REVIEW ARTICLE

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Heatstroke

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Heatstroke is the most hazardous condition in a spectrum of illnesses progressing from heat exhaustion to heatstroke, in which a shared finding is hyperthermia (i.e., the rise in core body temperature when heat accumulation overrides heat dissipation during exercise or exposure to environmental heat stress).[1] Clinically, heatstroke is characterized by central nervous system (CNS) dysfunction, multiorgan failure, and extreme hyperthermia (usually >40.5°C).[2,3] This review summarizes current knowledge about heatstroke, which is often misinterpreted or overlooked, focusing on its relevance for medical practitioners.

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Classification, Risk Factors, and Epidemiology

Depending on its cause, heatstroke may be categorized as either classic (passive) or exertional. Both types derive from failure to dissipate excessive body heat, but their underlying mechanisms differ. Classic heatstroke is due to exposure to environmental heat and poor heat-dissipation mechanisms, whereas exertional heatstroke is associated with physical exercise and results when excessive production of metabolic heat overwhelms physiological heat-loss mechanisms (Table 1).

Classic Heatstroke

Classic heatstroke frequently occurs as an epidemic among elderly persons whose ability to adjust physiologically to heat stress has become compromised, chronically ill persons, and those who cannot care for themselves.[4,5] Rising global temperatures causing heat waves, as well as urbanization with its attendant inner-city heat islands, are the major extrinsic factors.[5,6] According to the U.S. National Weather Service, heat waves kill more people, on average, than any other extreme weather event.[6] Multiple intrinsic physiological, social, and medical risk factors render elderly persons more vulnerable to ongoing heat owing to their diminished thermoregulatory capacity (Table 2).[4,5,7-9] Consequently, many elderly patients with classic heatstroke are hospitalized or are found dead within 1 to 3 days after a reported onset of illness,[10,11] and mortality from heatstroke among the elderly exceeds 50%.[1,5]

Prepubertal children are also regarded as a population at risk.[12] Children's susceptibility to classic heatstroke is attributed to a high ratio of surface area to mass (leading to an increased heat-absorption rate), an underdeveloped thermoregulatory system (impairing effective heat dissipation), small blood volume relative to body size (limiting the potential for heat conductance and resulting in greater heat accumulation), and a low sweating rate (reducing the potential for heat dissipation through sweat evaporation).[13] In infants, a major risk factor for death during hot weather is confinement in a closed car, where death can occur within a few hours.[14]

Table 1. Epidemiologic and Clinical Features of Classic and Exertional Heatstroke.

Feature*	Classic Heatstroke	Exertional Heatstroke
Age group	Prepubertal, elderly	Postpubertal and active
Occurrence	Epidemic (heat waves)	Sporadic (any time of year)
Concurrent activity	Sedentary	Strenuous
Health status	Chronically ill	Generally healthy
Medications	Often being used (prescribed medications)	Usually none being used (sometimes ergogenic aids, illicit drugs)
Mechanism	Absorption of environmental heat and poor heat dissipation	Excessive heat production, which overwhelms heat-loss mechanisms
Sweating	May be absent (dry skin)	Usually present (wet skin)
CNS dysfunction	Common	Common
Acid–base disturbance	Respiratory alkalosis	Metabolic acidosis
Rhabdomyolysis	Unusual	Frequent
Liver dysfunction	Mild	Marked to severe
Renal failure	Uncommon (<5%)	Common (25–30%)
DIC	Mild	Marked to severe
ARDS	Common	Common
Creatine kinase	Mildly elevated	Markedly elevated
Calcium	Normal	Low (hypocalcemia)
Potassium	Normal	Usually high (hyperkalemia)

* ARDS denotes acute respiratory distress syndrome, CNS central nervous system, and DIC disseminated intravascular coagulation.

EXERTIONAL HEATSTROKE

Exertional heatstroke is a medical emergency, sporadic in nature, and directly related to strenuous physical activity. It can strike athletes, laborers (e.g., firefighters and agricultural workers), soldiers, and others engaging in activities that many of them previously performed uneventfully under similar conditions of exercise intensity and duration and environmental exposure. Exertional heatstroke can occur even within the first 60 minutes of exertion and may be triggered without exposure to high ambient temperatures.[15,16]

Overmotivation and pressure from peers and coaches that drive people to perform beyond their physiological capability are major risk factors for exertional heatstroke.[17] In addition, functional and acquired factors and some congenital conditions increase susceptibility to heat, leading to exertional heatstroke (Table 2).[18,19] Alcohol and drug abuse, alone or in combination, which are often a feature of psychedelic-trance music parties or festivals, heighten the metabolic response to energetic music[20] and are risk factors for exertional heatstroke among participants in these events. In addition, amphetamine-like drugs and other stimulating agents[21] are a major risk factor for exertional heatstroke in athletes (Table 2). Although previous heatstroke has been suggested as a risk factor for a recurrent episode,[22] this is not supported by conclusive evidence.

The true incidence of exertional heatstroke is unknown because of frequent misdiagnosis (e.g., as dehydration or heat exhaustion). Epidemiologic surveys of U.S. high-school football players[23] and army personnel[24] reveal a steady increase in morbidity and mortality from exertional heatstroke during the past decade. Nevertheless, because exertional heatstroke most often affects healthy young persons and its recognition and treatment are usually prompt, mortality rates are low (<5%).[1,3]

PATHOGENESIS AND PATHOPHYSIOLOGY

The primary pathogenic mechanism of heat stroke involves transition from a compensable thermoregulatory phase (in which heat loss exceeds heat gain) to a noncompensable phase (in which heat gain is greater than heat loss), when cardiac output is insufficient to cope with the high thermoregulatory needs. Consequently, core body temperature continues to rise, leading to a direct cytotoxic effect and an inflammatory response, creating a vicious cycle, and eventually causing multiorgan failure (Fig. 1).[1,2,25-27]

INFLAMMATORY RESPONSE

The cascade of events underlying the systemic inflammatory reaction in heatstroke awaits full elucidation. Hyperthermia triggers a coordinated stress response involving endothelial cells, leukocytes, and epithelial cells, which provide protection against tissue injury and promote cell repair. This reaction is mediated by the molecular chaperone family of heat-shock proteins and by changes in plasma and tissue levels of proinflammatory and antiinflammatory cytokines.[28-30] With prolonged hyperthermia, the acute physiological alterations (including circulatory failure, hypoxemia, and increased metabolic demands) and direct

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