Heat hyperpyrexia: time to act

Heat wave continues to be a serious problem for the homeless and the very poor in India. The consequences of heat waves have been appalling, both in the West as well as the East, both in tropical and temperate regions of the world. The recent heat wave that swept Europe in 2003 with a death toll of over 35,000, France accounting for more than 14,000 of them, is but an example of the special vulnerability of the people, particularly the aged and the infirm. The recurrent heat waves in India during the last two years inflicted heavy loss of human lives. Over 1000 lives were lost in Andhra Pradesh (AP) when the temperature touched 122ºF in 2002 and over 1600 in 2003 in the whole of India. Yet, public perception of the hazards of high environmental temperatures is often poor and underplayed by public media and even the medical community. In an exhaustive review on the subject by the Earth Policy Institute\(^1\) a pointed reference is made to India, 'where heat-related fatalities in thousands are no longer uncommon', that the National Disaster Management Cell (NDMC) does not even classify Heat Waves as under 'Natural Disaster'.

Disturbance in the heat regulatory mechanism can lead to different manifestations such as heat exhaustion and heat stroke or hyperthermia, culminating in a 'multi-organ dysfunction syndrome'. Heat exhaustion represents mild to moderate illness due to loss of body fluids and depletion of salt following exposure to high environmental temperatures or intensive physical exercise resulting in intense thirst, weakness, dizziness and fainting and headache. Initially the core temperature may be slightly elevated. When it exceeds 40ºC, it is often accompanied by neurological manifestations such as delirium, convulsions or coma ending in 'heat stroke'. Rise in body temperature above the 'hypothalamic set point' results in hyperthermia. If the body or rectal temperature is below 39ºC, it is considered as mild hyperpyrexia and if over 40ºC as severe heat hyperpyrexia. Nowadays, 'cochleal temperature' is considered a better indicator. If the precipitating cause is high environmental temperature, it is designated as Classical Heat Stroke / Illness (CHS) and if it follows strenuous physical exercise, it is known as Exertional Heat Stroke / Illness (EHI). CHS occurs in young children and elderly persons in whom the thermo-regulatory mechanism is below par or impaired. On the contrary, EHI is encountered in young adults, following strenuous exercise or soldiers on rigorous duty, marathon runners and sportsmen etc. In the latter category there are additional features such as muscle cramps and pain, accompanied by destruction of muscle fibres or 'rhabdomyolysis'.

Historically, a corresponding condition especially in Armed Forces, called 'Exertional Heat Hyperpyrexia', was described in the past as 'Classic Fatigue Syndrome' by the British troops from the days of the Crimean War and Indian Mutiny\(^3\). Sir Victor Horsely an eminent neurosurgeon and pathologist is perhaps the most celebrated victim, who died on duty in the desert in 1916\(^4\). The exhaustive report\(^5\) on 125 cases of heat stroke is an oft-quoted and authoritative treatise on clinical and pathological aspects. A recent report\(^6\) of death due to EHI of a young British Officer Cadet was followed by a vigorous debate on several aspects of exercise schedules in the Royal Army Medical Corps (RAMC), therapy and possible legal implications\(^7\). From time to time, such studies have paved the way for development of more rational management and treatment of cases of heat hyperpyrexia.

Sporadic cases of classical heat hyperpyrexia were known for long throughout the Indian sub-continent, by different names such as, sun- stroke, heat exhaustion, and fatal heat hyperpyrexia. The situation gradually worsened, with increasing urbanisation, construction of 'cement jungles', laying down of asphalt roads and progressive denudation of foliage or forest cover\(^8\). The simultaneous spread of viral diseases and repeated outbreaks of 'encephalitis-like syndrome' in
children in places like Jamshedpur (Bihar) 1954, followed by UP, Delhi, Maharashtra and Tamilnadu, tended to obscure the etio-pathogenesis, since the initial attempts to isolate arbor viruses were non-contributory. However, in places like Nagpur, annually in the months of April to July, an increasing number of cases were seen especially in children. The disease was characterised by high fever of sudden onset, followed by convulsions and sensory disturbances of varying degrees, leading to a high case fatality of 50-60 per cent. When initial investigations by the ICMR during 1967 and 1968 failed to provide any clues to the aetiology of the syndrome, a comprehensive multi-disciplinary clinico-pathological investigation was launched.

It was conclusively established that there was no evidence of any inflammatory process of bacterial or viral aetiology. Neuro-pathological study of the 15 cases of autopsy of the brain demonstrated the total absence of stigmata of encephalitis, but confirmed the presence of 'encephalopathy', caused by high environmental temperature per se or secondarily in association with other endogenous causes. In many of the cases there was multi-organ damage with viscera like the liver, showing extensive degenerative changes, such as piecemeal necrosis, acidophil bodies, fatty infiltration of hepatic parenchyma and phagocytic activity of Kupffer cells, including 'erythropagocytosis'. It may be reiterated that the alternate diagnosis of the so-called Reye's syndrome is often based on liver biopsy findings alone, without taking into account the possible changes in the brain. Such a diagnosis may be passable or acceptable in true cases of endogenous hyperpyrexia occurring off-season. But, it may not be tenable as a separate clinico-pathological entity, arising from purely environmental factors. The distinction between the two was satisfactorily resolved in a primate model of experimental heat hyperpyrexia, on the basis of serial liver biopsies followed by a full autopsy.

To study the pathophysiology rats, rabbits and monkeys have been the preferred experimental animals as compared with dogs, which lack in sweat glands. The pathogenesis or evolution of lesions of multi-organ involvement were found similar to that in humans in a primate model of experimental heat hyperpyrexia. Subsequent studies in primates demonstrated the importance of lipo-polysaccharides as probable cause of hepatic changes as also antibodies against the LPS mitigated the lesions. Experimental heat stroke in rabbits and rats was found to be associated not only with production of IL-1β but was alleviated by 'interleukin-1 receptor antagonist' as well as by HSP expression. A subsequent exhaustive review discusses the present state of knowledge about the pathogenesis of heat stroke, systemic and cellular response to heat-stress including thermo-regulation, acclimatisation, 'acute phase response' and the generation of Heat Shock Proteins. The progression of heat stroke seems to be determined ultimately by the balance between two kinds of cytokine responses, represented by IL-1β and TNF-α as against anti-inflammatory cytokines such as 'acute phase proteins', IL-6 and HSP. It was also reiterated that IL-1 receptor antagonist and glucocorticoids have a protective role. Analogous to changes in sepsis, endotoxaemia and other 'toxic insults' by chemicals, endothelial activation/injury seems to be a major pathway in heat stroke. Microvascular thrombosis, coagulation and fibrinolysis finally result in disseminated intravascular coagulation (DIC). Similarly, adhesion molecule ICAM-1 might adversely affect the Blood Brain Barrier and cause brain lesions. Such vascular changes at the molecular level in the muscles of athletes might even explain rhabdomyolysis of EHI in sportsmen and military personnel, subjected to severe physical exercise. Further, studies are needed on the role of genetic factors in the susceptibility to heat stroke, and the role of the above factors such as cytokines, coagulation proteins and HSPs involved in the adaptation to heat stress.

Experience of physicians in the Middle East has indeed important lessons for the world at large. Perpetually confronted with the dry and high environmental temperatures across the sandy deserts, working conditions over the centuries appear to be appropriately re-adjusted according to the season, like the practice of working in early morning and late evening sessions in summer months and intervening 'mid-day siesta', which incidentally has spread to other Mediterranean countries. By contrast, countries like Israel, oriented to a different 'work culture', adopted a different strategy. Even up to the early 70's Israel imposed strict regulations 'that no
one shall die of heat stroke’. All suspected patients were to be shifted promptly to the nearest ‘Kibutz’ (like our Panchayats), for instituting effective treatment schedules, including ‘rapid cooling by conduction’. Patients were placed on 'large ice blocks' and aerated by big desert blowers. Saudi Arabia, has a very high death toll amongst the millions of Haj pilgrims to Mecca, especially when it coincides with peak of summer period, as per the local ‘Hijra Calendar’. It has contributed to a high level of clinical and scientific research on heat-related disorders. There has been significant progress in the clinical care and management based on new and emerging concepts of molecular biology2,17,18.

There are progressive improvements in the control of temperature in a more rational manner. The earlier practice of dissipation of heat by immersing the patients in ice water has given place to better methods, based on convection and evaporation with the help of tepid water sprays and rapid circulation of surrounding air with the help of fans. Locally adaptable ‘spray shower and blower fan’ technique is not only successful but preferable to ‘body cooling units or beds’ (BCUs). Although the latter may be suitable for certain situations, like military establishments etc, they are costly and unavailable at the site where the victims are located. The relative merits of ‘cold water immersion’ or ‘body cooling blankets’ as against ‘spray and fan techniques’ have been discussed17,18. The risks of peripheral vaso-constriction may have adverse effects on thermo-regulation. Further, from 1995 onwards, an ingenious method of ‘cold intravenous infusion’ has been tried successfully in the Haj pilgrims in Saudi Arabia20.

Confronted with perennial problem of heat hyperpyrexia in several parts of India and even in the Armed Forces and our increasing interests in sports, India should seriously address itself to several issues posed by both classical (environmental) and also exertional heat hyperpyrexia. Tremendous data have been generated in the recent times all over the world. Perhaps institutes like the ICMR's Desert Medicine Research Centre, Jodhpur, Defence Institute of Physiology and Allied Sciences(DIPAS), New Delhi, and the Sports Authority of India should work together to evolve appropriate regulations and therapeutic measures relating to heat hyperpyrexia. It would also be worthwhile to re-examine certain policy issues related to heat hyperpyrexia, like rhabdomyolysis and cramps etc. in the field of sports and evolve rational procedures and schedules so the sportsmen are not adversely effected.

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