Hyperthermia: *"I'm Hot Blooded; Check It and See"*

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Case #1

Found altered at bus stop

Pertinent History A 58-year-old male brought to the ED by EMS after bystanders found him at a bus stop on a 100 °F day. He smells of alcohol and is unable to supply a history due to his altered mental status. He has no visible signs of trauma. He is homeless and well known to the emergency department with multiple visits for alcohol intoxication.

PMH Alcoholic cirrhosis, hypertension, hepatitis C

Social History Homeless, smoker, chronic alcohol abuse, distant history of IV heroin use.

Pertinent Physical Exam

- BP 103/62 mmHg, Pulse 130 beats per minute, Temp 102.4 °F (39.1 °C) axillary, RR 18 breaths/minute, SpO2 95%

Except as noted below, the findings of the complete physical exam are within normal limits.

- General: Intoxicated, minimally responsive.
- HEENT: Normocephalic, atraumatic, pupils 3 mm ERRL.
- Back: Blistering and superficial burns noted to the upper back and buttocks.

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- Extremities: No deformities or edema. Burns with blistering noted over posterior calves and posterior arms.
- Neuro: Moans and opens eyes to painful stimuli, withdraws from pain, moves all extremities equally.

Pertinent Diagnostic Testing

Test	Result	Units	Normal range
WBC	16.2 ↑	K/μL	3.8–11.0 10^3 cells/mm^3
Hgb	12.8 ↓	g/dL	(Male) 14–18 g/dL (Female) 11–16 g/dL
Hematocrit	39.2	%	34.9–44.3%
Platelets	105 ↓	K/μL	140–450 K/μL
Sodium	136	mEq/L	135–148 mEq/L
Potassium	4.8	mEq/L	3.5–5.5 mEq/L
Chloride	100	mEq/L	96–112 mEq/L
Bicarbonate	18 ↓	mEq/L	21–34 mEq/L
BUN	31 ↑	mg/dL	6–23 mg/dL
Creatinine	1.2	mg/dL	0.6–1.5 mg/dL
Glucose	120 ↑	mg/dL	65–99 mg/dL
ALT	41 ↑	IU/L	8–32 IU/L
AST	62 ↑	IU/L	6–21 IU/L
Alk Phos	121 ↑	IU/L	32–110 IU/L
INR	1.3 ↑	–	≤1.1
CK	1340 ↑	U/L	30–220 U/L
pH	7.34	–	7.320–7.420
pCO_2	32	mmHg	36.1–52.1 mmHg
pO_2	256 ↑	mmHg	46.1–71.1 mmHg
Lactate	2.5 ↑	mmol/L	<2.0 mmol/L
Alcohol	380 ↑	mg/dL	<10 mg/dL
UA – specific gravity	1.040 ↑	–	1.001–1.035
UA – Leukesterase	Negative	–	Negative
UA – Nitrites	Negative	–	Negative
UA – Blood	Positive	–	Negative
UA – Ketones	Positive	–	Negative
UA – Protein	Negative	–	Negative

CXR No focal opacities, no pneumothorax, stable from prior exams.

CT Head No evidence of trauma, no intracranial hemorrhage.

CT C-Spine No fracture or dislocation.

EKG Sinus tachycardia, rate 132, no ectopy, normal ST segments.

Plan Observation pending sobriety.

ED Update The nurse obtained rectal temperature measuring 107.2 °F (41.8 °C). Active cooling measures with cold saline IV and evaporative cooling were initiated. The patient was intubated using rapid sequence intubation (RSI) and after

30 minutes of cooling had a core temperature of 39 °C. He was admitted to the ICU for further care.

Case #2 Partied Too Hard

Pertinent History A 26-year-old male is brought to the ED by EMS at 4 a.m. after partying all night. His friends state that they had been drinking and went to a "rave." When they were ready to leave, they went looking for their friend and found him altered and lying in the parking lot outside of the party. They immediately called EMS. They are unsure if he used any drugs but say that he "probably" did.

Social History Nonsmoker, binge drinks, and occasionally uses party drugs per friends.

Pertinent Physical Exam

- BP 115/62 mmHg, pulse 145 beats per minute, Temp 107.4 °F (41.9 °C) rectal, RR 24 breaths/minute, SpO_2 98%

Except as noted below, the findings of the complete physical exam are within normal limits.

- General: Diaphoretic, minimally responsive.
- HEENT: Normocephalic, atraumatic, pupils 8 mm ERRL.
- CV: Tachycardic, regular, no murmurs appreciated. 2+ capillary refill
- Neuro: Minimal moaning to painful stimuli, does not open eyes, moves all extremities equally, withdraws from pain. Slightly increased muscle tone with six beats of clonus.

Pertinent Diagnostic Testing

Test	Result	Units	Normal range
WBC	18.3 ↑	K/μL	3.8–11.0 10^3 cells/mm^3
Hgb	14.2	g/dL	(Male) 14–18 g/dL (Female) 11–16 g/dL
Hematocrit	44.5 ↑	%	34.9–44.3%
Platelets	284	K/μL	140–450 K/μL
Sodium	135	mEq/L	135–148 mEq/L
Potassium	4.7	mEq/L	3.5–5.5 mEq/L
Chloride	105	mEq/L	96–112 mEq/L
Bicarbonate	10 ↓	mEq/L	21–34 mEq/L
BUN	31 ↑	mg/dL	6–23 mg/dL
Creatinine	1.1 ↑	mg/dL	0.6–1.5 mg/dL
Glucose	105 ↑	mg/dL	65–99 mg/dL
ALT	29	IU/L	8–32 IU/L
AST	34 ↑	IU/L	6–21 IU/L
Alk Phos	115 ↑	IU/L	32–110 IU/L

Test	Result	Units	Normal range
INR	1.0	–	≤1.1
CK	2445 ↑	U/L	30–220 U/L
pH	7.24 ↓	–	7.320–7.420
pCO_2	25 ↓	mmHg	36.1–52.1 mmHg
pO_2	312 ↑	mmHg	46.1–71.1 mmHg
Lactate	4.1 ↑	mmol/L	<2.0 mmol/L
Alcohol	80 ↑	mg/dL	<10 mg/dL
UA – specific gravity	1.042 ↑	–	1.001–1.035
UA – Leukesterase	Negative	–	Negative
UA – Nitrites	Negative	–	Negative
UA – Blood	Positive	–	Negative
UA – Ketones	Negative	–	Negative
UA – Protein	Negative	–	Negative

CXR No focal opacities, no pneumothorax, stable from prior exams.

CT Head No evidence of trauma, no intracranial hemorrhage.

CT C-Spine No fracture or dislocation.

EKG Sinus tachycardia, rate 146, no ectopy, normal ST segments.

Plan The Patient was intubated immediately upon arrival using versed and rocuronium. Active cooling was initiated with cold saline bolus, evaporative cooling, ice packs in the groin and axilla, and he was kept sedated with fentanyl and versed drips. He was admitted to the ICU after cooling to 39 °C.

Learning Points: Hyperthermia

Priming Questions

1. What is the pathophysiology behind hyperthermia and the development of heat stroke?
2. What is the differential diagnosis for a patient with hyperthermia?
3. What are the complications of hyperthermia and heat stroke?
4. How is hyperthermia managed and what are the recommendations on cooling measures?

Introduction/Background

1. Hyperthermia can be the result of environmental exposure, physical overexertion, drug/medication use, or a combination of any of the above.
2. Heat stroke and hyperthermia can have various presentations based on the underlying etiology and can present on a broad spectrum from simple heat cramps to alteration in mental status.

3. About 618 people are killed by environmental heat–related illness in the United States every year according to the CDC [1].
   - Fluctuations in weather can lead to increased deaths. For instance, during a heat wave in France in 2003, there were an estimated 14,800 deaths from heat-related illness [2].
   - Heat related illness is almost always preventable with public education on the dangers of extreme heat exposure and common sense.
4. Illicit drugs use, particularly sympathomimetics such as MDMA, cocaine, and methamphetamine can cause significant hyperthermia, particularly when used in a warm environment and combined with physical activity (i.e., dancing for a prolonged period).

Physiology/Pathophysiology

1. The body's temperature is regulated through multiple mechanisms of heat dissipation and heat production and is maintained at the hypothalamic thermoregulatory center.
   - Hyperthermia occurs when the mechanisms of heat dissipation are overwhelmed, when the body generates excessive heat, or a combination of both. In essence, the body's natural cooling mechanisms are unable to bring the body temperature down to the (intact) hypothalamic "set point."
     - In contrast, a fever occurs when the hypothalamic set point is increased, typically in response to either infection or inflammation. Patients with a fever feel cold and shiver because the actual body temperature is below the set point. The body is acting the same way at 37 °C (98.6 °F) when the set point is 39 °C (102.2 °F) as it normally would at 35 °C (95 °F) when the set point is 37 °C (98.6 °C), because in both cases the body's actual temperature is 2 °C below the "set point." When the "set point" returns to normal, the patient begins to feel warm and sweat. A fever "breaking" is the body's natural response to lower the body temperature down to the newly reset, set point. This chapter focuses on hyperthermia, not fevers.
     - In rare cases, injury to the hypothalamus may also cause temperature dysregulation.
   - The core temperature is normally maintained between 36 and 38 °C (96.8–100.4 °F), and temperature regulation mechanisms become much less effective at temperatures >40 °C (104 °F) [3].
   - When the body's temperature rises, there are primarily four physiological responses: dilation of blood vessels, increased sweat production, decreased heat production, and behavioral changes.
   - The mechanisms of heat transfer away from the body are:
     - Radiation: transfer of heat from warmer object to cooler object by electromagnetic waves
     - Conduction: heat exchange between two surfaces in direct contact
     - Convection: heat transfer by air/liquid that is moving across the surface of another object
     - Evaporation: heat is lost by vaporization of water or sweat [4].

2. Heat stroke is severe hyperthermia (>40 °C (104 °F)) from heat exposure with altered mental status. Injury is directly related to how high the body temperature is and how long the temperature has been elevated [5].
   - Hyperthermia leads to a secondary increase in release of endotoxins, increase in vascular permeability, and a systemic inflammatory response that can lead to multiorgan failure [5, 6].
   - Elevated body temperature then leads to denaturing of proteins. Many proteins begin to denature at or above temperatures of 41 °C (105.8 °F) [7].
   - Prolonged hyperthermia overwhelms the body's natural thermoregulatory mechanisms, which leads to cellular death, resulting in excessive release of endotoxins causing multiorgan dysfunction and even death if not rapidly identified and treated.
   - Elderly patients have a decreased ability to compensate by the above mechanisms and are much more susceptible to hyperthermia when exposed to heat.
3. Hyperthermia may also be caused by increased metabolism and heat production by the body. This is most commonly due to physical exertion during sports, but other metabolic mechanisms can result in hyperthermia.
   - Sympathomimetic drugs, particularly amphetamines and cocaine, can increase the body's temperature by increased release and decreased reuptake of catecholamines:
     – Increased norepinephrine leads to a sympathomimetic toxidrome, which consists of tachycardia, hypertension, diaphoresis, anxiety, hyperreflexia, mydriasis, paranoia, seizures, etc.
     – Increased serotonin levels can lead to a clinical picture similar to serotonin syndrome, which consists of hyperthermia, agitation, hyperreflexia, tremor, diaphoresis, mydriasis, ataxia, and muscle rigidity [8, 9].
     – In addition, environments where these drugs are consumed (concerts, clubs, raves, etc.) are often warm and humid with poor ventilation and involve ongoing physical activity.
   - Serotonin syndrome, thyrotoxicosis, malignant hyperthermia, and neuroleptic malignant syndrome can also cause severe hyperthermia due to significantly increased metabolism.

Making the Diagnosis

Anything that can cause increased core body temperature with central nervous system dysfunction should be included in the differential.

The Differential Diagnosis

- Infectious: sepsis, meningitis, encephalitis, malaria, etc.
- Endocrinopathy: thyroid storm, pheochromocytoma, DKA
- Neurological: CVA, ICH, Status epilepticus
- Toxicological: anticholinergic, sympathomimetic, neuroleptic malignant syndrome, serotonin syndrome, salicylate overdose, etc.

1. The diagnosis of heat stroke should be suspected based on history and physical exam. While context clues can help with the diagnosis (high ambient temperatures, found in warm environment, etc.), the other possible causes listed above should be considered and excluded prior to making the diagnosis of heat stroke.
   - The prototypical non-exertional heat stroke patient will be an elderly patient with underlying chronic medical diseases such as cardiovascular disease, neurological disease, obesity, etc. These comorbidities limit the ability of the body to thermoregulate and often limit patient's ability to remove themselves from an excessively hot environment. They may have anhidrosis as well, but this is not a sensitive finding in heat stroke [5, 10].
   - Patients with heat stroke will often present with abnormal vital signs such as tachycardia, tachypnea, hypotension, and, of course, elevated temperature.
   - IMPORTANT: It is vital that an accurate temperature be recorded in these patients. Central monitoring probes should be used. Rectal thermometers will be most practical for the ED physician on initial assessment, but Foley catheters with temperature probes are very useful and easy to place for continuous temperature monitoring. For intubated patients, esophageal probes are also an option.
   - Central nervous system findings in heat stroke can vary and may be as minimal as confusion and/or irritability or as severe as seizures and coma, thus a high index of suspicion is key to prompting measurement of the core temperature as other methods may not reflect the true degree of hyperthermia [5].
   - History and physical exam should also focus on identification of possible toxidromes. Hyperreflexia and clonus may point toward serotonin syndrome or overdoses of drugs with serotonergic effects such as MDMA. Hyperreflexia may also be seen in thyrotoxicosis. Skin should be examined for moisture; dry flushed skin may point toward an anticholinergic toxidrome whereas diaphoresis may indicate sympathomimetic toxidromes.
2. Laboratory workup in hyperthermia should be broad and targeted at diagnosing complications of hyperthermia, primarily end organ damage, as well as identifying underlying etiologies if the clinical picture is unclear.
   - It is important to check CBC, CMP, ABG, coagulation studies, CK, urinalysis/UDS, EKG, and CXR. Other studies such as TSH may be indicated in the appropriate clinical setting.
   - If the patient's presentation is not clear, a CT of the head and LP to rule out CNS infection or hemorrhage may be indicated as well.

Treating the Patient

1. Like any critically ill patient, resuscitation should begin with the ABCs.
   - Airway: Patients who are unable to protect their airway should be intubated for airway protection similar to most patients presenting to the ED. Hyperthermic patients may gain additional benefit from intubation with paralytic agents as paralysis will reduce heat generation and prevent shivering.

- Breathing: Poor oxygenation may be due to aspiration, underlying infection, or poor respiratory effort. This can be assessed with CXR, ABG/VBG, and clinical exam.
- Circulation: Patients with heat stroke are often volume depleted due to excessive sweating and vasodilation. Fluid resuscitation should begin immediately in these patients. Avoid alpha agonists such as phenylephrine due to the fact that the peripheral vasodilation is needed to help with heat dissipation.
  - In contrast, patients with hyperthermia due to drug use may present hypertensive. Treatment of the hypertension should begin with benzodiazepines and if necessary, escalated to a titratable drip such as nicardipine.

2. All patients with hyperthermia will need rapid cooling.
   - Do not forget to remove the patient from the hot environment. If you are practicing in the ED, this is typically already accomplished by virtue of the patient's presence in the ED.
   - There is no evidence for any particular temperature endpoint, though endpoints as high as 39.4 °C (102.9 °F) have been used in the literature with good outcomes [11]. The ultimate goal is normothermia.
   - One of the most practical and effective methods of cooling in the ED is evaporative and convective cooling by exposing patients as much as possible and spraying tepid water on them with fans blowing air across their body.
   - A systematic review in 2009 showed immersive cooling is the most rapid method; however, this is rarely available in the ED. Additionally, immersive cooling may complicate monitoring and intravenous access. Lastly, the studies of immersive cooling have been conducted primarily in young healthy adults with no comorbidities, so generalization to elderly non-exertional heat stroke patients with multiple medical problems is unknown [5, 12, 13].
   - Other adjuncts include cooled oxygen, cooling blankets, cool IV fluids, bladder irrigation, intravenous temperature management systems, and gastric lavage. Often, many of these modalities are slow to initiate and the patient can be cooled to a safe temperature by other methods faster. In addition, gastric lavage may even cause water intoxication.
   - In a limited resource environment, simple ice packs can be used to help with cooling. Traditionally, it is taught that the most effective placement is in the groin, neck, and axilla. However, a randomized controlled trial with ten healthy adults showed that applying ice packs to the cheeks, palms, and soles in exercise-induced hyperthermia was more effective [14].
3. Other complications from hyperthermia and heat stroke that will need to be managed include respiratory dysfunction, arrhythmias, seizures, rhabdomyolysis, and end organ damage such as kidney and liver damage.
   - Respiratory complications: aspiration, noncardiogenic pulmonary edema, Acute Respiratory Distress Syndrome (ARDS), and pulmonary hemorrhage. These patients are often acidotic as well and will need intubation not only for airway protection but also for respiratory failure.
     - A study in India of 28 patients admitted for heat stroke found that 86% of the patients developed respiratory failure [15].

- Cardiac dysfunction: sinus tachycardia is the most common finding. Acute heart failure and elevated biomarkers with ST changes on EKG can be seen, but cases of stress-induced cardiomyopathy as a complication from heat stroke exist only as case reports [16].
- CNS dysfunction: patients present on a spectrum of CNS dysfunction from slightly altered cognition to seizures. While cooling is the definitive management, short-acting benzodiazepines can be used while cooling measures are being initiated.
- Other injuries to consider while managing these patients:
  - Rhabdomyolysis
  - Acute kidney injury
  - Hepatic injury
  - Coagulopathies such as DIC.
  - Hyponatremia from excessive water intake or drug effects [17].
  - Adverse effects from the underlying cause of hyperthermia
    - A case series in 2012 described three cases of intracranial hemorrhage in the setting of MDMA use. These patients were all in their twenties, and none were found to have underlying aneurysms [18].
    - There is also a case report of an aortic dissection that was "likely related" to the ingestion of ecstasy in a 29-year-old at a rave [19].

Case 1 Conclusion

The patient was admitted to the ICU with a normal temperature and extubated on hospital day 2. His mental status returned to his baseline, and he was discharged from the hospital on day 4 with normalizing labs and vital signs.

Case 2 Conclusion

The patient was admitted to the ICU, and his temperature continued to normalize. He was extubated the following day. His CK rose to 31,470 without evidence of AKI. He left the hospital against medical advice on hospital day 5.

Case Discussion

As presented in the cases above, hyperthermia may be fairly obvious on presentation but may also be somewhat subtle without high suspicion. Any altered patient brought from a hot environment, especially the elderly or otherwise impaired patient or patients suspected of using illicit drugs should have an accurate *core* temperature measured. Once identified, hyperthermia should be aggressively treated to reduce the core temperature to a safe range as underlying pathology and complications are managed.

Pattern Recognition

- Altered mental status
- Hyperthermia
- Hot ambient temperatures and/or
- Known drug abuse

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