr</td>
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<tr>
<td>Classically Implicated Medications</td>
<td>Pharmacogenetic</td>
<td>Phenothiazines, butyrophenones, thioxanthenes</td>
<td>Cocaine, amphetamines, phencyclidine</td>
<td>Antihistamines</td>
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<td>Halogenated inhalational anesthetic agents</td>
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<td></td>
<td>Depolarizing neuromuscular agents</td>
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<tr>
<td>Specific Treatment</td>
<td>Dantrolene</td>
<td>Bromocriptine (dantrolene)</td>
<td>Benzodiazepines</td>
<td>Physostigmine</td>
<td>Cyproheptadine</td>
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Have you ever been involved in the care of a patient with malignant hyperthermia?

- a. Yes
- b. No
- c. Not applicable, not in practice
Malignant Hyperthermia

- Rare genetic disorder manifesting after certain anesthetics: halothane and succinylcholine
  - Mutations in the RYR-1 gene located on chromosome 19q13.1
  - Incidence between 1:5,000 – 1:100,000
- Onset usually within 1 hour of anesthesia administration, rarely delayed up to 10 hours
- 50% of cases are inherited as autosomal dominant, rest are inherited in different patterns


Malignant Hyperthermia

- Early clinical findings include muscle rigidity, sinus tachycardia, increased CO₂ production, and skin cyanosis with mottling
- Marked hyperthermia (up to 45°C [113°F]) occurs minutes to hours later
  - Core body temperature tends to rise 1°C every 5-60 minutes
Malignant Hyperthermia Manifestations

- Hypotension
- Complex dysrhythmias
- Rhabdomyolysis
- Electrolyte abnormalities
- DIC
- Mixed acidosis

Diagnostic Evaluation of Malignant Hyperthermia

- Elevated rectal temperature
- Sinus tachycardia, tachypnea, widened pulse pressure, hypotension
- Chest x-ray may demonstrate pulmonary edema
- Dysrhythmia, conduction disturbances, nonspecific ST-T wave changes, or heat-related myocardial ischemia or infarction

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Hot Topics in Hyperthermia

Look at the Whole Picture

• Labs: CBC, coagulation studies, creatine kinase, and hyperphosphatemia myoglobinuria
• Myoglobinuria should be suspected in a patient who has a brown urine supernatant that is heme-positive, and clear plasma
• Toxicologic screening
• Head CT and lumbar puncture if CNS etiologies suspected

Look at the WHOLE Picture
Hot Topics in Hyperthermia

Look at the WHOLE Picture

Timing is everything

• In cases presenting >1 hr post anesthesia, may NOT be malignant hyperthermia

Malignant Hyperthermia Management

• Dantrolene administration is mainstay of treatment of malignant hyperthermia and should be initiated as soon as possible
  – In cases treated >50 min after symptom onset, rate of complications approaches 100%
  – Most common complication is renal dysfunction ~15%


TREAT THEM!

• Mortality of the fulminant syndrome has fallen from 70% to less than 10% when treated with dantrolene
• Dantrolene is a nonspecific skeletal muscle relaxant that acts by blocking the release of calcium from the sarcoplasmic reticulum, and thus decreases the myoplasmic concentration of free calcium and diminishes the myocyte hypermetabolism that causes clinical symptoms

Hot Topics in Hyperthermia

Dantrolene

• Out with the old and in with the new
• Supply
• The Joint Commission
• Anesthesia societies


Dantrolene Sodium for Injection

• Available since 1979, generics available
• Time
• Solubility
• Administration
• Cost


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Dantrolene Sodium for Injectable Suspension (Ryanodex)

- Solubility
- Volume
- Administration
- Cost

Ryanodex (dantrolene sodium) for injectable suspension prescribing information. 2014 Jul.

Dantrolene Dosing

- Malignant Hyperthermia Association of the United States (MHAUS) recommendation
  - Give 2.5 mg/kg rapid IV push
  - Repeat as frequently as needed until symptoms abate
    - >10 mg/kg may be required, but consider alternative diagnoses if no symptom resolution
- Manufacturers’ prescribing information suggests initial minimum dose of 1 mg/kg or maximum cumulative dose of 10 mg/kg, repeat if needed starting with 1 mg/kg

**Need For Treatment May Persist**

- After dantrolene administration, monitor body temperature for 48-72 hr
  - 25% of patients can experience increase in temperature
- After initial response, continue dantrolene orally using 4 to 8 mg/kg per day, in four divided doses for 3 days


**Consider Testing When Feasible**

- Muscle contracture test: caffeine halothane contracture test (CHCT)
  - Sensitivity: close to 100% (false negatives are rare)
  - Specificity: ~80% (~20% false positives)
- Genetic testing (ryanodine receptor [RYR1] gene sequencing)
  - Presence of causative mutation* in RYR1 gene is diagnostic for MH susceptibility

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Malignant Hyperthermia Treatment Cart

- Recommended by MHAUS and TJC
  - 36 20-mg vials of dantrolene sodium for injection
  - 3 250-mg vials of dantrolene sodium for injectable suspension (Ryanodex)

- Dantrolene sodium for injection vs. supportive care
  - 33 lives saved per year
  - Cost effectiveness ~ $200k/life saved


Case 3

- A 60-year-old man with a history of schizophrenia was working outdoors and is brought to your ED
- He is unconscious and needs to be intubated
- No further medical history available
- Temp 106°F, HR 145 bpm, BP 110/60 mm/Hg
  - What medications are preferred?
  - Should be avoided?
Case 3 (continued)

- Despite cooling, the patient still has an elevated temperature
- Would you consider adjunctive medications, such as dantrolene? Cyproheptadine? Bromocriptine?
- What labs should be performed?
- What fluids should be considered?

The best treatment for hyperthermia is _____.

a. Dantrolene sodium
b. Rapid cooling
c. Antibiotics for presumed sepsis
d. Acetaminophen
e. Succinylcholine
Hot Topics in Hyperthermia

Victims of heat stroke usually have ___.

a. Lack of sweating
b. Altered mentation
c. Current medication use
d. Muscle rigidity
e. Prior history of heat illness

Key Takeaways

- Supportive care is paramount in treating heat illness, and pharmacologic adjuncts are sometimes helpful
- Medications and drugs are a common and potentially avoidable cause of hyperthermia
- Dantrolene should be considered if malignant hyperthermia is suspected
Hot Topics in Hyperthermia

What will you do as a follow-up to today’s program?

• Share info about management of hyperthermic emergencies with colleagues
• Review my institution’s policy related to managing hyperthermic emergencies
• Participate in staff training to ensure all staff are prepared to respond to hyperthermic emergencies
• Ensure an adequate supply of dantrolene within my institution
• Consider potential effects of medications in patients with predisposition to hyperthermic conditions
• Review medical records or case reports of patients with hyperthermia and discuss strategies to improve care

Useful Resources: Heat Stroke

Hot Topics in Hyperthermia

Useful Resources: Malignant Hyperthermia

- Malignant Hyperthermia Association of the United States (MHAUS). www.mhaus.org

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Frank LoVecchio, D.O., M.P.H., ABMT, FACEP, is Vice-Chair and Research Director for the Maricopa Medical Center Department of Emergency Medicine in Phoenix, Ariz., and has been an emergency medicine physician for over a decade. He also serves as Professor in the Departments of Emergency Medicine, Pharmacology, and Internal Medicine at University of Arizona College of Medicine and Co-Medical Director at Banner Poison and Drug Information Center, both located in Phoenix.

After earning his Doctor of Pharmacy degree at the University of Minnesota, Dr. Hays built his practice in Rochester, N.Y., where he was the lead pharmacist on a grant from the Agency for Healthcare Research and Quality (AHRQ) to study the effect of a pharmacist on patient care in the emergency department. He contributed to two projects that were awarded ASHP Best Practice Awards. He has served on the Educational Steering Committee of the ASHP Section of Clinical Specialists and Scientists and as Chair for the Section Advisory Group on Emergency Care. He has written numerous chapters for text books in both pharmacy and emergency medicine practice related to the dynamics of emergency pharmacy. Dr. Hays is a Board Certified Pharmacotherapy Specialist and Fellow of ASHP.

Dr. LoVecchio earned his Doctor of Osteopathic Medicine degree at New York College of Osteopathic Medicine in Westbury, N.Y., and later completed a Master in Public Health degree from Harvard School of Public Health in Boston. He is board certified in addiction medicine, medical toxicology, medical forensics, and emergency medicine.

Dr. LoVecchio is a medical team leader for Arizona Task Force One for the Federal Emergency Medical Assistance (FEMA) program. He is the principal investigator (PI) for the Infectious Disease Network (IDNet) studies. He has also served as a site investigator for grants from National Institutes of Health (NIH) awarded through the Emergency Medicine Network (EMNet). In addition, Dr. LoVecchio served as a site PI for the ED-SAFE grant, which was a multicenter NIH grant to predict outcomes, behaviors, and risk reduction in acutely depressed patients.

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