Heat Stroke. Review

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DEFINITION

Heat stroke (HS), colloquially called sunstroke and formerly, solar stroke or heat stroke, heat apnea (sun stroke - heat apoplexy / heat apnea) is a clinical entity characterized by rapid increase in body temperature above 40 ° C, with concomitant neurological dysfunction expressed by delirium, convulsions or coma as a result of exposure to sunlight or strenuous exercise.

The two clinical criteria that should always be presented to suspect the diagnosis are the elevation of body temperature and neurological involvement, in the context of a warm atmosphere.

Demographics

The HS is an acquired disease that claims many lives as they pass the hottest stages of each year, taking a record in each country and sometimes increased mortality figures for this entity associated with hot flashes, which are Frequent daily as a result of natural disasters, pollution, sudden climatic changes, etc. There are multiple reports of waves of heat that charge lives protruding heat-related illness, heat stroke, especially in the Middle East and parts of Europe that have experienced heat waves with high morbidity and mortality.[20, 33]

In Mexico, according to data of the 3rd National Communication to the Framework Convention of the United Nations on Climate Change, held in October 2006 and conducted by the National Institute of Ecology, is discussed as the population group most at risk adults older population that is over 65 years old and people with pre concomitant diseases. The states with the highest mortality are Sonora and Baja California (north of Mexico), with increased mortality 1.2% and 1.3%, respectively. Using climate and mortality records 1979-2003, 1998 was the year in which older HS deaths were documented, being the warmest year of the last decades. It is expected to have increments of 1 and 2 ° C in the next twenty years in these regions of Mexico. In the south-southeast, Veracruz is one of the states that occupy the 2nd place in the step of mortality, with reports of 14-55 cases in that period. From January to October 2008, 30 deaths have joined in Mexico by HS. [16]

CLASSIFICATION

In It has made the distinction between two pictures HS defined according to its evolution and severity, as despite being a mild and one severe form, provided they meet the clinical criteria. The division is in classic HS and postexercise. (See Table 1)

Pathophysiology

The initial hyperthermia that is caused by exposure to sunlight, especially during heat waves (where the ambient temperature tends to rise above 32.2 ° C for 3 consecutive days), or excessive exercise, start settings in body economy in order to maintain homeostasis. The first stages of that process begin with what has been called heat stress (body temperature between 37-40 ° C), which is the feeling of discomfort when being in a hot environment and is perceived subjectively, to a greater extent during physical work. If the continuous heat stimulus, the process called thermoregulation starts, in which an increase in blood temperature lower than 1 ° C, stimulates peripheral heat and hypothalamic receptors bringing the hypothalamic thermoregulatory center is activated, and its response, a peripheral sympathetic activation stimulating cutaneous vasodilation, increasing blood flow in the dermal 8 l / min.

The second mechanism for maintaining homeothermia is evaporation which occurs to vaporize sweat to saturate the air around the body surface, mentioning that 1.7 ml of vaporized sweat, consumes 1 kcal of heat or heat induced even mentioned in a dry environment, this process can dissipate about 600 Kcal / hr, however about 1 liter of sweat is needed, leading to dehydration.

Even people with activity in chronic hot environment, tend to have a phenomenon called acclimatization or thermotolerance during weeks in which he gives a series of adjustments for the body to tolerate the heat gradually, mainly: activation the renin-angiotensin-aldosterone system, salt retention by the kidneys and sweat glands, also the ability to expel sweat, plasma volume expansion, improved cardiovascular performance, increased glomerular filtration rate increases and increases the ability to resist rhabdomyolysis. Unfortunately, these changes do not occur in the context of a HS.

Highs reviews identified in humans ranges from 41.6 to 42 ° C, for 45 minutes to 8 hours, after which tissue destruction is imminent and irreversible. A extreme temperatures 49 to 50 ° C, all cell structures are destroyed and cell necrosis occurs in less than 5 minutes. There are reports of forensic medicine, in which the rectal temperature remained high even hours after death (> 41 ° C), which speaks of persistent hyperpyrexia, even after cessation of metabolic activities. [33]

In case of further heat stress, in aggregate, it gives an acute phase response, activation of endothelial, epithelial cells and leukocytes, which aims to encourage the protection, thus avoiding tissue damage and promote cell repair. Initially, these reactions are local level muscle tissue not so in leucocytes circulating, having cytokine release, particularly IL-6, IL-10 and IL-1 (called cytokines thermogenic, involved in thermal stimuli as fever, hyperpyrexia, etc, primarily through production of prostaglandin E2, which is finally activated thermal hypothalamic receptors in the anterior hypothalamus-preoptic area), which will generate a shallow acute inflammatory response, and in turn control the levels of other proinflammatory cytokines. Moreover, they stimulate hepatic synthesis of acute phase inflammatory proteins, called heat shock proteins (heat shock proteins - HSP), thereby producing reactive oxygen species and release of proteolytic enzymes from activated leukocytes inhibits . Besides these acute phase proteins, stimulate the adhesion and proliferation of endothelial cells and angiogenesis, thereby attempting the maintaining tissue integrity.

Continuing the thermal stimulus and the first mechanisms ineffective, now, the systemic inflammatory response and becomes severe, with leukocyte activation and production of so-called heat shock proteins; both cytokine response as the production of these proteins is primarily controlled at the genetic and the initial stimulus secondary transcription. When this happens, the first response of the organism is, generate peripheral vasodilatation mainly at the dermal-epidermal as well as splachnic vasoconstriction, as the main compensatory mechanisms to sharp increase in body temperature.

The heat shock proteins confer protection from both the nervous system (there is evidence accumulation of these central nervous tissue abundantly) as cardiovascular, being of major proteins 60, 70 and 72 (HSP 60, HSP 70 and HSP 72), the latter two say something known as thermotolerance, the HSP 70 induces tolerance in tissues and HSP 72 causes it is maintained over time, unfortunately it seems to be a limit to the time after which overexpression of these proteins decay; in animal models ranging from 16 to 48 hrs, depending on the tissue which has expressed the synthesis of such proteins. Furthermore HSP 72 induces protection against cerebral ischemia and circulatory shock. [18]

Protection mechanisms by which these proteins act are: to serve as intracellular „chaperones" to other proteins, carting to avoid heat denaturation and act as key regulators of the baroreceptor reflex response, which generates bradycardia and hypotension, thereby exercising its neurocardioprotección. (See figure 1)

Product splanchnic vasoconstriction, another player in the genesis of inflammation and coagulation disor-

der, this being intestinal ischemia with subsequent increase in permeability. This damage anoxo-intestinal ischemia stimulates the production of reactive oxygen and nitrogen species that accelerate the damage to the intestinal mucosa; these changes generate mucosal hyperpermeability direct pass into the systemic circulation together with bacterial endotoxin translocation, further promoting the acute inflammatory response, causing hemodynamic instability and subsequently death, similar to what happened in severe sepsis. Also activation of endothelial cells and endothelial release of vasoactive factors such as nitric oxide and endothelin is induced; Thus cytokines such as endothelium-derived factors alter thermoregulation, exerting inhibition control sweating and to alter the splanchnic vascular tone, leading to precipitate hypotension, hyperthermia and at the same stroke calor. [4, 5, 11]

Subsequently, decrease occurs in the production of heat shock proteins, and neurocardiovascular protection conferred is lost. There is an imbalance between anti-inflammatory cytokines (IL-6, IL-10, soluble p55 and p75 TNF receptors) and proinflammatory (TNFα IFNγ IL-1B), going forward fan, generating damage associated with inflammation and refractory immunosuppression, making patients more prone to infection and concomitant sepsis, increased intracranial pressure, decreased cerebral blood flow, severe neuronal damage. [17, 18, 21, 22, 43]

As is known the endothelium controls vascular tone and permeability, leukocyte movement and maintains a balance between procoagulant and anticoagulant substances.

The hyperthermia itself in vitro, thus favoring a proinflammatory state as a prothrombotic state. Along with the severe inflammatory response is brewing, a second actor, of equal magnitude and importance, that is the activation of the coagulation cascade, starting with the endothelial cell damage, diffuse microvascular thrombosis, as well as complex formation thrombin-antithrombin III, soluble fibrin monomers, low levels of protein C, protein S and antithrombin III. The highly activated fibrinolysis expressed with increased levels of D-dimer and plasmin-α2 complex -antiplasmin, also is decreased plasminogen. Also they found high circulating levels of von Willebrand factor, thrombomodulin, endothelin, nitric oxide metabolites, E-selectin and intercellular adhesion molecules.

Finally, and of great importance in modulating the expression of integrin-B2 characterized by increased modulation and CD11b low modulation CD11a on the surface of circulating lymphocytes, suggesting an active live interaction in between leukocytes and endothelial cells, which explains calls starting inflammation and clotting cascades simultaneously, which despite the normalization of temperature and removal of the heat stimulus, once triggered not return to normal and tend to multiple organ dysfunction, similar to what happened in other processes with severe inflammatory response. (See Figure 2)

In an animal model of heat stroke, using baboons who are subjected to elevated temperatures, it was found that there is damage to the ultrastructure characterized by extensive hemorrhage and thrombosis, as well as transmural leukocyte migration and microvascular endothelial damage; Immunohistochemistry showed increased endothelial von Willebrand factor, tissue factor and endothelial interaction of leukocytes and platelets. He showed extensive apoptosis in spleen, intestines, lungs and hematopoietic cells that reside in those bodies. Activating enzymes as caspase-3 to interact with tissue factor in apoptoícas cells was also evidenced. All this suggests that there microvascular injury, thrombosis, inflammation and ultimately apoptosis. [11]

Diagnosis and Clinical Manifestations

As mentioned, the diagnosis is clinical, history of exposure to sunlight or strenuous exercise, increase in body temperature above 40 ° C and CNS involvement, they are the basis for this.

To classify, take into account the characteristics previously discussed, which refer to a mild illness or a severe one, classic HS or after exercise, respectively. No paraclinical or cabinet analysis is not required for diagnosis, but they are important for monitoring of possible complications, even from the very moment in which the entity is brewing, especially if it has encompassed the patient as HS postexercise, which tends to be a severe and often fatal form.

All patients have tachycardia and hyperventilation. The incidence of hypotension is on average 25% in classic HS, and HS postexercise in this increase, although no figures highly correlated data, but severe inflammatory response that is feasible.

In classical HS respiratory alkalosis; HS after exercise, often coexist respiratory alkalosis and lactic acidosis. cor pulmonale and respiratory distress syndrome may develop, similar to acute lung injury sepsis, which together with cardiovascular failure, favors the development of pulmonary edema.

Primary involvement is given to muscular level, which undergoes degeneration and necrosis by direct effect of heat, being more intense in the HS after exercise. Secondarily generated rhabdomyolysis, which increases the incidence of irreversible renal failure, nephropathy by secondary to myoglobinuria.
Often develop some degree of acute renal failure accompanied by hipoelectrolitemia mainly hypocalcemia (favored by the extensive muscle damage), hypokalemia (which is considered the first electrolyte disorder and favoring others, mediated by the initial sweating and in advanced stages by the hypokalemic

nephropathy associated with HS), hypophosphatemia (mediated renal failure and acute respiratory alkalosis) and hypomagnesemia. When hypercalcemia and hyperproteinemia is evident, they are almost always secondary to hemoconcentration.

Interestingly, neurological impairment, which is one of the diagnostic criteria for this entity and the first organ to be affected in both types of HS. It is characterized by greater involvement at the spinal and cerebellar level, even with pancerebelosos syndromes, since it has been demonstrated that nerve fibers conduct, called Purkinje fibers are sensitive to the toxic effects of heat in addition conditioning of cerebellar involvement, cerebral edema vasogenic, and local bleeding neuronal death, which explain the neurological symptoms. There are also reports of involvement imaging with both the cerebellum, thalamus, hippocampus, caudate, putamen, external capsule and the subcortical white matter, being a metabolic etiology and toxic damage secondary to heat. Neurological sequelae in survivors of heat stroke patients, do they have a shorter survival given comorbidity, which favors same complications of various kinds (poor functional quality, malnutrition, infections, abandonment syndrome, etc). [6, 18, 45]

In the cardiovascular area electrocardiographic data consistent with secondary myocardial ischemia as well as atrioventricular conduction disturbances, with this leading to further cardiovascular failure in severe cases factor. [42]

A gastrointestinal level, no direct mucosal damage by heat, which initially results in mucosal hypoperfusion with increased permeability, and subsequent development of ulcers and bleeding favoring endotoxemia. The liver is particularly sensitive to the effects of heat, and hepatic necrosis and cholestasis is observed on the 2nd day of HS postexercise cases, may be the cause of death in 5-10%. [31]

Haematological failure starts with reactive leukocytosis in response to the inflammatory process, however later alterations in platelet aggregation which is inactivated exist, just as there Hyperviscosity favoring thrombosis; hepatic involvement contributes to decreased synthesis of coagulation factors and subsequently the dreaded Disseminated Intravascular Coagulation with severe thrombocytopenia, which is likewise mediated by direct insult of heat on megakaryocytic line, which decreases its production appears 50% survivors resulting abnormal platelets, thus increasing the risk of both thrombosis and various bleeding.

Finally, there are secondary endocrine manifestations, the most frequent hypoglycemia by a comprehensive metabolic state. In classic HS, there is usually hyperglycemia and even elevations of serum cortisol, even when evidence of adrenal hemorrhage pericorticales (usually in postexercise HS), no concomitant adrenal insufficiency. Hyperaldosteronism and hipersomatostatinismo coexist in an attempt to preserve the blood volume. [28, 29, 37, 38, 40]

TREATMENT

The main objective of treatment involves cooling the body in the shortest possible time (within 30-60 minutes into heat stroke or diagnosis have been made), the goal, lower body temperature of 38-39 ° C and lower rectal 39 ° C, and that depends where there is no involvement of the target organ and systemic inflammation and coagulation eventually lead to irreversible organ failure and death are activated. 34, 36 Both in-hospital management and in the hospital itself, it is always necessary to maintain the basic ABC resuscitation and start cooling measures ranging from the stripping of clothes patient, keep in a cool and aerated, apply compresses ice water throughout the economy and transfer him to a hospital unit specializing in certain sophistication to the appropriate treatment of these patients (having critical care unit, trauma room-shock, etc.), but as will be seen later these measures are poor therapeutic value.

As discussed are vital first minutes, as well as monitoring of core body temperature and ideally rectal (as translated intra-abdominal temperature) greater than 40 ° C and 40.6 ° C respectively as diagnostic criteria, but being able to raise the rectal between 42-49 ° C and maintained, despite the attempts of cooling the surface, there is even evidence of continued high rectal temperature corpses, 2-3 hrs after the death occurred, hence the current importance filing. 33 Once in hospital, there are various methods of cooling, external and internal, invasive and noninvasive, which have differences in technology, complexity, effectiveness, pursuing the same goal. [39, 44, 46] (See Table 2)

The cooling methods are on hand of any hospital unit range from convective, evaporative and conductive methods. Convective use the physical principle of convection to try to dissipate heat through an air stream; They employ evaporative cold water or atomized spray or freeze for that purpose and finally the conductive methods, of greater height currently relate to dip various body parts or even the whole body in cold or ice water, taking advantage of the ability of water to dissipate heat. Unfortunately methods like gelatinized apply compresses or cold packs or ice water, air conditioning or cooling rate are low so they are not recommended, or partially and in conjunction recommend to other cooling methods, as in the case of the famous Body Cooling Units (BCU) that have been used in military medicine and desert regions with differing results between different studies, but as current treatment option; Cooling rate of 0.03 ° C to 0.1 ° C / min. It is said that with this technique, the temperature drops 0.1 ° C every 11 minutes, so that the time taken to decrease to 39.4 ° C would be approximately 60 minutes. Less efficient than the

immersion temperature drop, but better tolerated in patients with classic HS (often elderly people with chronic diseases). [2, 32]

It is mentioned that an individual is cooled to 4 times faster in water than in an air stream at the same temperature, since water has a higher heat conductivity, 630.5 mW / m2 vs. 26.2 mW / m2, and that water, the contact surface is higher than with air. That's why the conductive method is currently considered the gold standard of treatment, but has significant technical difficulties but has shown a higher rate of cooling in less time.

Mentioned techniques that contribute a cooling rate above 0.20 ° C / min are those with better prognosis for the patient, which are: immersion in ice water (1-3 ° C) 50% of body immersion cold water (20 ° C) almost the entire body except the head, and immersion in ice water respecting head; a study on the effectiveness of these three techniques demonstrated to lead a temperature of 43 ° C to 40 ° C in just 15 minutes. Technical a cooling rate of 0.10-0.20 ° C / min takes 30 minutes (immersion in cold water of 5 ° C to 20 ° C) and having an index of 0.03-0.10 ° C to 100 minutes (packages cold water on the body, cooling to 22 ° C, body cooling units, and mixtures thereof).
The cooling rates with this technique are 0.16 to 0.20 ° C / min, and when mixed with other techniques and influenced by other factors (air conditioning, dipping from the entire body except the head, medium height, post-exercise), this increases up to 0.35 ° C / min.

Characteristic is found, the Currie phenomenon, which is characterized in that, paradoxically, when attempting to cool the body that maintains, or even increases the temperature for 8 to 10 minutes (in normotensive, 20-30 minutes), to homeotermia maintain, lease and later met the target. This physiological phenomenon is more common in normothermic in hyperthermic, but still present, having to take into account to avoid misinterpretations during the dive.

Finally, it is mentioned that the pharmacological management, with common antipyretics, NSAIDs and even dantrolene, has no proper effect and can lead to complications, especially liver. However, there is another current drug group that is under investigation, highlighting those with anti-inflammatory and anticoagulant power, as in the case of activated protein C, which has been used in patients with severe sepsis and septic shock, but without an adequate response and few studies in patients with HS and several animal models, which seem to promise good results. There are other drugs still under investigation in animal models, such as etanercept, which increases the levels of IL-6 and TNF, as well as increases the thermotolerance and avoid hypotension; Polymerase inhibitors or ADP-ribose 1 (PARP-1 inhibitors), the enzyme involved in cell death processes for generalized inflammatory conditions, PJ34 and 3-AB have been shown to improve liver function, increased levels of proteins heat shock (HSP-70 and HSP-27, in particular) increased thermotolerance and most importantly, by blocking this enzyme deficient immune response whereby systemic inflammation and coagulation is not expressed, thus increasing the survival of patients occurs . [7, 8, 19, 26, 27]

Now, as to the methods of internal cooling, there was a great boom during the decade of the 80s and 90s, regarding the use of peritoneal washings (saline to 9 ° C), gastric, colonic and bladder (saline at 20 ° C), supported with various probes and catheters to infuse cold or iced saline, however, it has shown common side effects such as abdominal cramps, diarrhea, latent risk of water intoxication and not the rhythm is controlled infusions and as to bladder washing, cooling is temporary, so that is not currently recommended.

The soluterapia with ice cold saline or solution has shown effectiveness in animal models, but still unknown data in humans, poor control over the rate and cooling rate.

The methods of extracorporeal cooling or hemodyalitics have some effectiveness but are inaccessible and expensive, coupled not have in all hospital units are highly complex and poor control over the degree of thermal reduction., But recently has been described team with intravenous catheters and external feedback microtermistor with bladder temperature (CoolGard 3000 and CoolLine®, ALSIUS Company), which has proved effective in terms of thermal control and maintenance of core body temperature, and is fully manageable with such equipment, coupled to reversibility of the inflammatory response was also demonstrated following use. Proven in humans as an indication for induction of hypothermia in cardiac arrest, acute ischemic heart disease, severe ischemic cerebral vascular disease, neurosurgery, anoxoischemic encephalopathy, hyperpyrexia states; HS effectiveness in isolated case reports said. Cooling rates of 0.6 ° C / hr (max 2-2.5 ° C / hr), sustainable and modified at will, for an indefinite period and according to requirements. [3, 30, 35]

As you can see there are a variety of methods from the most common and colloquially reasonable as the stripping of clothes the patient, place him in a cool and shaded, through methods of external cooling, little or partially effective in combination, and internal cooling methods that unfortunately, the simplest and that could be implemented in any hospital unit 1st or 2nd level of care are not effective in achieving the goals of treatment, and the most complex and effective that same unfortunate way, not found in all care units. Conclude and agree that this should be called the Gold Standard treatment and this Immersion in ice water, which involves immersing the patient in water at temperatures between 1-3 ° C, partially or completely and can be implemented in a special area

any hospital in 2nd or 3rd level, especially if we are in a geographical area for heat waves, high incidence of heat stroke or risk of the same. [12, 13, 14, 15, 24, 25]

Finally mention a treatment that is being widely used in China, where herbal origin, called Xuebijing, which is an injection of extracts of five plants used since ancient times in traditional Chinese medicine, which has undergone several studies demonstrating effectiveness in reducing and abate the systemic inflammatory response of various processes such as sepsis, DIC and heat stroke in the latter category have been tested in murine models, showing after application of the compound, improvement of hepatic, pulmonary, hematologic and kidney damage, which encourages naturist to this product, however more studies must be done before it can be applied in allopathic medicine. [47]

PROGNOSTIC FACTORS

It is fully demonstrated that increased levels of CPK (> 1000U / L) and transaminases (twice the normal value) as well as metabolic acidosis from admission of the patient are poor prognosis and translate higher incidence of multiple organ failure. Similarly, the high procalcitonia without evidence of prior or concomitant infection, acts as predictor of severity but not mortality. He recently commented, elevated troponin I and T, but could not prove specific association probably translate secondary myocardial damage and subsequent cardiovascular failure that accompanies multiple organ failure. [9, 10, 23, 41]

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Tab.1: Classification of heat stroke.
Tab.2: Gold standard in heat stroke treatment.

TAB. 1. CLASSIFICATION OF HEAT STROKE

Findings	Classic HS	HS postexercise
	Common to both entities	
hyperthermia	> 40°C (body)	> 40°C (body) > 40.6°C (rectal)
CNS condition	Delirium, convulsions, coma.	Delirium, convulsions, coma.
Hypotensión	Present in 20-30%	incidence is unknown, probably 20-65%
	Distinctive	
Age	Older adults, with chronic degenerative diseases. Infants and pediatric	Young, athletes
Skin	Hot, dry.	Hot, profuse sweating..
Rhabdomyolysis	Mild to moderate, absent	Severe
Renal failure	Rare, absent	Common
Lactic acidosis	Mild to moderate, absent	Severe
Glycemia	Hyperglycemia, normal	Hypoglycemia
Disseminated intravascular coagulation (DIC)	Mild to moderate, absent.	Severe
Etiology or triggers	Hot flashes and consumption of some drugs simultaneously (including antihistamines, antiparkinsonian, diuretics and phenothiazines anticholinergic). Similarity to malignant hyperthermia	After exercise Prolonged exposure to heat

TAB. 2. GOLD STANDARD IN HEAT STROKE TREATMENT

Findings	Classic HS	HS postexercise
Ice packs (on large arteries)	0.025	100 minutes or more
Air conditioning fanning 22 ° C	0.025	100 minutes or more
Ice packs (full body)	0.03	30-100 minutes
Ice water + air conditioning	0.03	''
+ Ice + ice water air conditioning	0.03	''
Air conditioning fanned + ice water	0.04	''
Thermal control unit (BCU)	0.05	''
Immersion in water at 15 ° C	0.05	''
Manual cooling device	0.06	''
Atomized water and air (31 ° C)	0.07	''
Wet-cold gauze and ventilation	0.08	''
Air conditioning and shadow	0.10	15-30 minutes
Splashing cold water or ice	0.14	''
Immersion in cold water at 14 ° C	0.15	''
Immersion in cold water (variable temperature)	0.15	''
Immersion in cold water (1-3 ° C) log	0.15	''
Cold water immersion, hands and feet	0.16	''
Immersion in cold water (14 ° C)	0.16	''
Immersion in ice water (5 ° C), Variable time	0.16	''
Immersion in ice water (20 ° C), Variable time	0.19	''
Immersion in ice water (8 ° C), Variable time	0.19	''
Immersion in ice water (1-3 ° C) Body 50%	0.20	0-15 minutes
Immersion in cold water (14 ° C), whole body	0.25	0-15 minutes
Immersion in ice water (2 ° C), whole body	0.35	0-15 minutes
Cool Gard 3000® and Cool Line®	0.6-2.5°C/hour	0-15 minutes

Red and yellow, which is considered the gold standard today

FIG. 1. COMPENSATORY MECHANISMS (BEFORE THERMAL STIMULUS) LEADING TO HOMEOTERMIA AND THEREFORE TARGET ORGANS (ESPECIALLY BRAIN AND HEART) ARE PROTECTED

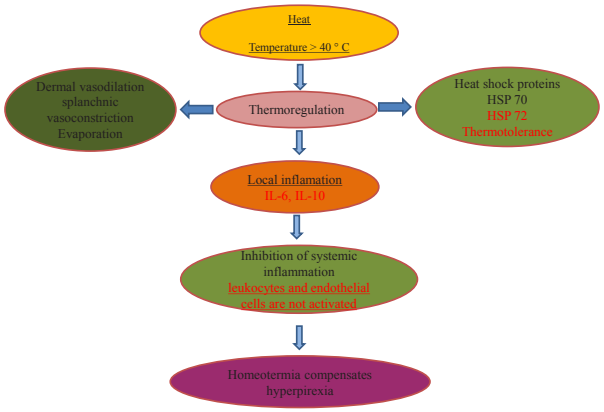
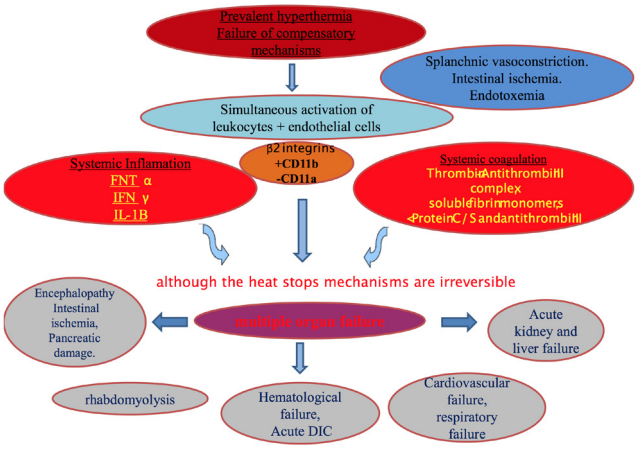


FIG. 2. MECHANISM LEADING TO MULTIPLE ORGAN FAILURE AND DEATH



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