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HYPERTHERMIC CONDITIONS IN NEUROSURGICAL PATIENT

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Abstract

Thermoregulation during anesthesia – general or regional – is often significantly impaired. Any shifts from a body core temperature of 36.6°c±0.2°c results in either hyperthermia or hypothermia, causing pathophysiologic reactions.

Hyperthermic disorders are very dangerously and critical for patients. Hyperthermia is caused by a variety of clinical states. It is important to differentiate controlled and uncontrolled hyperthermia and evaluate the underlying cause. In this paper we discuss most frequently pathologic state, monitoring of hyperthermic disorders and adequate clinical management.

Temperature control occurs by feedback mechanisms operating through the preoptic area of the hypothalamus. Heat-sensitive neurons in this area increase their rate of firing during artificial heating. Receptors in the skin, spinal cord, abdominal viscera, and central veins primarily detect cold and provide feedback to the hypothalamus signaling an increase in heat production. The hypothalamus maintains body temperature at 37.1 C (98.78 F). Stimuli that begin to change the core temperature result in drastic changes in heat loss or production.

Even a mild elevation in brain temperature may be detrimental to the hypoxic, ischemic and injured brain. Hyperthermic states may be caused by a wide variety of clinical disorders which are divided into two major groups: 1) Controlled hyperthermia – resulting from a deviation of thermoregulatory set points and thresholds, 2)

Table 1 lists major causes of hyperthermia.

Increased heat production	Impaired heat loss	Surgical and Medical conditions	Drugs

• Metabolic rate
• Fever
• Heat stroke
• Thyrotoxicosis, thyroid storm
• Pheochromocytoma
• Drugs: amphetamines, hallucinogens
• Malignant hyperthermia
• Neuroleptic malignant syndrome
	• High ambient temperature and humidity
	• Excessive heating
	• Cardiovascular disease
	• Hypokalemia
	• Dehydration
	• Old age
	• Skin disease
	• Cystic fibrosis
		• Hypothalamic bleeding
		• Fourth ventricle bleeding
		• CNS lesions
		• Hemispherectomy
		
		• Infection causes
		  • Meningitis
		  • Encephalitis
		  • Cerebral abscess
		  • Subdural Emphysema
		  • Medullar abscess
		  • Sepsis
			• Anticholinergics
			• Monoamine oxidase inhibitors
			• Serotonin releasers
			• Serotonin reuptake inhibitors
			• Amphetamines
			• Ecstasy
			• LSD
			• Tricyclic antidepressants
			• Analgesics
			• Antihistamines
			• Phenothiazines
			• Butyrophenones
			• Thiothixenes
			• Barbiturates
			• Anti-Parkinsonian agents
			• Diuretics
			• Beta-blockers
			• alcohol

Uncontrolled hyperthermia – resulting from impaired thermoregulatory responses or excessive heat production. Numerous studies have found pyrexia to be associated with increased mortality and morbidity after stroke. Early fever is associated with a poor Glasgow Coma Scale score in traumatic brain injury patients. Patients with subarachnoid hemorrhage are at increased risk for cerebral ischemia due to vasospasm. Hyperthermia may potentially worsen this vasospasm mediated brain injury. Several studies have shown hyperpyrexia to be an independent risk factor, predicting worse outcomes in TBI, SAH and ischemia. Blood in the cerebrospinal fluid induces fever in experimental models, and temperature is thus a likely marker for the primary severity of the hemorrhage.

Patophysiology

The major damage of hyperthermia is a result of direct cellular toxicity, i.e. deterioration of mitochondrial activity and, alterations of enzymatic reactions and cell membrane instability. Cellular effects may progress to widespread organ pathophysiologic reactions. Muscle damage, degeneration, and necrosis are direct results of extreme heat production and are associated with significant elevation in muscle enzymes. Cardiovascular effects caused by elevated core body temperature are associated with high cardiac output due to an increase in demand and diminished peripheral vascular resistance (secondary to vasodilation and dehydration), and tachyarrhythmias (sinus tachycardia, SVT and also VT/VF). High-output cardiac failure and heat-induced myocardial damage often lead to various degrees of systemic hypotension.

Cerebral blood flow and cerebral metabolic rate (CBF and CMR) are increased by elevated body temperature (between 37°c and 42°c), but above 42°c cerebral oxygen consumption decreases due to cellular enzymatic degradation. Uncoupling of central nervous system (CNS) metabolism may lead to further damage if CBF is compromised, and may have deleterious effects on the non compliant brain by raising intracranial pressure (ICP). Other effects of hyperthermia on the injured and ischemic brain include: direct brain and spinal cord toxicity associated with cell death, alterations in membrane stability, enzyme function and neurotransmitter release, brain-blood barrier (BBB) disruption, cerebral edema and local hemorrhage, epileptic activity and increased peritumoral edema. These processes may lead to profound stupor, coma and seizures. In conscious patients - ataxia, dysmetria and dysarthria may be seen. Cerebral spinal fluid (CSF) analysis may reveal increased protein levels, xanthochromia and slightly elevated lymphocyte count. Any underlying pathological condition of the central nervous system (traumatic brain injury, ischemic stroke, intracranial hemorrhage) may be adversely affected by hyperthermia, and clinical outcomes may be worse. Coexisting hyperthermia and impaired brain autoregulation in brain-injury may put patients at risk for cerebral hypoperfusion during periods of low blood pressure, whereas they may be prone to the development of vasogenic edema, vascular engorgement, and worsening of intracranial hypertension during periods of high blood pressure.

Hyperthermic reactions may cause acute renal failure (incidence 5%) secondary to dehydration, hypotension and muscle damage. Acute tubular necrosis with moderate proteinuria is more common. In the gastrointestinal tract, hyperthermia frequently leads to ischemic ulcerations that may result in bleeding, elevated liver enzymes, cholestasis and hepatic necrosis.

White blood cell count is frequently elevated in hyperthermic patients. In cases of fatal hyperthermia disseminated intravascular coagulation syndrome (DIC) may evolve, leading to bleeding diathesis and multiple organ failure. Laboratory blood tests will reveal hyperglycemia, elevated serum cortisol, and elevated growth hormone and aldosterone levels. Electrolyte disorders include decreased serum potassium, mild hypophosphatemia and hypocalcemia. Pulmonary thermal injury may cause cor-pulmonale and acute respiratory distress syndrome (ARDS). Pulmonary edema is also common.

Prevention - Hyperthermia

Core body temperature should be measured continuously throughout the entire perioperative period. Core temperature is best reflected by measurements in five sites: tympanic membrane, pulmonary artery, distal esophagus, nasopharynx, and bladder. Rectal temperature tends to lag behind core body temperature. Vascular temperature are used to determine cardiac output by thermodilution. These require insertion of a pulmonary artery multilumen catheter with thermistors at ports located in the right atrium and pulmonary artery.

Crisis management - Hyperthermia

Hyperthermia is suggested by recording above normal core temperature. The diagnosis is confirmed by history and physical examination of the patient. A thorough examination and diagnostic evaluation for all vital signs (pulse, blood pressure, oxygenation, $ETCO_2$, arterial blood gas analysis) should be conducted to identify the particular cause of hyperthermia. Differential diagnosis must include most common causes of hyperthermic state (Table 1). The most common cause of intraoperative hyperthermia is passive hyperthermia caused by excessive insulation and heating.

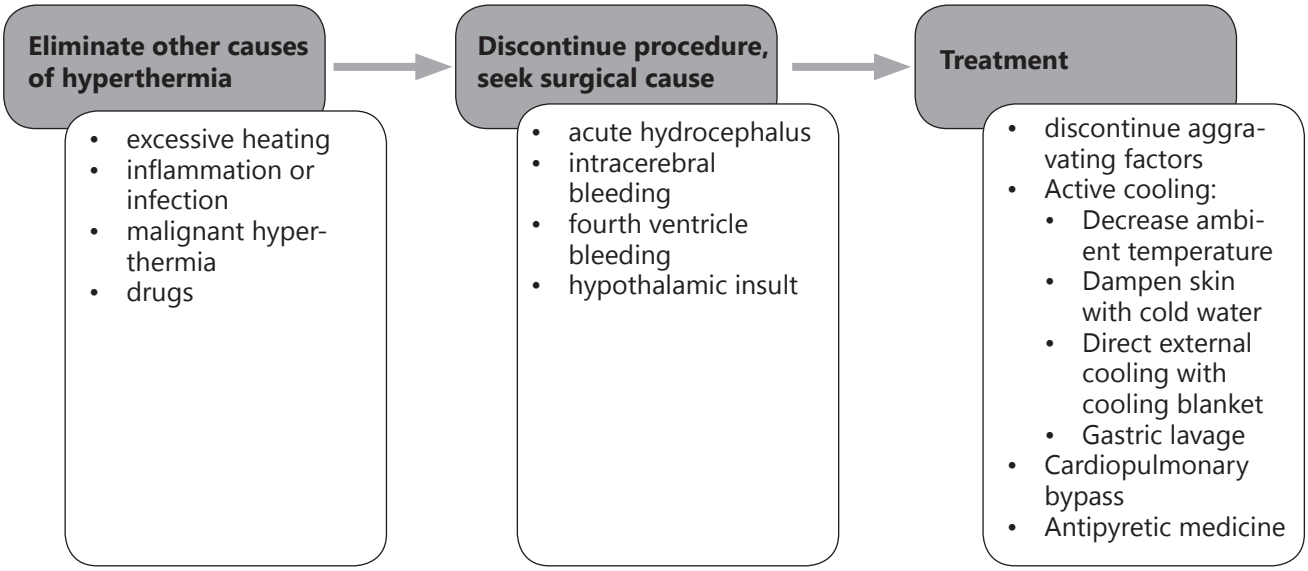
Hypothalamic tumors or intraoperative brain hemorrhage may produce hyperthermia by elevating core body temperature and may be distinguished from heat stroke or severe infection, by noting asso-

ciated clinical conditions such as diabetes insipidus and anhydrosis. Central nervous system infections are characterized by relevant history, clinical signs, and elevated enzyme and white cell count in CSF.

While the underlying cause of hyperthermia should be sought, symptomatically correcting fever in the brain damaged patient is warranted, minimizing damage and improving outcomes. The ideal method (Physical cooling or Pharmacologic) for treating hyperpyrexia is not yet clear. Disadvantages of physical cooling include: patient discomfort, limited effectiveness and elevation of CMR and catecholamine levels – particularly in instances of "controlled" fever. Some evidence exists, demonstrating advantages in pharmacologic control of hyperpyrexia in brain injured patients. Nevertheless, the benefits of pharmacologic antipyretic therapy, compared with associated risks, have not been clearly established.

Malignant hyperthermia (MH) is a rare but fatal phenomena encountered in anesthesia. Most commonly, it occurs under severe stress and after administration of triggering anesthetic agents (most notable – volatile anesthetics and succinylcholine). Several reports have associated brainstem hemorrhage with MH like symptoms. Hyperthermia is usually a late sign, and is preceded by masseter muscle contraction, tachyarrhythmia, combined respiratory and metabolic acidosis, muscle rigidity and hypertension. Aberrations in calcium homeostasis may contribute to increased neuronal damage. The cerebellum has been noted to be particularly vulnerable. Neuroleptic malignant syndrome may be diagnosed by history of use neuroleptic agents (butyrophenones, phenothiazines, thioxanthenes, dopamine-depleting agents and others). A wide variety of other drugs not included in this category have been suspected to cause hyperthermia as well. The use of Haloperidol for treatment of agitation in TBI patients is increasing. Several reports have shown TBI patients to have greater risk of developing NMS following this treatment, and particular attention should be given to early detection. If malignant hyperthermia is suspected, Dantrolene (IV Dantrolene Sodium 1-10 mg/kg) must be administered as soon as possible. Forced diuresis and hemodialysis may be indicated to treat rhabdomyolysis and renal failure. Supportive therapy aimed at treating systemic disturbances (tachyarrhythmias, hypotension, decreased urine output, metabolic acidosis) associated with hyperthermia should be initiated. Continuously monitoring arterial blood gas analysis, urine output and serum electrolytes are critical in the management of the acute crisis.

The following approach is suggested **Figure 1:**



Conclusion

Treatment of hyperthermic disorders depends on the etiology of underlying cause. Continuous temperature monitoring is essential, and may be an indicator of a life threatening syndrome. Malignant hyperthermia is life threatening and should be treated promptly. Elevated core temperature lags behind other signs and symptoms. Surgical intraoperative causes of hyperthermia include: acute hydrocephalus, fourth ventricle bleeding, hypothalamic insult, and intracerebral bleeding. Treatment depends on etiology, and includes active cooling and pharmacologic antipyretic therapy, and is warranted particularly in the injured brain.

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