Exhibit 4

Heat Stroke and Cutaneous Burns

Hyperthermia is an elevation of the body temperature. It occurs as a result of 3 mechanisms: increased heat production, decreased elimination or as a result of lesions to the body's internal thermal regulatory center and peripheral responses. Normal physiological thermo-regulatory mechanisms include increased heart rate, increased respiratory rate, peripheral vasodilation, and diaphoresis. Central nervous system responses include restlessness, irritability and eventually convulsions.

Internal body temperatures above 42.5C result in numerous functional physiological disturbances which include generalized vasodilation (increased diameter of the body's blood vessels), cardiac malfunction leading to failure and maladaptive respiratory patterns. Overall internal temperature elevations above 41 or 42C are not compatible with life.

Heat stroke refers to a form of hyperthermia that occurs when the body is exposed to very high ambient temperatures in the setting of altered thermo-regulatory cooling processes. It occurs in two forms, exertional and non exertional heat stroke. Exertional heat stroke usually effect young healthy adults who perform excessively vigorous exercises. Non exertional heat stroke usually effects infants, young children, the chronically ill and the elderly, a group whose ability to adapt to thermal insults are either underdeveloped or compromised.

Overall it is difficult to determine the effects of a single temperature or temperature range on the body. The reason for this is due to the fact that both the actual temperature exposure, rate of temperature change, and duration of exposure are each individual and distinct variables that determine the body's adaptation to the exposure. Moreover the thermoregulatory mechanisms are distinctly different per individual and are affected by medications, chronic illness, age, level of hydration and cardiovascular reserve. Overall a combination of external variables such as type and duration of heat exposure and internal variables such as effectiveness of individual thermoregulatory control make it difficult to determine how the body would respond to a given temperature. For example the body's thermoregulatory mechanisms may be able to sustain a high ambient exposure for a short duration; however the same temperature exposure for a longer duration of time may exhaust the thermoregulatory mechanisms and lead to failure to thrive. Furthermore there are no studies published which have outlined the effects elevated ambient temperature on the body due to ethical and lawful reasons. However as stated earlier, it is generally accepted that internal temperatures above 41C are devastating and require immediate emergent intervention.

An index of heat related injury severity exists, named the Wet Bulb Globe Temperature. This index is used to evaluate heat related injuries and is based on 3 variables: temperature, humidity and radiant heat. There is low risk if the WBGT is < 65 º F, moderate risk if it is between 65-73 º F, high risk if between 73-82 º F, and very high risk >82 º F.

Although it is difficult to determine what types of responses would occur to the human body at 100C due to numerous external and internal variables, it could be expected that human thermoregulatory mechanisms would be exhausted within minutes. Widespread denaturation of proteins and destabilization of cell membranes would cause widespread cellular apoptosis and the release of numerous cytokines which would result in rapid onset multi-organ failure. Widespread systemic vasodilation and circulating denatured proteins, heat shock proteins and inflammatory cytokines would result in cardiovascular collapse, acute respiratory distress syndrome, acute kidney injury, and central nervous system irritability leading to seizures and coma. With precipitous deterioration multiple organ systems, it is reasonable to assume that death would occur within minutes. It should be noted that these opinions are not strongly supported by scientific data and these statements are not those of an expert on the study of hyperthermia, heat stroke or burns.

Cutaneous Burns:

A form of localized hyperthermia that like heat stroke is highly dependent on both the absolute temperature elevation and also the rate of temperature change. For instance a sustained (10 min.) 50C exposure may not result in tissue death, whereas a limited 70C exposure for as little as a few seconds may produce necrosis of the entire superficial skin layer.

Cutaneous burns are categorized into three categories based on severity:

First Degree Burns: associated with pain and vascular congestion, but no tissue death. Localized injury to blood vessel walls results in vasodilation, vascular permeability and localized edema. An example of a first degree burn is sunburn

Second Degree Burns: Burns which result in necrosis of the entire epidermal layer, sparing the underlying dermis. These types of burns result in the formation of blisters as the epidermis separates from the underlying dermis. The skin appears pink and moist and is exquisitely sensitive to touch.

Third Degree Burns: Burns which produce injury and necrosis to the epidermis, dermis and underlying tissue. These types of burns are pale and painless due to necrosis of the underlying nerve and vessel.

Overall, it is difficult to determine the extent of injury from a thermal exposure to the skin due to variables associated with the exposure such as absolute temperature and duration of exposure. In general soft tissue can withstand heat of 44C for several hours before it is injured. However temperature increases above this cause a logarithmic increase in tissue destruction. Therefore it is accepted that skin is significantly burned when exposed to temperatures above 46C. The extent of damage again depends on temperature level and duration of exposure.

At 100C, it could be expected that the individual would experience extensive third degree burns within seconds. The tissue damage would be expected to penetrate well below the dermis and possible effect muscle, fascia, bone and neurovascular bundles. Again, it should be noted that

the opinion about damages sustained at 100C are loosely supported by scientific data and these statements are not those of an expert in the field of burn physiology.

Eric Feuchtbaum
Medical Student (Year 4)
University of Virginia School of Medicine

References:

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