Project: Ghana Emergency Medicine Collaborative

Document Title: Environmental Hyperthermia

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Environmental Hyperthermia

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Clinical Professor of Emergency Medicine
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Bethesda, Maryland, U.S.A.
Heat-Related Illnesses: History

- Death reported from field labor: (Old Testament, II Kings 4:18-20)
- Roman Army in Arabia decimated by heat: 24 B.C.
- King Edward & Crusaders lost battle against Arabs: 3rd Crusade
- Heat wave in Peking, China: 11,000 deaths: 1743
- 123 British troops died in Black Hole of Calcutta: 1856
- U.S. Army: 125 reported deaths in basic training: 1941-44
- 820 U.S. reported deaths / "heat wave year" (1952-55, 1966)
- Several thousand deaths in heat wave in Greece/Italy: 1987
- ? > 10,000 deaths in France in 2003
Heat-Related Illness: Incidence

- About 4000 deaths / year in U.S.A.
- Second leading cause of death in amateur athletes (head trauma is first)
- Can cause mass numbers of deaths during "heat wave"
- Some cases mistakenly attributed to heart disease
Controversies or Unclear Points

• Environmental Hyperthermia
  • What is the most effective central cooling method?
  • What is the best method to limit shivering?
  • Are any medications helpful as adjunct therapy?
Hyperthermia: Causes

- Infections
- Drug reactions
- Neuroleptic malignant syndrome
- Malignant hyperthermia
- Environmental
Mechanisms of Heat Transfer

- **Conduction (2 %)**
  - Transfer of heat by direct physical contact
- **Convection (1 to 40 %, depends on wind velocity)**
  - Transfer of heat to air / water vapor circulating around body
- **Radiation (30 to 65 %)**
  - Heat transfer by infrared waves
- **Evaporation (10 to 80 %)**
  - Conversion of liquid sweat to vapor (0.58 Kcal / cc of H2O evaporated)
Mechanisms of heat transfer from the skin
Predisposing Factors to Heat-Related Illness (Excluding Drugs)

- Exogenous heat gain
- Endogenous heat gain
- Impaired heat dissipation
Sources of Exogenous Heat Gain

- Closed spaces (locked cars, etc.)
- Bright sunshine (150 Kcal/hr)
- Hot tubs
- Lack of air conditioning
- Hot soil (can transmit heat thru shoes)
Sources of Endogenous Heat Gain

- Exercise (300 to 900 Kcal / hr)
- Agitation / restraint
- Fever / infection
- Hypermetabolism / hyperthyroidism
Baseline Energy Metabolism

- Basal metabolism (adult male)
  - 65 to 85 Kcal/hr or 50 to 60 Kcal/hr/m² body surface area
- For every 100 calories produced:
  - O₂ consumption is 20 liters
  - CO₂ production is 20 liters
  - 100 ml water is needed (for sweat and respiratory loss)
## Energy Expenditure During Different Activities

<table>
<thead>
<tr>
<th>Activity</th>
<th>Kcal / hr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LABOR</strong></td>
<td></td>
</tr>
<tr>
<td>Shoveling</td>
<td>570</td>
</tr>
<tr>
<td>Hand sawing</td>
<td>450</td>
</tr>
<tr>
<td>Pushing wheelbarrow</td>
<td>300</td>
</tr>
<tr>
<td>Carrying bricks</td>
<td>216</td>
</tr>
<tr>
<td>Light assembly work</td>
<td>108</td>
</tr>
<tr>
<td>Typing</td>
<td>84</td>
</tr>
</tbody>
</table>
### Energy Expenditure During Different Activities (cont.)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Kcal / hr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPORTS &amp; RECREATION</strong></td>
<td></td>
</tr>
<tr>
<td>Football</td>
<td>102</td>
</tr>
<tr>
<td>Wrestling</td>
<td>114</td>
</tr>
<tr>
<td>Hockey</td>
<td>173</td>
</tr>
<tr>
<td>5-mile run</td>
<td>360</td>
</tr>
<tr>
<td>Walking (4 mph)</td>
<td>340</td>
</tr>
<tr>
<td>Basketball</td>
<td>344</td>
</tr>
<tr>
<td>Swimming</td>
<td>660</td>
</tr>
</tbody>
</table>

*Calorie expenditure per event given as increment above basal requirement*
Causes of Impaired Heat Dissipation

- High environmental temperature
- High environmental humidity
- Lack of acclimatization
- Excessive clothing
- Obesity
- Diabetes / autonomic neuropathy
- Sweat gland dysfunction (dehydration, cystic fibrosis, ectodermal dysplasia, scleroderma, extensive scars)
- Previous heatstroke
Hyperthermia: Types of Causative Drug Reactions or Effects

- Hypersensitivity
- Hypermetabolism
- Impaired thermoregulation
- Impaired heat dissipation
- Impaired cardiovascular compensation
- Direct pyrogens
Representative Drugs Causing Hyperthermia

- **Hypersensitivity**
  - Antibiotics
  - Antiarrhythmics
  - NSAID's
  - Phenytoin
- **Pyrogens**
  - Antibiotics
  - Cancer chemo Rx
- **Hypermetabolism**
  - Salicylates
  - Thyroid
- **Impaired Heat Dissipation or Compensation**
  - Phenothiazines
  - Ethanol
  - Diuretics
  - Laxatives
  - Beta blockers
- **Muscle Hyperactivity**
  - Cocaine
  - Amphetamines
  - Phencyclidine
  - MAO inhibitors
Children at Greater Risk of Heat Stress

- Obesity
- Febrile state
- Cystic fibrosis
- Diabetes mellitus
- Diabetes insipidus
- Ectodermal dysplasia
- GI infection
- Chronic heart failure
- Caloric malnutrition
- Anorexia nervosa
- Mental deficiency
- Peripheral vascular disease
Environmental Causes of Hyperthermia

- Mild forms of heat illness:
  - Heat edema
  - Heat cramps
  - Heat syncope
  - Prickly heat

- Heat Exhaustion:
  - Sodium depletion type
  - Water depletion type

- Heatstroke:
  - Classic
  - Exertional
Treatment of Mild Forms of Heat Illness

- Heat edema (usually only hands, feet, ankles)
  - Elevation, support hose (do not use diuretics)
- Heat cramps (due to Na depletion)
  - Cooling, PO fluids containing some salt
- Heat syncope (usually due to mild fluid depletion)
  - Rest, PO fluids
- Prickly heat
  - Skin cleansing, loose clothing, antibiotics if pustular
Acclimatization to Heat Exposure

- Improved metabolic efficiency (increased aerobic metabolism, decreased heat wasted in making ATP)
- Sweating promoted at lower core temperature
- Rate of sweating increases from 1.5 to 3 liters / hr
- Stroke volume increases, cardiac output increases, heart rate decreases
- Aldosterone secretion increases (Na in sweat decreases from 30 to 5 meq / liter)
- Potassium retention
Acclimatization to Heat Exposure

- Gradual: takes 10 to 20 days
- Full tolerance may take 2 months
Heat Exhaustion: Sodium Depletion Type

- **Etiology**
  - Usually in unacclimatized
  - Usually young age
  - Exercise in hot environment
  - Mildly inadequate fluid intake & moderate inadequate Na intake
Heat Exhaustion: Sodium Depletion Type

- **Sx**: + febrile, headache, weakness, fatigue, nausea, diarrhea, cramps, + hypotension / tachycardia

- **Rx**: Rest, cooling, fluids (PO or IV) with sodium
Heat Exhaustion: Water Depletion Type

- Etiology: Usually elderly with inadequate free water intake; can lead to heatstroke
- Sx: Febrile, thirst, weakness, confusion
- Rx: Cooling, rest, hypotonic fluids; if elderly, may need hospital admission
Heatstroke: Items Required for Diagnosis

- Exposure to heat stress: internal or external
- Elevated body temperature (usually > 40 °C)
- Major CNS dysfunction (bizarre behavior, seizures, coma, etc.)
- Usually tachypneic, tachycardic, hypotensive
- Usually anhydrotic
Heatstroke

- A true emergency
- Rapid dx and Rx essential
- Two types:
  - Classic
  - Exertional
Classic Heatstroke

- Usually elderly
- Occurs after exposure to heat for $\geq 1$ week
- Mortality 70% untreated, 10 to 20% treated
Exertional Heatstroke

- Usually younger age
- Usually after heavy exertion
- May still have sweating
- May have rhabdomyolysis / renal failure
- Mortality 30% untreated, < 10% treated
Table 3: Comparison of Classic and Exertional Heatstroke

<table>
<thead>
<tr>
<th></th>
<th>Classic</th>
<th>Exertional</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of patients</strong></td>
<td>Elderly</td>
<td>Younger</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td>Epidemic (heat waves)</td>
<td>Sporadic</td>
</tr>
<tr>
<td><strong>Predisposing diseases</strong></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Sweating</strong></td>
<td>Absent</td>
<td>Often present</td>
</tr>
<tr>
<td><strong>Acid/base disturbance</strong></td>
<td>Resp. alkalosis</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td><strong>Renal failure</strong></td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Rhabdomyolysis</strong></td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Disseminated intravascular coagulation</strong></td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Hyperuricemia</strong></td>
<td>Mild</td>
<td>Marked</td>
</tr>
</tbody>
</table>
Heatstroke: Differential Diagnosis

• Meningitis / encephalitis: do LP if not sure
• Cerebral falciparum malaria
• CVA / traumatic intracranial bleed
• DKA with infection
• Thyroid storm
• Neuroleptic malignant syndrome*
• Malignant hyperthermia*

*These should show muscle rigidity
Heatstroke: Emergency Treatment Protocol

- Airway management: intubate if comatose; High flow O2 for all
- Large bore IV and rapid bolus 500 to 1000 cc NS
- Draw blood (CBC, lytes, BUN, glucose, creatinine, PT, PTT, platelets, lactate, calcium, LFT's, CPK, ABG)
- Rapid external cooling: fully undress patient; ice bath with skin massage (Hubbard tank) or cool skin soaks and fans
- Foley and NG tube insertion: iced NG lavage
Heatstroke: Emergency Treatment Protocol (cont.)

- Monitor core temp. (high rectal probe or esophageal); stop external cooling when core temp. ≤ 102°F
- Monitor for hypotension, hypocalcemia, arrhythmias, seizures, acidosis, ARF
- Admit to ICU
- Acetaminophen (do not use aspirin)
- Consider low dose phenothiazine (chlorpromazine 25 mg IV) or diazepam IV to promote heat loss and lessen shivering
Heatstroke:
Early Complications & Treatment

- Shivering: generates heat so should be suppressed with chlorpromazine or thiopental
- Hypotension: usually Rx with increased IV fluids
- Rhabdomyolysis / renal failure: usually only need Rx with fluids but may need bicarb + mannitol
- Acidosis
- Hypocalcemia
- Hypoglycemia: Rx with IV glucose
- Seizures: standard Rx with diazepam or lorazepam, phenytoin
Heatstroke: Late Complications

- DIC
- Hepatic necrosis / failure
- Renal failure with hyperkalemia
- Acute MI; reported but uncommon
- Muscle compartment syndrome
- CNS damage
- Permanently impaired thermoregulatory control: susceptible to heatstroke again under even milder conditions
# Heatstroke: Mortality Reports

<table>
<thead>
<tr>
<th>Setting</th>
<th>Type</th>
<th>Treatment</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 military series</td>
<td>exertional classic mixed</td>
<td>ice bath ice bath BCU</td>
<td>0 / 66 14% 11%</td>
</tr>
<tr>
<td>Heat wave (U.S.)</td>
<td>mixed</td>
<td>ice bath</td>
<td>14%</td>
</tr>
<tr>
<td>Mecca pilgrimage (1979)</td>
<td>mixed</td>
<td>KSU bed</td>
<td>11%</td>
</tr>
<tr>
<td>Mecca pilgrimage (1986)</td>
<td>classic exertional</td>
<td>fan, ice packs ice packs only</td>
<td>0 / 25 7% 24%</td>
</tr>
<tr>
<td>1986 U.S.A. series</td>
<td>classic</td>
<td>ice packs, sheets</td>
<td>21%</td>
</tr>
<tr>
<td>younger patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1967 series,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1977-1983 Louisville, KY</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Heatstroke: Rate of Cooling Effect on Mortality

<table>
<thead>
<tr>
<th>Author</th>
<th>Mortality Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vicario</td>
<td>33% if 1 hr. temp. &gt; 38.9°C</td>
</tr>
<tr>
<td></td>
<td>15% if 1 hr. temp. &lt; 38.9°C</td>
</tr>
<tr>
<td>Yaqub</td>
<td>18% if &gt; 1 hr. to 38.5°C</td>
</tr>
<tr>
<td></td>
<td>5% if &lt; 1 hr. to 38.5°C</td>
</tr>
</tbody>
</table>
Heatstroke: Rapid Body Cooling Techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Reported Cooling Rate (°C / min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ice water immersion</td>
<td>0.21 to 0.23</td>
</tr>
<tr>
<td>BCU (net / spray)</td>
<td>0.11 to 0.17</td>
</tr>
<tr>
<td>Iced gastric lavage</td>
<td>0.08 to 0.11</td>
</tr>
<tr>
<td>High freq. jet ventilation</td>
<td>0.06</td>
</tr>
<tr>
<td>Dantrolene treatment</td>
<td>0.04</td>
</tr>
<tr>
<td>Spontaneous (no treatment)</td>
<td>0.03 to 0.06</td>
</tr>
</tbody>
</table>
Khogali's Objections to Ice Water Immersion (Favoring Use of BCU)

• Peripheral vasoconstriction shunting blood from skin ( ? rise in core temp.)
• Induction of shivering : raises heat production
• Extreme discomfort to patient
• Difficulty performing CPR
• Difficulty monitoring VS
• "Unpleasant and unhygienic" conditions if emesis or diarrhea occur
Other Cooling Methods

• Groin, neck, axillae, or scalp ice packs
  • Limited effectiveness
• Iced peritoneal lavage
  • Only a few case reports
• Cold O2 / Cold IV fluids
  • Minimal heat exchange
• Iced enemas
  • Minimal heat exchange
• Cardiopulmonary bypass
  • Effective but time consuming to set up
Probably the best cooling method is water spray and fans with the patient on an open stretcher.
Heatstroke: Prognosis (Px)

- If coma < 3 to 4 hrs.: px good
- If coma > 10 hrs.: likely fatal
- SGOT < 1000 in first 24 hr.: px good
- SGOT > 1000 in first 24 hr.: likely fatal
- Temperature > 42.2 °C on admission: worse px but can have complete recovery
Heat Illness: Prevention

- Time exertion to avoid sunlight exposure and the hottest daytime hours (10:00 am to 3:00 pm)
- Light loose clothing permitting airflow over body surface
- Consume 400 to 500 cc fluid before exertion and 200 to 300 cc at 20 min. intervals during exertion
- Check body weight before practice: if wt. down 3%, increase PO fluids; if wt. down 5%, cancel participation that day; if wt. down 7%, immediate fluids & consider medical attention
- Use only low osmolal fluids (< 2.5 g glucose and < 0.2 g NaCl per 100 cc)
- Extra NaCl and potassium intake during acclimatization
- Cancel event if WBGT > 30°C
Potential Problems with Salt Tablet Use

- Delayed gastric emptying
- Osmotic fluid shift into gut
- Gastric mucosal damage
- Hypernatremic dehydration
- May impair acclimatization
- May exacerbate potassium depletion
Hyperthermia : WBGT

- Wet bulb globe temperature = Heat Index
- WBGT = 0.7 X wet bulb temperature
  + 
  0.2 X black globe temperature
  + 
  0.1 X dry thermometer temperature
**Wet-Bulb Globe Temperature (WBGT) and Recommended Activity Levels**

<table>
<thead>
<tr>
<th>C °</th>
<th>F °</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>60</td>
<td>No precautions</td>
</tr>
<tr>
<td>19-21</td>
<td>66-70</td>
<td>No precautions as long as H2O, salt &amp; food easily available</td>
</tr>
<tr>
<td>22-24</td>
<td>71-75</td>
<td>Postpone sports practice, avoid hiking</td>
</tr>
<tr>
<td>24</td>
<td>76</td>
<td>Lighter practice, work only with rest breaks</td>
</tr>
<tr>
<td>27</td>
<td>80</td>
<td>No hiking or sports</td>
</tr>
<tr>
<td>28</td>
<td>82</td>
<td>Only necessary heavy exertion with caution</td>
</tr>
<tr>
<td>30</td>
<td>85</td>
<td>Cancel all exertion for unacclimatized; Avoid sun exposure even at rest</td>
</tr>
<tr>
<td>31.5</td>
<td>88</td>
<td>Limited brief activity for acclimatized, fit personnel only</td>
</tr>
</tbody>
</table>
Figure 1. Weather guide for prevention of heat illness during prolonged strenuous exercise. (Reproduced with permission from Mathews-DK, Fox EL: The Physiological Basis of Physical Education and Athletics, ed 3. New York City, CBC College Publishing, 1981.)
Neuroleptic Malignant Syndrome (NMS)

- **Definition**:
  - Idiosyncratic reaction to neuroleptic agents (phenothiazines, etc.) that consists of fever, mental status changes, muscle rigidity, autonomic dysfunction, respiratory distress and possible rhabdomyolysis; May cause as many as 4000 deaths / year
  - Occurs with therapeutic doses of neuroleptics and is not related to duration of therapy
  - Occurs with phenothiazines, butyrophenones, thioxanthines, metaclopramide (Reglan) and withdrawal from amantadine or levodopa
NMS : Symptoms / Signs

• Fever (in 100 %)
• Parkinsonism (98 %)
  • Muscle rigidity, tremor, bradykinesia, dystonia
• CNS symptoms (in 77 %)
  • Agitation, stupor, coma, seizures, ataxia, nystagmus
• Tachycardia / tachypnea
• Diaphoresis
• Increased WBC, LFT's, CPK, and catecholamines
• May have rhabdomyolysis / acute renal failure
NMS

- Occurs with therapeutic doses of neuroleptics
- Not related to duration of therapy
- Subsequent exposure does not always cause recurrence
- Most reported cases in young males
NMS: Incidence

- First described 1968
- Affects < 1 % of patients on neuroleptics
- 9 to 30 % mortality in reported cases
- ? 4000 deaths / year

52
NMS Symptom Complex

- **I**: Hyperpyrexia (may reach 41°C)
- **II**: Generalized Rigidity; Akinesia
- **III**: Altered Consciousness
  - Dazed mutism
  - Stupor
  - Coma
- **IV**: Autonomic Dysfunction
  - Diaphoresis
  - Dyspnea
  - Urinary incontinence
  - Labile blood pressure
  - Tachycardia
NMS : Causative Agents

- Haloperidol / fluphenazine : 1/2 of reported cases
- Chlorpromazine / other phenothiazines
- Thioxanthenes
- Metaclopromide
- Withdrawal from amantadine or levodopa
- ? more severe if neuroleptic plus lithium
NMS Onset and Duration

- Usually gradual onset: over 1 to 3 days
- Lasts 1 to 2 weeks after stopping oral neuroleptics
- May last several weeks after stopping IM neuroleptic ("depot" preparations)
NMS : Treatment

- Basic Rx same as for heatstroke
  - O2, cooling, IV fluids, cardiac monitoring, ICU admission
  - Stop the neuroleptic!
- Consider use of adjunctive drugs : (To restore CNS dopamine levels)
  - Bromocriptine 2.5 to 20 mg PO tid
  - or Amantadine 100 mg PO tid
  - or Levodopa 100 to 230 mg PO tid
  - or Dantrolene 1 to 10 mg / Kg / day IV or PO
- Consider ECT (for Rx of the original condition) if the neuroleptic cannot be restarted
Malignant Hyperthermia

- **Definition:**
  - Inherited condition (autosomal dominant with variable penetrance) causing fever, acidosis and muscle rigidity in response to halogenated general anesthetics and depolarizing neuromuscular blockers (succinylcholine)
  - Probably due to excessive release of intracellular calcium in muscle; Can rarely occur in predisposed patient from stress alone
Malignant Hyperthermia: Incidence

- 1 per 200,000 patients exposed to general anesthesia
- Has occurred in response to stress with only local anesthesia
- Untreated mortality 70%
Etiologic Drugs for Malignant Hyperthermia Syndrome

• Halogenated general anesthetics
• Succinylcholine
Malignant Hyperthermia

- Usually occurs early intraoperatively
- Can rarely present postoperatively
- Can rarely present from stress alone
- Can occur in patient who has had uneventful prior surgery & anesthesia
Malignant Hyperthermia: Patients at Risk

- Positive family history
- Family history of neuromuscular diseases
- Increased muscle bulk
- Frequent muscle cramps
- Excessive anxiety
- Twitches / fasciculations at rest
- Diagnostic muscle biopsy / contracture test available at some centers
Malignant Hyperthermia: Family History

- Always specifically ask about family history of problems with general anesthesia (and also pseudocholinesterase deficiency) prior to anesthetic administration.
- If any question of malignant hyperthermia, use narcotic / benzodiazepine / N2O but not halogenated anesthetics or succinylcholine.
Malignant Hyperthermia: Diagnosis

- Fever: sudden rise: often 41°C
- Tachycardia / tachypnea
- Muscle rigidity (may first note masseter spasm)
- DIC (may first note capillary bleeding in the surgical wound)
- Ventricular arrhythmias (may first note PVC's)
- Acidosis
- Hypotension
- Rhabdomyolysis / myoglobinuria
Malignant Hyperthermia: Treatment

- Discontinue the anesthetic immediately (use new tubing or new anesthesia machine)
- Ventilate with 100 % O2
- Discontinue the surgery and close the wound quickly
- Call for help
- Start external cooling: Ice packs to scalp, groin, axillae: hypothermic blanket: uncover patient
- Insert NG and foley: start iced NG lavage
- Draw blood (SMA6, CBC, LFT's, PT, PTT, CPK, Ca, ABG)
- IV fluid bolus ± bicarb ± mannitol
- Give dantrolene 1 mg / Kg IV every 3 to 5 min. (until symptoms subside or dose of 10 mg / Kg reached)
Malignant Hyperthermia: Complications

- Vascular collapse
- CNS deficits
- Renal failure
- Bleeding
Prevention of Malignant Hyperthermia

- Choose other anesthetics (local, regional, spinal, N2O + narcotics + pancuronium)
- Pretreat with 1 mg / Kg dantrolene PO q8h X 4 doses prior to surgery or 2.5 mg / Kg IV 30 min. before surgery
- Have cooling materials and adequate dantrolene in OR prior to inducing anesthesia
- 24 hour malignant hyperthermia hotline: (209) - 634-4917
The **Only 2 Things of Important Relevance to Ask About in the Family History**

- Malignant hyperthermia
- Pseudocholinesterase deficiency
Factors that Help Differentiate Neuroleptic Malignant Syndrome (NMS) from Malignant Hyperthermia (MH)

<table>
<thead>
<tr>
<th>Precipitating factors</th>
<th>NMS</th>
<th>MH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>90% within 14 days; up to years</td>
<td>Minutes to hours</td>
</tr>
<tr>
<td>Cardinal signs</td>
<td>Temp. as high as 105.8°F (41°C), autonomic nervous system dysfunction</td>
<td>Temp. as high as 111.2°F (44°C), rigid jaw muscles</td>
</tr>
<tr>
<td>Genetic predisposition</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Factors that Help Differentiate Neuroleptic Malignant Syndrome from Malignant Hyperthermia (cont.)

<table>
<thead>
<tr>
<th></th>
<th>NMS</th>
<th>MH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated creatine kinase levels when asymptomatic</td>
<td>Rare</td>
<td>Often</td>
</tr>
<tr>
<td>Localization of thermoregulatory deficit</td>
<td>Hypothalamus</td>
<td>Muscle (sarco-plasmic reticulum)</td>
</tr>
<tr>
<td>Treatment</td>
<td>Supportive care, dopaminergics, dantrolene</td>
<td>Supportive care, dantrolene</td>
</tr>
<tr>
<td>Mortality</td>
<td>Up to 20 %</td>
<td>Up to 60 %</td>
</tr>
</tbody>
</table>