Management of the hyperthermic patient

Undifferentiated body temperature of greater than 38°C can herald a number of important clinical syndromes essential to diagnose besides just infectious aetiologies. This review examines the pathophysiology, clinical features and approach to the management of hyperthermia that will lead to appropriate diagnosis and treatment.

Fever is a frequent cause of urgent and emergent presentations to health-care facilities accounting for 6% of all adult visits for patients aged 18–65 years (Shah et al, 1998). In many of these cases, infectious agents are the cause of fever. However, elevated core temperature can be secondary to a number of different processes and can lead to significant morbidity and mortality.

The human body's regulation of temperature requires complex mechanisms that maintain an important balance between heat production and heat dissipation. The hypothalamus acts as the thermostat, coordinating endocrine and autonomic responses to maintain a temperature set point, normally around 37.0°C (Dalai and Zhukovsky, 2006). There are two separate situations in which the body's temperature is above this normothermic set point: fever and hyperthermia. Fever is generally defined as a core temperature of >38.3°C (O'Grady et al, 1998). Hyperthermia occurs when there is failure of thermoregulation and the body produces more heat than it can dissipate. Core temperatures in this disease state usually reach temperatures of >41°C.

This review examines the clinical features of hyperthermia and the approach to initial and ongoing management. Emphasis is placed on the most common reasons for substantial hyperpyrexia beyond infection, drug-related toxicity and environmental exposure.

Pathophysiology of hyperthermia

The preoptic nucleus of the anterior hypothalamus has heat-sensitive receptors that increase firing when the blood temperature rises above the thermal set point, and decrease firing when it falls below. The same area of the hypothalamus receives information from peripheral heat-sensitive receptors in the skin, abdomen and spinal cord. Under normal conditions, these receptors increase their output as the body's temperature rises above the set point, signalling the hypothalamus to enact several mechanisms of heat release. Inhibition of the sympathetic nervous system results in vasodilation of the blood vessels to the skin and activation of sweat glands. Metabolic activity – a large source of heat production in the body – is downregulated and the stimulation of panting increases evaporative heat loss from the lungs.

In the febrile state, the hypothalamic thermal set point is shifted upward to a higher temperature by elevated prostaglandin (PG) E_2 levels. The hypothalamus then, perceiving a normothermic temperature as hypothermic, stimulates mechanisms for heat production (Dinarello, 2004). 'Thermogenesis' is activated in the body's fat stores, uncoupling proteins to release adenosine triphosphate and heat. Shivering produces heat as a byproduct of mechanical energy production in the muscles, and vasoconstriction in the periphery shunts blood centrally, increasing body temperature and also creating the sensation of chill. Behaviours that decrease the sensation of coldness, such as layering clothing and seeking warm environments, increase core temperature by decreasing radiative heat loss. Older individuals have lower body temperature than younger patients and thus pathologically elevated body temperature may not be recognized (Norman and Yoshikawa, 1996).

The pyrogenic substances implicated in fever are both exogenous and endogenous. Exogenous pyrogens involve microbes and microbial toxins, whereas endogenous pyrogens include cytokines released by leukocytes in response to inflammatory processes. These cytokines cause elevations in PGE_2 that stimulate the hypothalamus to increase the thermal set point (Dinarello, 2004). A patient core temperature of >40°C is termed 'hyperpyrexia'.

In contrast to fever where the body attempts, under hypothalamic direction, to increase its temperature to a new thermal set point, in hyperthermia the body's temperature rises uncontrollably, outstripping the body's mechanisms to dissipate heat despite a normothermic set point. Causative factors include both environmental heat exposures and either toxic or metabolic derangements that disrupt the body's natural processes of heat loss. Exertional hyperthermia tends to affect young, fairly healthy patients (such as athletes) with heat production as a result of physical activity on top of elevated environmental temperatures and sometimes inappropriate layering of clothing that impedes radiative and evaporative heat loss. In contrast, physiological changes that occur with ageing, such as decreased number of sweat glands and diminished vasomotor control, place elderly patients at higher risk for hyperthermia, as do medications that interfere with these processes (such as anticholinergics, diuretics, antihypertensives, neuroleptics and drugs of abuse). Chronic illnesses often also play a role, and factors such as dementia

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or immobility may limit older patients' behavioural responses to remove themselves from hot environments (Bouchama et al, 2007). In any age group, hyperthermia is rapidly fatal without intervention and thus reinforces the need to quickly identify the causative aetiology.

Differential diagnosis of hyperthermia

There are numerous causes of elevated body temperature in patients presenting to emergency departments or outpatient clinics. The differential diagnosis for hyperpyrexia is listed in *Table 1*. Even though infection is the most common cause of fever, others need to be considered while approaching a patient with this complaint.

Table 1. Differential diagnosis of hyperpyrexia

Drug associated	Toxicity	Anticholinergic
		Stimulant toxicity (phencyclidine, cocaine, amphetamine, ephedrine, MDMA)
		Salicylate toxicity
	Serotonin syndrome	
	Neuroleptic malignant syndrome	
	Malignant hyperthermia	
	Drug withdrawal syndrome: ethanol withdrawal	
	Drug-induced fever	
Infections	Generalized infections, e.g. bacterial sepsis, malaria, typhoid, tetanus	
	CNS infections: meningitis, encephalitis, brain abscess	
Endocrine derangements	Thyroid storm, phaeochromocytoma	
Neurologic	Status epilepticus	
	Cerebral haemorrhage	
Environmental exposure	Heat exhaustion	
	Heat stroke	
Blood clots	Deep venous thrombosis, pulmonary embolism, deep-seated haematomas	

Table 2. Environmental heat illness

Heat exhaustion	Vague malaise, fatigue, headache
	Core temperature may be normal or elevated to less than 40°C (104°F)*
	No altered mental status (coma or seizures)*
	Tachycardia, orthostatic hypotension, clinical dehydration
	Liver function tests: aspartate aminotransferase and alanine aminotransferase may be normal or elevated to several thousands
Heat stroke	Exposure to heat stress, endogenous or exogenous
	Signs of severe CNS dysfunction (coma, seizures (75%), delirium)*
	Core temperature usually above 40.5°C (105°F), but may be lower*
	Tachycardia, orthostatic hypotension, clinical dehydration
	Liver function tests: aspartate aminotransferase and alanine aminotransferase are elevated to tens of thousands

* main differentiating features

Two of these more common causes will be emphasized in this article: heat illnesses and drug-related hyperthermia.

History and physical examination

A comprehensive history and exam must be obtained in all stable patients. A source of infection must be diligently sought out, especially in the presence of chronic illnesses, immunocompromised state or indwelling catheters. Soft tissue and joint infections or intra-abdominal abscess can be missed if the patient is not rigorously assessed. A core temperature must be obtained, preferably using a rectal probe. The degree of fever should not sway the physician away from the diagnosis of sepsis, as a certain temperature does not make sepsis less likely (Cunha and Shea, 1996). While altered mental status can result from sepsis, muscular rigidity, cerebellar signs, myoclonus and hyperreflexia often point to an alternative cause. A careful medication history should be obtained, including medications that were discontinued in the past 6 weeks. A history of illicit substance use must be obtained. Signs and symptoms of volume depletion are frequently encountered in febrile patients. The severity must be assessed to guide subsequent therapy.

Heat exhaustion

Head exhaustion is the result of exposure to excessive temperatures and/or decreased capacity to disseminate heat coupled with significant dehydration. Heat exhaustion is usually more common in the elderly, in patients with preexisting psychiatric conditions and in children. Children are especially susceptible because of their large surface area-to-mass ratio, associated with a relatively low number of sweat glands. Other risk factors include inadequate fluid intake, inappropriate dressing and concomitant use of medications that predispose to hyperthermia, whether through causing anhidrosis or other mechanisms. Skin diseases such as miliaria (prickly heat rash), extensive burns, scleroderma and cystic fibrosis impair sweating and thus adequate heat dissipation.

Patients usually present with symptoms of vague malaise, fatigue and a headache. The core temperature may be normal, and if elevated, does not exceed 40°C (104°F). Mental function is preserved, with no delirium, coma or convulsions. Signs and symptoms of volume depletion are common but sweating persists, as the body's compensatory mechanisms are not yet overwhelmed.

Heat stroke

Heat stroke is a more severe form of heat illness, with mortality reaching up to 20%, and 33% of survivors suffering from moderate to severe functional impairment (Bouchama and Knochel, 2002). The body's physiological compensatory mechanisms are overwhelmed and are unable to adequately cool the body. Vasoconstriction of vasculature leads to end-organ ischaemia manifesting as the cardinal signs of heat stroke, elevated liver enzymes and CNS dysfunction with a core temperature >40°C.

Heat stroke can be differentiated from heat exhaustion by the presence of neurological symptoms, and a (usually) higher core temperature (*Table 2*). The presence or lack of sweating is unreliable for differentiation, as up to 50% of patients with heat stroke have some degree of sweating (Tek and Olshaker, 1992). Neurological symptoms can manifest in the form of bizarre behaviour or hallucinations, opisthotonus, decerebrate rigidity, oculogyric crisis or cerebellar dysfunction. Seizures can be mimicked by profound muscle rigidity, coarse tremors and dystonia (Yeo, 2004). While a number of lab abnormalities may be seen, elevated liver function tests up to the tens of thousands are a prominent hallmark and reflect the degree of centrilobular liver necrosis. Coagulation abnormalities, found on day 2–3, may manifest as purpura, or in more severe cases, gastrointestinal or CNS bleeding. Care must also be taken to look for coexisting infections which can be seen in up to 30% of patients. While heat stroke has been classified as classic *vs* exertional, this differentiation is of less pragmatic clinical use as the treatment for both is similar.

Drug-induced hyperthermia

Drug-induced hyperthermia describes an elevation of body temperature directly secondary to an ingested pharmacological agent. The mechanisms are diverse and involve impaired heat dissipation, an increased rate of metabolism, evoked immune response or mimics of endogenous pyrogens. There are a large number of drug classes that can cause hyperthermia. These are summarized with their sentinel clinical features and individual treatments in *Table 3*. Consideration of these agents early on in the differential diagnosis is essential for timely administration of specific drug therapy.

Acute stabilization of hyperthermia

Regardless of the underlying cause, acute management of the hyperpyrexic patient includes evaluation and stabilization of airway, breathing and circulation, placement of a rectal thermometer for accurate temperature monitoring and the mainstay of hyperthermia management: rapid cooling. As the initial survey is conducted and cooling therapy is initiated, patients should be attached to continuous cardiac monitoring, a foley catheter placed for accurate monitoring of urine output, pertinent lab work drawn, and a 12-lead electrocardiogram and intravenous access should be obtained (*Table 4*).

Patients with severe fever or hyperthermia are often obtunded and are at risk for aspiration pneumonia, pulmonary oedema and seizures. They may also not be able to meet the increased respiratory demand of the hypermetabolic hyperthermic state. Thus, early definitive control of the airway is essential, using intubation as necessary.

Most hyperthermic patients have a hyperdynamic circulation, and tachyarrhythmias and hypotension are common (Platt and Vicario, 2009). Dysrhythmias should resolve with cooling; electric cardioversion should be avoided until the temperature has come down and the myocardium has recovered. Hypotension is a result of peripheral vasodilation and dehydration, and pulmonary oedema can lead to right heart strain and high-output failure. With cooling efforts vasoconstriction contributes to normalization of blood pressures, but the patient will likely need additional resuscitation with intravenous crystalloids, with attention to respiratory status as a result of risk of worsening pulmonary oedema. Central venous pressure monitoring may be indicated to assess intravascular volume, with the caveat that it may be falsely elevated in the setting of right heart failure.

Table 3. Drug-induced hyperthermia*

	Mechanism	Clinical features	Medications	Treatment
Anticholinergic syndrome	Anticholinergic	Tachycardia and hypertension Mydriasis Urinary retention Altered mental status, seizures, myoclonus (no rigidity)	Antihistamines Tricyclic antidepressants Anti-Parkinsonian	Benzodiazepines Physostigmine (in agitated delirium)
Stimulant toxicity	Sympathomimetic	Tachycardia and hypertension Mydriasis Altered mental status, seizure Muscle rigidity Diaphoresis	Phencyclidine Cocaine Amphetamine Ephedrine	Benzodiazepines Sodium bicarbonate (for wide complex dysrhythmias)
Salicylate toxicity	Uncoupling of oxidative phosphorylation	Tachycardia Intractable acidosis, renal failure, pulmonary oedema CNS disturbances	Salicylates	Urinary alkalinization Haemodialysis
Serotonin syndrome	Serotonergic	Triad: mental status change, autonomic hyperactivity and neuromuscular abnormalities	Selective serotonin-reuptake inhibitors Monoamine oxidase inhibitors	Benzodiazepine Cyproheptadine or chlorpromazine
Neuroleptic malignant syndrome	Anti-dopaminergic	Slowly progressive muscle rigidity ('lead pipe') Altered mental status Autonomic instability	Antipsychotics Dopaminergically active antiemetics (less common) Lithium	Benzodiazepine Bromocriptine or dantrolene (controversial)
Malignant hyperthermia	Uncontrolled calcium release in skeletal muscle	Fulminant muscle rigidity and rhabdomyolysis Intense hyper-metabolic reaction Hypercarbia and acidosis	Volatile anaesthetic agents Succinylcholine	Dantrolene
Drug-induced fever	Hypersensitivity, other mechanisms	Can be caused by virtually any drug More frequently encountered in inpatient setting	Anticonvulsants, minocycline, antimicrobials, allopurinol, heparin	Discontinuation of offending drug

*Supportive care and discontinuation of offending drug for all cases of drug-related hyperthermia.
From Eyer and Zilker (2007)

The mortality rate in hyperthermia increases proportionally to body temperature, and the faster the patient is cooled the better the survival rate (Vicario et al, 1986). Aggressive reduction of body temperature to <38.9°C within 30 minutes of presentation improves survival (Dematte et al, 1998). There are several methods of rapid cooling but non-invasive methods such as evaporative cooling and ice-water immersion are the most evidence based and widely used.

Ice-water immersion is considered by some to be the gold standard of cooling therapy, and can cool at a rate of 0.15°C/min, but can be difficult to accomplish in the emergency department and limits patient monitoring capabilities and concurrent resuscitation efforts (Costrini, 1990). Evaporative cooling, which uses fans to blow warmed air (45°C) over the patient as he/she is sprayed with cooled, atomized water (15°C), has a cooling rate of 0.08°C/min (Graham et al, 1986). This provides a slightly slower rate of cooling but with fewer impracticalities and a decreased shivering response.

Owing to their lesser cooling efficacies, other therapies can be used as adjuncts but should not be used alone. These include ice-packing (either whole-body or strategically at the neck, axillae, and groin), use of cooling vests or blankets, cooled humidified oxygen or cooled intravenous fluids, or more invasive methods such as cold gastric or rectal lavage. Peritoneal lavage has marked benefit with a cooling rate of up to 0.5°C/min, but is invasive and should not be the first-line therapy if non-invasive methods will be effective. Cooling should be discontinued after the temperature measured by the rectal probe reaches 39°C to prevent overshooting normothermia.

Medications used in acute hyperthermia management include intravenous benzodiazepines as needed to increase patient comfort during rather uncomfortable interventions and to minimize heat production by shivering. In addition, cooling may precipitate seizures also best treated with benzodiazepines. As the pathophysiology of hyperthermia is not related to PGE_2 elevations, the acute management of heat illnesses does not include use of antipyretics. Salicylates may worsen hyperthermia and coagulopathies, while acetaminophen administration may worsen possible hepatic damage. If there is concern about malignant hyperthermia or neuroleptic malignant syndrome, intravenous dantrolene is an appropriate intervention, but has not borne out as a useful therapy in other causes of hyperthermia (Bouchama et al, 1991).

Table 4. Work up of hyperthermia

Diagnostic tests	Findings of interest
Complete blood count, basic metabolic panel, liver function tests, prothrombin time or partial thromboplastin time, fibrinogen, fibrin split-products, lactate dehydrogenase, creatine kinase-MB, myoglobin, lactate, troponin, toxicology screen	Infection, haemoconcentration, thrombocytopenia, electrolyte abnormalities, renal failure, uraemia, transaminitis, coagulopathy or disseminated intravascular coagulopathy, haemolysis, rhabdomyolysis, hypoperfusion, possible ischaemia, intoxication
Arterial blood gas	Respiratory alkalosis or metabolic acidosis
Urine analysis, urine toxicology screen	Myoglobinuria, acute tubular necrosis, toxic causes
Electrocardiogram, cardiac monitor	Dysrhythmias, ischaemic changes
Chest X-ray	Pulmonary oedema, acute respiratory distress syndrome
Computed tomography, lumbar puncture	Cerebrovascular accident, traumatic brain injury, intracranial haemorrhage

Treatment of complications

Initial resuscitation and maintenance of airway and circulation should be prioritized followed by appropriate cooling and supportive measures. Ongoing therapy then should be tailored to the specific aetiology. If hyperpyrexia is thought to be secondary to sepsis, the mainstay of therapy is goal-directed haemodynamic optimization with early initiation of antibiotics. Adequate fluid resuscitation, with continuous monitoring of the vital signs, lactic acid and central venous oxygen saturation, is linked to decreased mortality (Rivers et al, 2001).

Complications from hyperthermia manifest with a characteristic early (described above) and late phase. From a pulmonary standpoint, direct thermal insult to the alveolar endothelium can lead to pulmonary oedema, acute respiratory distress syndrome and cor pulmonale (Tek and Olshaker, 1992). The usual cardiac response is tachycardia, decreased systemic vascular resistance and increased cardiac output. In patients with a history of cardiac illness, these findings may not be seen; it is also crucial to take note of patients without heart history who have more of a hypodynamic picture with low stroke volumes – this is often a sign of impending cardiovascular collapse. Direct myocardial thermal injury and coronary hypoperfusion place even patients with normal coronaries at risk for infarction and resultant heart failure.

Renal failure is a frequently seen complication of heat illness. Severe heat causes direct cellular damage leading to increased vascular permeability; this acts in tandem with vasodilatory efforts at heat loss to cause relative renal hypoperfusion and prerenal failure. Exertional, thermal and/or toxic muscle injury cause rhabdomyolysis and acute tubular necrosis secondary to renotoxic myoglobin circulating in the bloodstream. Thus, strict attention to electrolyte repletion, fluid balance and urinary output is essential. Hepatocyte damage is very common, and hepatic failure leads to build up of lactate and deregulation of clotting factors and platelet production, placing the patient at risk for disseminated intravascular coagulation, a major cause of mortality in heat stroke and hyperthermia (Leon and Helwig, 2010). In renal failure, uraemia can cause platelet dysfunction, compounding the concern of having a significant bleed. Disseminated intravascular coagulation should be treated with supportive measures and alpha amino caproic acid avoided as it is associated with an increased risk of rhabdomyolysis.

Thermal injury in the CNS combined with fluid shifts secondary to dehydration and electrolyte abnormalities cause cerebral oedema and neuronal death, while the coagulopathy of hyperthermia predisposes the patient to intracranial haemorrhage (Yaqub and Al-Deeb, 1998). Any of these complications put the patient at risk of seizure, coma, permanent disability or death. The cerebellum is particularly heat sensitive, and cerebellar signs may become permanent if the patient survives (Yeo, 2004). Agitation is best controlled with short-acting benzodiazepines. Barbiturates are best avoided, as they are hepatically cleared, so their duration of action can be erratic.

Hyperthermia can be seen after ischaemic stroke as well as traumatic brain injury and is caused by autonomic deregulation leading to sympathetic overactivation. Even a few degrees of temperature elevation can have negative effects on morbidity and mortality for brain-injured patients, emphasizing the importance of early recognition and treatment of hyperthermia.

For patients in whom hyperthermia is secondary to a drug effect, the therapy after initial resuscitation should be mainly supportive with specific pharmacological adjuncts used dependent on the toxidrome (*Table 3*). A comprehensive discussion of all drugs causing hyperthermia is beyond the scope of this article. However, many of these drug-induced hyperthermic patients will manifest excited delirium syndrome characterized by agitation, delirium acidosis and hyperadrenergic autonomic dysfunction. This syndrome is the common manifestation of multiple clinical syndromes such as heat stroke, sympathomimetics, serotonin syndrome and neuroleptic malignant syndrome. If de-escalation techniques fail, chemical sedation is the intervention of choice. Agents most commonly used are benzodiazepines, antipsychotics (with preceding QTc measurement) and occasionally ketamine (Vilke et al, 2011). Sedation is important not solely for safety purposes, but also because physical struggle results in catecholamine surge and possible worsening of the pre-existing metabolic acidosis, which has been linked to poor outcome and increased mortality (Roberts, 2007).

Conclusions

The underlying pathophysiological processes associated with fever and hyperthermia create a variety of complications with which the physician must be familiar. Heat itself causes direct damage through disruption of metabolic reactions, protein denaturation and destabilization of cell membranes. These disturbances affect each organ system and without intervention can spiral into multi-organ system failure and death. Clinical vigilance begins with prompt stabilization, resuscitation and cooling with a vigorous search for the purported cause of hyperthermia. Early antibiotics and fluids are critical for surviving sepsis. A high index of suspicion for drug-related hyperthermia will allow for initiation of appropriate treatment. Fulminant heat illness manifesting as heat exhaustion or heat stroke must be identified in a timely manner to avoid associated morbidity and mortality. BJHM

Conflict of interest: none.

Bouchama A, Knochel JP (2002) Heat Stroke. *N Engl J Med* **345:** 1978–88

Bouchama A, Cafege A, Devol E, Labdi O, El-Assil K, Seraj M (1991) Ineffectiveness of dantrolene sodium in the treatment of heatstroke. *Crit Care Med* **19:** 176–80

Bouchama A, Dehbi M, Mohamed G et al (2007) Prognostic factors in heat wave-related deaths. *Arch Intern Med* **67:** 2170–6

Costrini A (1990) Emergency treatment of exertional heatstroke and comparison of whole body cooling techniques. *Med Sci Sports Exerc* **22:** 15–54

Cunha BA, Shea KW (1996) Fever in the intensive care unit. *Infect Dis Clin North Am* **10**(1): 185–209

Dalai S, Zhukovsky D (2006) Pathophysiology and management of fever. *J Support Oncol* **4:** 9–16

Dematte JE, O'Mara K, Buescher J et al (1998) Near fatal heat stroke during the 1995 heat wave in Chicago. *Ann Intern Med* **129:** 173–81

Dinarello CA (2004) Infection, fever, and exogenous and endogenous pyrogens: some concepts have changed. *J Endotoxin Res* **10:** 201

Eyer F, Zilker T (2007) Bench-to-bedside review: Mechanisms and management of hyperthermia due to toxicity. *Critical Care* **11:** 236

Graham BS, Lichtenstein MJ, Hinson JM, Theil GB (1986) Nonexertional heat stroke: Physiologic management and cooling in 14 patients. *Arch Intern Med* **146:** 87

Leon LR, Helwig BG (2010) Heat stroke: role of the systemic inflammatory response. *J Appl Physiol* **109**(6): 1980–8

Norman DC, Yoshikawa TT (1996) Fever in the elderly. *Infect Dis Clin North Am* **10:** 93

O'Grady NP, Barie PS, Bartlett J et al (1998) Practice parameters for evaluating new fever in critically ill adult patients. Task Force of the American College of Critical Care Medicine of the Society of Critical Care Medicine in collaboration with the Infectious Disease Society of America. *Crit Care Med* **26:** 392–408

Platt M, Vicario S (2009) Heat Illness. In: Marx J, Hockerberger R, Walls R, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice.* Mosby/Elsevier, Phila: 1882–92

Rivers E, Nguyen B, Havstad S et al (2001) Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* **345:** 1368–77

Roberts JR (2007) Rapid tranquilization of violently agitated patients. *Emerg Med News* **29:** 15–18

Shah SM, Searls L, Weihl AC (1998) The febrile adult—Parts 1 and 2. *Emerg Med Rep* **19:** 17

Tek D, Olshaker JS (1992) Heat illness. *Emerg Med Clin North Am* **10:** 299

Vicario SJ, Okabaque R, Haltom T (1986) Rapid cooling in classic heatstroke: effects on mortality rates. *Am J Emerg Med* **4:** 394

Vilke G, Debard ML, Chan TC et al (2011) Excited delirium syndrome: defining based on a review of the literature. *J Emerg Med* **2:** 1–9

Yaqub BA, Al-Deeb S (1998) Heat strokes: Etiopathogenesis, neurologic characteristics, treatment and outcome. *J Neurol Sci* **156:** 144

Yeo TP (2004) Heat stroke: a comprehensive review. *AACN Clin Issues* **15**(2): 280–93

KEY POINTS

- In hyperthermia the body's temperature rises uncontrollably, outstripping the body's mechanisms to dissipate heat despite a normothermic set point.
- Hyperthermia is a complex syndrome that can be caused by multiple different aetiologies.
- The most common causes of hyperpyrexia are infectious, environmental heat illness and drug related.
- For all hyperthermic presentations, acute stabilization involves resuscitation with concomitant rapid cooling.
- The most effective cooling modality is evaporative cooling with adjunctive use of ice packs and more invasive measure dependent on the degree of hyperthermia.
- Drug-related hyperthermia requires a high index of suspicion and should be specifically sought via history and recognition of characteristic toxidromes.
- Heat stroke carries a particularly high morbidity and mortality rate which can be mitigated through early recognition and rapid appropriate therapy.