Severity Classification of Heat Illness Based on Pathophysiology

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Abstract

Pathophysiology of aggravation and death due to heat illness includes high fever, circulatory failure and systemic inflammatory response syndrome (SIRS), as well as disseminated intravascular coagulation (DIC) and multiple organ failure. DIC and multiple organ failure are the important determinants of severity and mortality of heat illness.

Recently, Grade I through III classification of heat illness is widely being used in Japan in emergency medicine to avoid underdiagnosis and misdiagnosis. Grade I is a mild case, such as heat cramp and syncope. In Grade III, the core body (rectal) temperature is 39°C or higher due to exposure to hot environment, and is accompanied by brain dysfunction, liver/kidney dysfunction, and/or DIC. When all 3 prerequisites are present, it is called a *complete* type. Grade II heat illness is diagnosed after excluding Grade I and Grade III heat illness.

In this paper, we discuss the significance of understanding the Class III as a syndrome. It is easy to remember the care and treatment for early stage of heat illness as *FIRE*, (*Fluid, Ice*, *Rest*, and *Emergency*). A mnemonic for prevention, on the other hand, is *A* (*Acclimatization*) + *FIRE*, as in "a fire."

Key words Heat illness, Classification, Syndrome

What Is Heat Illness?

During the summer of 2003 in Europe when a heat wave raised the temperature 3.5°C above normal for 2 weeks, there were 22,000 to 45,000 heat illness-related deaths.[1] Many homes and hospitals in Europe were not equipped with air-conditioning at that time, which increased the sacrifice.

Heat illness is a general term for a condition that results from physical adjustment disorders in hot environments. As the aging of the society progresses, the interest in the heat illness among the elderly is growing. On the other hand, there have been reports of young individuals undergoing strenuous physical activity in hot environments who died from or developed permanent neurological damage. The likelihood of death or sequela in a severe case of heat illness is 30% or higher, and prevention and early diagnosis is critical. All medical professionals, including primary care physicians, must possess the knowledge of heat illness.

Pathophysiology of Aggravation and Death Due to Heat Illness

In patients with heat stroke, high fever was believed to induce cytotoxicity resulting in organ damage and death. However, recent studies show that important factors in heat illness are: high fever (Factor 1), circulatory failure (Factor 2), and systemic inflammatory response syndrome (SIRS) (Factor 3)[2,3]; and disseminated intravascular coagulation (DIC) (Factor 4) and multiple organ failure (Factor 5). Among these, DIC and multiple organ failure are the important determinants of the severity of a case.

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Factor 1: High fever Based on the observation of volunteers and the cancer patients undergoing systemic hyperthermia therapy, the maximum body temperature that a human can endure is 41.6–42.0°C for the duration of 45 minutes to 8 hours.[4] High body temperature has cytotoxicity, causing tissue and organ damage.

Factor 2: Circulatory failure The vasodilation on the skin and vasoconstriction of visceral organs are the natural physiological response of a human body in a hot environment to facilitate heat dissipation. However, it causes hypoperfusion and ischemia in visceral organs under extreme conditions (high temperature and high humidity, strenuous exercise, etc.), which leads to organ damage.

Factor 3: SIRS Insufficient blood flow to visceral organs damages intestinal mucosa, and endotoxin is released into the bloodstream, triggering SIRS.[3]

Factor 4: DIC In a severe case of heat illness, coagulation factors in the blood become activated from the early stage. Once activated, the coagulation system cannot be quickly deactivated even when the body temperature is lowered.[5]

This coagulation system disorder that cannot stop once activated causes DIC and further leads to multiple organ failure, which is described next.

Factor 5: Multiple organ failure Cytotoxicity from high fever, circulatory failure and SIRS damages organs. And also DIC causes multiple organ failure by disrupting the microvessels in organs.

Risk of Underdiagnosis in the Old "Heat Stroke" Classification

In the past, the most severe case of heat illness was referred to as "heat stroke" in many literatures. In this old classification, it often used 3 factors as the key diagnostic indicators: disturbance of consciousness, high fever (40°C or higher), and dry skin with no sweating. However, satisfying all these 3 conditions would mean that the condition of a patient is in an extremely advanced stage. As Shapiro et al.[6] states, a patient with a severe case of heat illness with disturbed consciousness may not necessarily exhibit the arrest of sweating or a high grade fever above 40°C during the first examination. Relying heavily on the arrest of sweating or a fever above 40°C can lead to misdiagnosis at the early stage. There have been reports of many severe cases of heat illness that did not fulfill all 3 factors, in which the patients did not show the arrest of sweating nor the fever above 40°C when first brought in by an ambulance but later diagnosed as being severe. The concept of "heat stroke" in the old classification has a risk of underdiagnosis, incorrectly diagnosing severe cases as non-severe. The major reason of underdiagnosis is that old classification neglects the pathophysiological determinants of severity, DIC and multiple organ failure. DIC and multiple organ failure could evolve even if sweating continues or body temperature is lowered or even consciousness is regained.

Grade I Through III Heat Illness Classification to Avoid Underdiagnosis and Misdiagnosis

Classification of burn depth, severity of a subarachnoid hemorrhage, cancer grades, and many other diseases are expressed numerically in the medical field, which is referred to as the ordinal scale. Without using confusing terminology, we have classified heat illness into 3 grades (I through III) and distinctively defined Grade III (**Table 1**).[7–10]

Grade I is a mild case with innocuous heat cramp or syncope. In order to clearly distinguish between Grade II and Grade III at the initial examination, the presence of any one of the 3 conditions (brain dysfunction, liver/kidney dysfunction, and DIC) is used as the prerequisite. Again, in order to avoid underdiagnosis, the prerequisite is *any* of the 3 conditions. A case with all 3 conditions will be referred to as the *complete* type, which has higher mortality compared to the *incomplete* types with 1 or 2 prerequisites.

Main target organs in severe heat illness are brain and nervous system, liver, kidney, blood coagulation system, and striated muscles; however, striated muscles were removed from the diagnostic reference because rhabdomyolysis can occur in any grades of heat illness. If rhabdomyolysis is accompanied by renal failure, it is considered to be Grade III. If a person who had been exposed to a hot environment or in the conditions that increase heat production shows a high fever, and the possibility of all other diseases has been excluded and heat illness is suspected, then, the presence of any one of the 3 prerequi-

Table 1 Diagnostic criteria of Grade III heat illness

If a patient is under heat stress, the possibility of other diseases including head trauma has been denied, and the core body temperature is 39°C or higher (or 38°C or higher in the axilla), then, heat illness is suspected. The presence of any of the 3 following prerequisites will indicate Grade III heat illness.	
(1) Brain dysfunction	Loss of consciousness, delirium, cerebellar symptoms and generalized convulsion
(2) Liver and kidney dysfunction	Elevated levels of AST, ALT, BUN, and creatinine, and presence of blood/urine myoglobin
(3) Disseminated intravascular coagulation (DIC)	Platelet count, D-dimer and FDP levels, PT time, and fibrinogen level
If all 3 are present, then, it is called a *complete* type. If not all 3 are present, then, it is called an *incomplete* type. (Note: A complete type has higher mortality than an incomplete type.)	

• The elevated levels of CPK and myoglobin are commonly observed with rhabdomyolysis. They are essential for diagnosing and predicting the onset of acute renal failure due to myoglobinuria.

• Grade II heat illness is diagnosed after excluding Grade I and Grade III heat illness.

(Extracted from Yasuoka.[7])

sites above will mean the Grade III diagnosis. Here, core body (rectal) temperature of 39°C or axillary temperature of 38°C is considered a high fever. Body temperature assessment should be based on core body temperature (i.e., rectal) since axillary temperature has higher risk of overlooking hyperthermia; however, in practice it is extremely rare to take rectal temperature for diagnosis. Axillary temperature may falsely show the body temperature to be below 38°C when the axillary region has been treated with cold packs in the scene of sports activity or during transportation by ambulance, so caution is required.

In addition to disturbed consciousness, other possible brain dysfunction that must not be overlooked includes cerebellar symptoms such as ataxia, and psychoneurotic symptoms such as delirium or strange behaviors. In our classification, an episode of disturbed consciousness that only lasted several seconds without any other neurological symptoms are considered as a mere orthostatic dizziness or fainting and are excluded from the diagnostic reference; the episode of disturbed consciousness that lasted 1 or 2 minutes or longer are considered in the diagnosis. Before the sudden loss of consciousness, a person may become unsteady during walking or running (cerebellar symptoms) or may be delirious. Not overlooking such cerebellar symptoms or delirium state and bringing a patient to an emergency medical facility for proper treatment as early as possible could spell the difference between life and death.

If a patient had exhibited disturbed consciousness, delirium, and/or cerebellar symptoms when he/she first fell, the patient should be diagnosed as Grade III heat illness even if the patient has already regained consciousness at the time of medical examination.

To check for liver or kidney dysfunction and DIC, the blood and urine screening should be conducted. When testing blood, a blood count (including platelet count), erythrocyte sedimentation rate, biochemistry (including AST, ALT, BUN, creatinine, myoglobin, CPK, Na, and K) as well as arterial blood gas analysis are required. When testing urine, the possibility of myoglobinuria should be checked. To test for the presence of DIC, D-dimer, FDP, prothrombin time and fibrinogen should be checked, in addition to a platelet count.

The diagnosis of Grade II should be made after ruling out the possibility of Grade III. In other words, the difference between Grades II and III is the presence of damages among target organs (brain and nervous system, liver and kidney, and/or blood coagulation system). The evidence of damage to these target organs is extremely useful for detecting severe cases during the early stage of the disease and also for the follow-up observation. The elevated CPK or myoglobinuria accompanied by rhabdomyolysis can be observed in Grade I or II cases, so those are not included in the definition of Grade III.

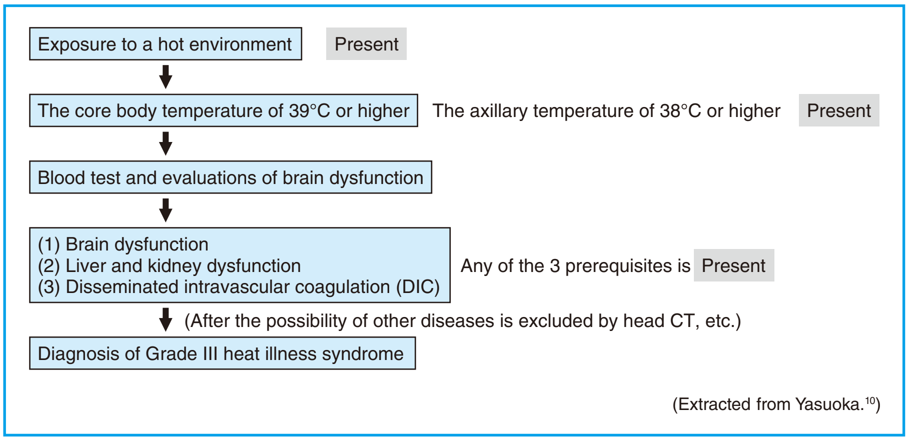

Fig. 1 The diagnostic process of Grade III heat illness

Nonetheless, they are extremely useful for differentiating from other diseases such as head trauma. Myoglobinuria is also significant in predicting renal tubular disorder and renal failure. Recently, this classification of Grade I through III is widely used in many emergency hospitals in Japan.[11]

Significance of Considering the Diagnostic Criteria of Grade III Heat Illness as a "Syndrome"

The past court cases include one that a patient with heat illness was wrongly diagnosed as "head trauma" at a facility specialized in neurosurgery and another that mistakenly treated the patient for "myocarditis" at a facility specialized in cardiovascular diseases. The first physician examining a patient with heat illness must have sufficient knowledge of the disease. The old textbook on internal medicine by Harrison[12] says, "The diagnosis is greatly simplified if a given clinical problem conforms neatly to a well-defined syndrome, because only a few diseases need to be considered in the differential diagnosis." Significance of this "well-defined syndrome" remains unchanged today.

Memorizing the diagnostic criteria of Grade III in the heat illness classification of Grade I through III (**Table 1**) as one important "syndrome" can help clarify the concept of the disease and prevent misdiagnosis. Diagnostic process of Grade III heat illness syndrome can be schematized, as shown in **Fig. 1**.

Cautions When Diagnosing Grade III Heat Illness

The main points to note in the diagnosis of Grade III heat illness are as follows.

(1) Stroke can become progressive, called progressive stroke. Grade III heat illness can become progressive just as stroke, so it requires caution. One must not rush to make a final assessment based only on the initial examination; the possibility of progressive aggravation should be noted in the patient's medical record, and such risk should be explained to the patient and his/her family.

(2) Keep in mind that a patient who showed only mild level of disturbed consciousness at the initial examination may actually be a severe case of heat illness. Particularly in a case with abnormal coagulation system or with kidney dysfunction due to rhabdomyolysis severity could be independent of consciousness level. Note that the coagulation system abnormality can be exacerbated into a progressive type in a few days (**Fig. 2**).

(3) Pay attention to the difference between the ambient temperatures announced by the weather stations and the actual temperatures at sites of onset as well as the difference in heat stress. According to the study that compared the Wet Bulb Globe Temperature (WBGT) index among various activity environments,[13] the difference between an outdoor sports arena and an indoor gymnasium can be as much as 4.0°C, and the difference between an arena and city streets

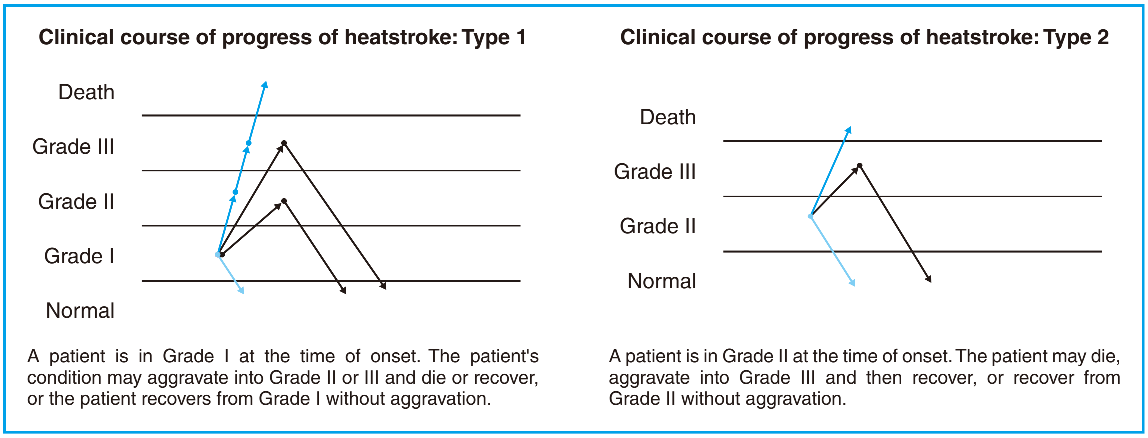

Fig. 2 Clinical course of progress of heat illness based on Grade I through III classification, schematized

among high-rise buildings (both outdoor) can be as much as 3.4°C. These data suggests that the difference in WBGT index among different environments has considerable quantitative effect on the risk of heat illness onset. In other words, people may develop heat illness even when the temperature announced by the weather stations is in the 20s°C, and thus its possibility must be considered when making initial diagnosis at the first examination. Heat illness may occur regardless of the season. In particular, the months of April through November require great caution.

A "hot spot" is a term that originally refers to the spot, place, or area at which a certain value or activity is locally high or active. In Japan, it is often used to refer to the local spots with intense radioactive contamination since the Fukushima nuclear accident in March 2011. Beside in radiology, this term has been traditionally used in criminology and environmental studies as well. Using the term "hot spots" to refer to the risk of heat illness onset will help promoting the awareness that we cannot solely rely on the temperature announced by the weather stations and that we need to measure the WBGT values of the activity sites to understand the risk of onset accurately.

Main Diseases to Be Differentiated

Diseases that should be differentiated when diagnosing heat illness include: 1) head trauma and cerebrovascular disease, 2) various infections such as meningitis or sepsis, 3) hyperventilation syndrome, 4) status epilepticus, 5) malignant syndrome, 6) thyroid crisis, 7) diabetic coma, 8) delirium tremens, and 9) drug intoxication.

Elevated levels of AST and ALT, the liver enzymes, are useful for differential diagnosis. In many diseases that induces high fever and disturbance of consciousness, liver function remains normal or show mild abnormality. In Grade III heat illness, however, the levels of liver enzymes will rise from the early stage, and liver function exacerbate over several days.

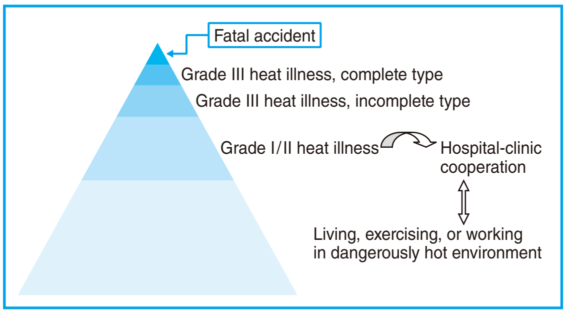

Fig. 3 The conceptual diagram of hospital-clinic cooperation in heat illness (from the Heinrich's Law)

Hospital-Clinic Cooperation in Heat Illness Accident (From the Heinrich's Law) (Fig. 3)

The Heinrich's Law is a rule of thumb developed by Heinrich in 1930s through studying the incidence probability of workers' accidents. Its idea has been used not only for the prevention of

Table 2 Initial care and treatment for heat illness and its prevention

The initial care and treatment at the site of onset: *FIRE*	
F (fluid):	Oral ingestion or intravenous drip of fluid (water + salt)
I (ice):	Body cooling and air conditioning
R (rest):	Completely stop the exercise/labor
E (emergency):	If the disturbance of consciousness is present, secure the airway, ABC of emergency care, and request for an ambulance
***A*+*FIRE* ("a fire") for prevention**	
A (acclimatization):	Acclimation to the heat (it takes a week or more to acclimate to the heat)
+	
F (fluid):	Fluid (water + salt) intake
I (ice):	Body cooling (water spray, mist, ice)
R (rest):	Good rest during the practice/shifts
E (emergency):	Preparation and arrangements based on the expected emergency

industrial accidents, but also for the prevention of medical accidents. The Heinrich's Law, as well as other rules developed by researchers, has one common idea in their foundation. *Never underestimate any small abnormalities or accidents that are easy to be overlooked; designing a system to prevent them will prevent a major accident from happening.*

This basic idea can be also used in the prevention of heat illness accidents. When a person develops heat illness, the worst response is to turn Grade III heat illness and the fatal accident into a question of personal talent, or neglect and disregard Grade I and II cases as mild ones. That would be no different from holding only one medical staff accountable for a medical accident or not actively analyzing and evaluating near-miss incidents. Establishing a culture or system of good information gathering and evaluation of cases of heat illness will contribute to the prevention of serious accidents. When examining a patient with Grade I or II heat illness, the case should not be taken lightly; the patient care should be transferred from an emergency room of a hospital to a clinic (i.e., hospital-clinic cooperation). And the conditions of living environments or sports activity and safety management of the patient must be reviewed together by the attending physicians and those involved. That will lead to the prevention of Grade III heat illness and fatal accident at schools, work places, and homes.

"FIRE" and "A FIRE" as Mnemonic for the First Aid and Prevention of Heat Illness

Care and treatment for early stage of heat illness boils down to *FIRE*, namely: *fluid*, *ice*, *rest*, and *emergency* (**Table 2**). Heat illness is a kind of disease in which the proper care and treatment at the site of onset is extremely important. The mnemonic *FIRE* will help to remember the concepts of heat illness at the sites. The mnemonic for prevention, on the other hand, is *A* (*acclimatization*) + *FIRE*, and it is easy to remember as "a fire." The author has mentioned about this in campaigns and talks with the media as well as on the internet. This proposal to use the mnemonic *FIRE* is fortunately well accepted.

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