Submitted by the expert from Australia

Informal document GRSP-76-01
75th GRSP, 2 – 7 December 2024
Provisional agenda item 24

Heatstroke- Fatal and Non-fatal Conditions

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1. CLIV Heatstroke is caused by Vehicles

When a child is left in a car, the primary cause of paediatric vehicular heatstroke (PVH) is the increase in a car's internal temperature. This increase is associated with a car left out of the shade in average or high ambient temperatures, with a sustained solar irradiance. A secondary cause includes body water loss from the child, increasing humidity inside the vehicle. Most cases occur during day between 4am and 5pm, making up 88% of cases, when ambient temperatures are generally highest (Hammett et. Al., 2021).

Children being left in or gaining access to vehicles causes heatstroke when the previously outlined conditions are met. These children are often unable to leave the vehicle themselves. They also are unable to thermoregulate as well as adults, due to smaller blood volume for heat transfer, higher surface area to body mass ratio and less effective sweating mechanism (NHTSA, 2014; Booth et. Al., 2010). Children are particularly vulnerable to heatstroke due to a variety of factors, some previously covered. This is well borne out in various studies, listing children's size and limited thermoregulation (Booth et. Al., 2010; Forsyth and Solan, 2022)

Heatstroke occurs in people when core body temperature reaches beyond 40°C (Ishmine, 2024). Simulations and measured temperature display that it takes between 20 – 45 minutes to reach 40°C in a vehicle during summer months (Xuhao, 2020; Duzinski et. Al., 2014). Vehicle temperature also reaches above 40°C in most months after a sustained period, while also reaching these within an hour (Kirk and Ewing, 2022; Xuhao, 2020; Duzinski et. Al., 2014). Vehicle paint doesn't change the internal temperature significantly, with both reading 40°C in a similar time, around 35 – 40 minutes

(Kirk and Ewing, 2022; Bazille et. Al., 2005). Furthermore, a review in how ambient extreme heat affects child morbidity found associations with heat-related illness (e.g: heatstroke and heat exhaustion) and high temperatures (Uibel et. Al., 2022).

With these factors, we can say with certainty that CLIV can suffer heatstroke more easily in vehicles due to a rapid increase in temperature, including their inability to thermoregulate compared to adults. Therefore, leaving children in a vehicle with high ambient temperatures results in heatstroke if internal temperatures increase above normal rates.

2. Many Adults Leaving Children Unattended in Cars

A recent survey of US caregivers gave insight into how commonly parents will leave their children in cars. 12% of US adults report leaving their child in a car at least once or being unsure if they have (Sartin et. Al., 2023). Of those that leave their children in cars;

- ~54% left them unattended more than twice per month
- ~19% left them in their car more than 6 times per month
- 12.3% reported leaving them in the car for 16 minutes or more
- 87.7% leaving their child in their car unattended for 15 minutes or less
- 74.3% left them in the higher risk seasons of spring, fall and summer
- ~1.47% of respondents left their children in the car for more than 15 minutes.

It's important to state that this isn't necessarily out in high ambient temperatures. They also sought out caregivers in higher risk states, such as California, Texas and Florida, so the proportions above may be higher than the overall US population. However, with the number of children under 5 in the US being ~22.4 million, there are conservatively tens of thousands of children left in cars for a dangerous amount of time every year (Childstats.gov, 2022).

There are a large number of children who are left in cars but do not die of heatstroke. In only the Australian state of Queensland, over 1113 callouts to rescue children occurred in FY2023 (RACQ, 2024). In South Australia and Victoria, the number of children rescued from cars in 2023 was 308 and 1160 children respectively (Ambulance Victoria, 2023; RAA, 2024). NRMA also reported in 2022 that at least 1882 children were locked in cars that year (Antrobus, 2023). These also don't account for the number of children left in their car that are not rescued by emergency services. As there have only been approximately 30 confirmed Australian deaths from hot cars over the last 25 years, there are likely hundreds or thousands of times more children left in vehicles every year.

This is dangerous, as there is an average increase in 1.77°C (3.2°F) per 5 minutes after a vehicle is parked out in the sun. On average, there is approximately a 22.2 C increase on ambient temperatures of 22.2 – 35.5 C (72 – 96 F) inside a vehicle, with 80% of this increase occurring within the first 30 minutes (McLaren et. Al., 2005).

Therefore, it is possible that many more children experience heat stress or heatstroke while not passing away. We are reaching out to relevant authorities to determine how often emergency services and ambulances are called to the scene. Understanding the non-fatal effects of heatstroke is therefore important, as it might cause a lot of currently unmeasured damage to children and families.

3. Heatstroke - Effects on the Body

There are several ways to define heatstroke, however, most sources agree that it involves core body or body temperature rising above the range of 40 – 40.5°C. Occasionally, patients may have the criteria of heatstroke with body temperatures below this range (Hifumi et. Al., 2018). People can suffer two broad types of heatstroke, exertional and non-exertional. They have slightly different symptoms (Epstein and Yanovich, 2019). Non-exertional occurs while sedentary, sweating may be absent, liver dysfunction may be milder and kidney/liver failure may be less common (<5%). Exertional is sporadic and induced from excess heat production rather than from ambient temperatures. Kidney/liver failure is also more common (25 – 30%). However, they both involve the failure of the body's heat-loss mechanisms, dysfunction in the central nervous system and stress the body's organs (Epstein and Yanovich, 2019).

Criteria for signs of heatstroke from the Japanese Association for Acute Medicine's (JAAM) Committee Related to Heatstroke (HS) were released in 2014 and updated by a working group (WG) in 2016 (Hifumi et. Al., 2018). These include central nervous system, liver system and renal system related criteria. Another common definition of heatstroke used worldwide is Bouchama's definition, involving core body temperature >40°C, exposure to environmental heat and no liver system criteria. The updated JAAM-HS-WG criteria are:

1. Glasgow Coma Scale (GCS) score ≤14
2. Hepatic/Renal dysfunction (Creatinine or bilirubin levels ≥1.2 mg/dL)
3. Coagulation Disorder (JAAM Disseminated intravascular coagulation score ≥ 4).

As body temperature increases, sweating response increases, leading to loss of salts and water causing dehydration and salt depletion (Hifumi et. Al., 2018; Bouchama et. Al, 2022). Sustained loss of water and dehydration impairs thermoregulation and the ability for the body to supply blood and nutrients to the lungs, heart, digestive, excretory, reproductive or circulatory organs. The coagulation response and inflammation that follows leads to blood clots, injury of the inner wall of veins and arteries, as well as suppression of platelet release from bone marrow (Bouchama et. Al., 2022). In addition, this increase in inflammatory and coagulation proteins may be associated with high intracranial pressure, decreased cerebellar blood flow, and severe neuron injury (Shimada et. Al., 2020).

Heatstroke commonly causes brain injury from restricted blood flow, metabolic disorder, release of proteins that induce fever and brain edema. In addition, excess swelling in the brain impairs nerve and blood vessel function (Asmara, 2020). Central nervous system alteration is also a defining feature of heatstroke, including manifesting in coma-like symptoms.

Therefore, heatstroke as a condition causes multiple organ failure, due to and in addition to blood clots, as well as damage to the cardiovascular system. The proportion of heatstroke victims that suffer from coagulation disorder or dysfunction of the central nervous, cardiovascular, kidney, respiratory or liver system is variable. However, presence of organ dysfunction is very common in heatstroke victims, and it's presence is used to diagnose heatstroke (Bouchama et. Al., 2022; Hifumi et. Al., 2018; Asmara, 2020; Bazille et. Al., 2005). [1.]

1. Note: This is a relatively short summary of a very complex and multifactored health issue, and the details of these injuries will not be fully explored in this paper. A recent and comprehensive review can be found at the following link: Classic and exertional heatstroke | Nature Reviews Disease Primers

4. Heatstroke Effects on Adults

Heatstroke manifests in high proportions of the conditions outlined in Section 3 (Schlader et. Al., 2022).

In terms of fatal outcomes for adults, mortality is imprecise, as many often die outside of the hospital during heatwaves. For those admitted to the hospital, mortality ranges from 10 – 65% (Mahri and Bouchama, 2018). Other estimates approximate mortality at <5% for exertional heatstroke (Esptein and Yanovich, 2019). There are also delayed mortality outcomes, with ~10-20% mortality at 1 to 2 years after hospital discharge (Mahri and Bouchama, 2018). Survivability in adults is typically high when not deemed critically ill with heatstroke (Hausfater et. Al., 2010).

Non-fatal outcomes and conditions vary significantly, however, 18% of the surviving patients displayed impairment in their autonomy up to 1 year after the incident (Hausfater et. Al., 2010). Furthermore, due to the damage to arteries, veins and the increase in coagulation of blood, there is also a heightened risk of cardiovascular disease following a single heatstroke occurrence (Schlader et. Al., 2022). This is supported by heatstroke causing the coagulation of blood, leading to blockage in micro-blood-vessels, which are small blood vessels that transport fluid, oxygen and nutrients between blood and surrounding tissue, including the heart, brain and lungs (Bouchama et. Al., 2022). Epstein and Yanovich, 2019). This coagulation induced micro-vessel blockage is supported by lung blockage being found in 60% of post-autopsy heatstroke patients (Bouchama et. Al., 2022).

Lastly, long term neurological conditions, or varying degrees of irreversible brain injury, occur in approximately 10 – 28% of patients who survive either exertional or non-exertional heatstroke (Bouchama et. Al., 2022; Yeo, 2004). Also, core temperatures 38.5° - 40°C can still cause heatstroke in the elderly, as they are similarly vulnerable as children to heat increase from malfunctioning bodily heat loss systems (Bouchama et. Al., 2022). This is concerning, as vulnerable adults are both at high risk of long-term neurological conditions and need a lower core body temperature to suffer from heatstroke.

This further reinforces that a significant number of people who suffer from heatstroke don’t necessarily die from it. There is also a medical consensus that there are medium-long term effects in a proportion of those that suffer from heatstroke. Lastly, not all of those that will eventually die from heatstroke die immediately. Therefore, heatstroke patients could die later after heatstroke and have their deaths or conditions be misattributed to the organ damage caused by heatstroke itself.

If children suffer from the same or similar outcomes as adults from non-fatal heatstroke, then there is a previously unaddressed area of CLIV that has severe implications. As previously established, many more children are left in cars, and likely more don’t die of heatstroke immediately. If mortality of CLIV can occur years after the event then many could have long term conditions or die due to conditions caused by heatstroke.

The concept of long-term cognitive effects is of interest, and will be examined further in the section 5.

5. Heatstroke Causes Long Term Neurological Conditions

Brain tissue is particularly vulnerable to heatstroke based on the available evidence. Particularly vulnerable is the outer layer of the cerebellum at the base of the brain stem, the midbrain, hippocampus and thalamus (Bouchama et. Al., 2022). These areas of the brain control various functions:

- Cerebellum – muscle control, balance, movement (Jimsheleishvili and Dididze, 2023)
- Midbrain - movement and reflexes (Caminero and Cascella, 2022)
- Hippocampus – memory, learning, spatial navigation, emotional behaviour (Anand and Dhikav, 2012)
- Thalamus - relaying motor and sensory information from the body to the brain, as well as pain/arousal regulation, mood and motivation (Torrico and Munakomi, 2023)

This brain damage is illustrated by more than 95% of patients suffering from acute neurological symptoms at the time of heatstroke (Lawton et. Al., 2019). As previously mentioned, central nervous system dysfunction is used to diagnose heatstroke and 10 – 28% of patients develop long-term neurological conditions due to heatstroke (Hausfater et. Al., 2010; Bouchama et. Al., 2022; Bazille et. Al., 2005, Yeo, 2004; Lawton et. Al., 2019). Specifically, these long-term neurological conditions are related to the brain regions mentioned above, particularly in the cerebellum, due to atrophy and cell loss/death (Bazille et. Al., 2005; Bouchama et. Al., 2022; Epstein and Yanovich).

Some of these conditions may persist for weeks after heatstroke and be sustained for years after recovery (Bouchama et. Al., 2022; Epstein and Yanovich, 2019; Argaud et. Al., 2003). Brain damage can be temporary, or result in permanent injury (Shimada et. Al., 2020). Survivors of exertional heatstroke had significantly more severe CNS injury. This was exhibited by higher severe Glasgow Coma Score, and significantly impaired cooling ability (Mengmeng et. Al., 2017). Furthermore, there is often no evidence of structural damage through MRI brain imagery immediately after heatstroke, but evidence of damage to the cerebellum, prefrontal cortex or hippocampus can be found after imaging months after the incident (Leon and Bouchama, 2011). In adults, about 60% of patients who died or suffered long-term neurological conditions had no documented pre-existing medical condition, with an average age of 47 (Lawton et. Al., 2019).

There are several possible causes of these long-term neurological conditions, but heatstroke does likely cause these conditions. Neurological issues are used to diagnose heatstroke, and >95% of heatstroke sufferers present to hospital with acute neurological symptoms. Therefore, it’s highly likely that heatstroke does cause these conditions. For example, greater central nervous system injury, a lower Glasgow Coma Scale (GCS) score, within 24 hours of a hospital visit due to heatstroke was associated with greater risk for long term neurological conditions (Mengmeng et. Al., 2017). The duration of these sustained neurological injuries is unknown, however, significant alterations in neurologic function and brain tissue occur when cerebral temperatures exceed 38°C (Mengmeng et. Al., 2017).

Section 5 displays that long-term neurological conditions can result in severe outcomes for adults who suffer from heatstroke and survive, predominantly with cerebellar conditions (muscle/balance/movement control conditions). Section 6 is an analysis of evidence for these effects presenting in children.

6. Heatstroke Effects on Children: Possible Neurological and Long Term Conditions

Those with impaired heat loss and thermoregulation are commonly represented in the previous section on adults that suffer from heatstroke. It requires a lower ambient temperature for people with limited thermoregulation to attain heatstroke (Bouchama et. Al., 2022). Therefore, as children have much less effective thermoregulation than adults, they are at a higher risk of heatstroke and can suffer from heatstroke at lower temperatures. Heatstroke in children appears to correlate with neurological changes, brain dysfunction or changes in brain structure.

A Hong Kong infant aged 3 suffered from near fatal heatstroke in an enclosed car. This caused multiple organ failure, temporary kidney failure and coagulation of blood causing blood clots (Ozcetin et. Al., 2012). He was in the car unattended for five hours, with a core temperature >40.0°C for 30 minutes after admission to the emergency room. Despite treatment with intensive cooling, neurological conditions persisted. He was discharged from the hospital after 17 days with weaker light reaction reflexes, inability to follow objects, abnormal response to visual stimuli and regression of developmental milestones. There was no follow-up on this case, however, it’s unknown if the child recovered or if the effects lasted long-term.

However, these are similar to long term effects on older adolescents and adults. For example, after a 17-year-old army recruit suffered from exertional heatstroke and an MRI and cognitive reassessment was conducted. These tests showed his intellectual capacity was still present, however, he demonstrated severe memory impairment and rapid forgetting, impaired attention, mental slowing (Romero et. Al., 2000). He also developed personality traits different to those present prior to heatstroke, displaying social impairment and less social inhibition.

The post-mortem findings of children suffering from heatstroke in cars is also similar to adults who died of heatstroke. In autopsies of children left in parked cars for a median time of 4 hours, there were haemorrhages found in the lungs of most victims, as well as the heart and brain in several (Adato et. Al., 2016). This study found that these conditions are consistent with autopsies of adults who died of exertional heatstroke (Adato et. Al, 2016).

Changes in brain structure, or encephalopathies, have been found to have significant correlation with higher environmental temperatures in children under 15 in the Muzaffarpur region in India (Singh et. Al., 2023). These were largely correlated to the heat, rather than infectious causes. This included previous outbreaks of acute encephalopathy. Lastly, some accepted diagnostic criteria for heatstroke in adults includes signs of encephalopathy, core temperature greater than 38 - 40°C and absence of infection (Forsyth et. Al., 2022). Higher body temperature has also been associated with brain edema (Kuki et. Al., 2022).

This section demonstrates some possible harmful effects of heatstroke in children. Children are also more susceptible than the general population (Epstein and Yanovich, 2019). Pre-existing disability is likely not a factor, as children who pass away from PVH have disability and chronic illness similar to the general population (Chandler et. Al., 2023).

7. Conclusions and Limitations of this Paper

Generally, not accounting for heatstroke, it is accepted to avoid hyperthermia in children, especially as brain overheating and other vital physiological functions can be impacted in a developing infant (Bach and Libert, 2022). The information in previous sections describes the effects of heatstroke, the plausible effects on children, as well as how adult studies can represent what may happen in children. The information presented in this paper outlines the following claims:

1. CLIV causes PVH by temperature rising in vehicles while they are trapped inside
2. Not all CLIV die of heatstroke and many adults leave their children unattended in cars, at a rate of ~100 – 1000 times that of CLIV deaths every year
3. Children are more vulnerable to heatstroke than average, due to worse thermoregulation mechanisms, like in the elderly
4. Heatstroke effects are damaging in some form to most visceral organs in the body in adults, including the heart, brain, lungs, arteries and liver/renal systems. Acute/immediate damage to these organs is essential for diagnosing heatstroke
5. Non-exertional and exertional heatstroke have common characteristics, with exertional heatstroke being slightly more severe given equal circumstances, with lower mortality.
6. The neurological effects on adults can be long lasting, with permanent changes to the brain and evidence of neurological conditions lasting at least 1 – 2 years after heatstroke
7. Heatstroke in adults causes long term neurological conditions to occur in 10 - 28% of patients
8. Heatstroke in children left in vehicles does cause damage to organs in similar ways to adult heatstroke based on autopsy results
9. Case studies of heatstroke in children/adolescents from being left in vehicles resulted in neurological conditions present afterwards

If exertional heatstroke in adults is similar in effect on children left in cars in autopsies, and exertional heatstroke has a lower fatality, there could be many more cases of CLIV that suffer from heatstroke and don't die. Heatstroke also causes many long-term conditions and delayed mortality in adults, and the effects of heatstroke seem similar in adults and children. Therefore, we can conclude that its highly likely many more children suffer long-term conditions or delayed mortality after suffering from heatstroke.

It is important to identify the limitations of this paper. Firstly, identifying heatstroke in the hospital is difficult, particularly in children, as many symptoms of heatstroke are similar to sepsis and other diseases (Biswas and Agarwal, 2022). These diseases can be confused as heatstroke, where heatstroke is not the cause of these long-term conditions (Forsyth et. Al., 2022). In addition, post-mortem heatstroke signs are nonspecific. Therefore, haemorrhage, organ failure or other conditions cannot easily be directly associated with autoptic or histological findings, unless all other diseases can be ruled out (Cioffi et. Al., 2024).

Heatstroke in these studies has clearly been identified as the cause of death. Based on the available evidence presented in this paper, heatstroke can cause similar maladies in CLIV as with adults (Adato, 2016). Organ failures are used to diagnose heatstroke in adults, particularly from the GCS and measurement of other biomarkers as with the JAAM, so it's unlikely that child heatstroke patients don't suffer organ damage and organ failure (Hifumi et. Al., 2018; Bouchama et. Al., 2022).

There is also little evidence that children have fewer disabling conditions compared to adults who suffer from heatstroke, either from autopsy results or pathological features. This is because children have lower thermoregulation abilities, which also contributes to adults who suffer from heatstroke. Further, even though heatwaves generally don't increase infant deaths consistently, they may still pose a threat to the infant up until they are 1 year old (Xu et. Al., 2011; Bach and Libert, 2022).

Lastly, as many more children are left in cars than die from them, including in high risk scenarios, we do not know exactly how many children may be placed at risk of non-fatal injuries. We also cannot conduct a causal study to examine if PVH directly causes long term conditions in children, as this study design would be inherently unethical. Children's brains are also developing and may be more vulnerable. We are seeking expert guidance on whether children's developing brains are more vulnerable to permanent damage than adults.

In conclusion, there is worrying evidence of non-fatal injuries due to heatstroke. The costs associated with long term cognitive and organ dysfunction could be significantly larger than previously realised. Ultimately, CLIV is not only about the children that die from heatstroke, but also non-fatal injuries or delayed mortality. The contracting parties to the working group should consider this possibility, as there is growing evidence to support it. Lack of regulation or ineffective regulation may result in greater public scrutiny following the growing body of evidence.

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References

Adato, B., Dubnov-Raz, G., Gips, H., Heled, Y., Epstein, Y. Fatal heat stroke in children found in parked cars: autopsy findings. Eur J Pediatr 175, 1249–1252 (2016). https://doi.org/10.1007/s00431-016-2751-5

Ambulance Victoria. Paramedics urge Victorians to be summer smart - Ambulance Victoria, Ambulance Victoria (2023). https://www.ambulance.vic.gov.au/paramedics-urge-victorians-to-be-summer-smart/

Anand KS, Dhikav V. Hippocampus in health and disease: An overview. Ann Indian Acad Neurol. 2012 Oct;15(4):239-46. doi: 10.4103/0972-2327.104323. PMID: 23349586; PMCID: PMC3548359.

Antrobus, B. 'Highest in five years': Grim detail as NRMA reveals number of kids rescued from hot cars. News.com.au. Available at: https://www.news.com.au/national/nsw-act/news/highest-in-five-years-grim-detail-as-nrma-reveals-number-of-kids-rescued-from-hot-cars/news-story/f9bc1f2f357d6b0658f540b9895ea0fe

Argaud, L. et al. Short- and long-term outcomes of heatstroke following the 2003 heat wave in Lyon, France. Arch. Intern. Med. 167, 2177–2183 (2007). doi: https://doi.org/10.1001/archinte.167.20.ioi70147

Asmara IGY. Diagnosis and Management of Heatstroke. Acta Med Indones. 2020 Jan;52(1):90-97. PMID: 32291378.

Bach V and Libert J-P (2022) Hyperthermia and Heat Stress as Risk Factors for Sudden Infant Death Syndrome: A Narrative Review. Front. Pediatr. 10:816136. doi: 10.3389/fped.2022.816136

Bazille, C., Megarbane, B., Bensimhon, D., Lavergne-Slove, A., Catherine Baglin, A., Loirat, P., Woimant, F., Mikol, J., Gray, F. Brain Damage After Heat Stroke, Journal of Neuropathology & Experimental Neurology; 64(11) (2005), Pages 970–975, https://doi.org/10.1097/01.jnen.0000186924.88333.0d

Agarwal, S. (2022) 'Autopsy Diagnosis of Deaths from Heat Stroke' Biswas, G. Recent *Advances in Forensic Medicine & Toxicology: Volume 3*. Pp. 132 – 143. ISBN: 978-93-90595-32-7

Booth JN 3rd, Davis GG, Waterbor J, McGwin G Jr. Hyperthermia deaths among children in parked vehicles: an analysis of 231 fatalities in the United States, 1999-2007. Forensic Sci Med Pathol. 2010 Jun;6(2):99-105. doi: 10.1007/s12024-010-9149-x. Epub 2010 Mar 4. PMID: 20204546.

Bouchama A, Abuyassin B, Lehe C, Laitano O, Jay O, O'Connor FG, Leon LR. Classic and exertional heatstroke. Nat Rev Dis Primers. 2022 Feb 3;8(1):8. doi: 10.1038/s41572-021-00334-6. PMID: 35115565.

Caminero, F., Cascella, M. Neuroanatomy, Mesencephalon Midbrain. NBK551509. PMID: 31855353

Chandler, M., Schnitzer, P., Dykstra, H., MacKay, M Pediatric vehicular heatstroke: An analysis of 296 cases from the National Fatality Review Case Reporting System. Traffic Injury Prevention. 2023 25(3):400-406. doi: https://doi.org/10.1080/15389588.2023.2290454

(2022) POP1 Child population: Number of children (in millions) ages 0–17 in the United States by age, 1950–2022 and projected 2023–2050. Childstats. Federal Interagency Forum on Child and Family Statistics. Available at: https://www.childstats.gov/americaschildren/tables/pop1.asp

Cioffi. A., Cecannecchia, C., Baldari, B., Simone, S., Cipolloni, L. Fatal Heat Stroke: A Case Report and Literature Review. Forensic Sci. 2024, 4(3), 417-431; https://doi.org/10.3390/forensicsci4030026

Duzinski, S., Barczyk, A., Wheeler, T., Iyer, S., Lawson, K. Threat of paediatric hyperthermia in an enclosed vehicle: a year-round study. Inj Prev 2014;20: 220–225. doi:10.1136/injuryprev-2013-040910

Epstein, Y., Yanovich, R. Heatstroke. N Engl J Med 2019; 380:2449-59. doi: 10.1056/NEJMra1810762

Forsyth, N., Solan, T. It's getting hot in here: heat stroke in children and young people for paediatric clinician. Paediatrics and Child Health 2022; 32(12). Doi: https://doi.org/10.1016/j.paed.2022.10.004.

Hammett, Deborah L. DO∗; Kennedy, Thomas M. MD†; Selbst, Steven M. MD†,‡; Rollins, Amber BSW§; Fennell, Janette E. BA‖. Pediatric Heatstroke Fatalities Caused by Being Left in Motor Vehicles. Pediatric Emergency Care 2021; 37(12):p e1560-e1565. doi: 10.1097/PEC.0000000000002115

Hausfater, P., Megarbane, B., Dautheville, S. et al. Prognostic factors in non-exertional heatstroke. Intensive Care Med 36, 272–280 (2010). https://doi.org/10.1007/s00134-009-1694-y

Hifumi, T., Kondo, Y., Shimizu, K. et al. Heat stroke. j intensive care 6, 30 (2018). https://doi.org/10.1186/s40560-018-0298-4

Jimsheleishvili, S., Dididze, M. Neuroanatomy, Cerebellum. StatPeals 2023. PMID 30844194

Kirk, A., Ewing, J. (2022) Temperature in Cars Survey, RACQ, pp. 1 – 10. Available on request

Kuki, I., Inoue, T., Nukui, M., Okazaki, S., Kawawaki, H., Ishikawa, J., Amo, K., Togawa, M., Ujiro, A., Rinka, H., Shiomi, M. Effect of higher body temperature and acute brain edema on mortality in hemorrhagic shock and encephalopathy syndrome. Journal of the Neurological Sciences 2022; 439. Pp 120321 . doi: https://doi.org/10.1016/j.jns.2022.120321.

Lawton EM, Pearce H, Gabb GM. Review article: Environmental heatstroke and long-term clinical neurological outcomes: A literature review of case reports and case series 2000-2016. Emerg Med Australas. 2019 Apr;31(2):163-173. doi: 10.1111/1742-6723.12990. Epub 2018 May 31. PMID: 29851280.

Leon, L.R. and Bouchama, A. (2015). Heat Stroke. In Comprehensive Physiology, R. Terjung (Ed.). https://doi.org/10.1002/cphy.c140017

Bouchama, A., Mahri, S. Chapter 32 – Heatstroke. Handbook of Clinical Neurology (2018); 157. Pp. 531-545. ISBN 9780444640741

McLaren, C., Null, J., Quinn, J. Heat Stress From Enclosed Vehicles: Moderate Ambient Temperatures Cause Significant Temperature Rise in Enclosed Vehicles. Pediatrics July 2005; 116 (1): pp. e109–e112. 10.1542/peds.2004-2368

Mengmeng, Y. MDa; Li, Zhi MD, PhD; Zhao, Yan MD; Zhou, Feihu MD, PhD; Zhang, Yu MD; Gao, Jingli MD; Yin, Ting MD; Hu, Xin MD; Mao, Zhi MD, PhD; Xiao, Jianguo MD; Wang, Li MD; Liu, Chao MD;

Ma, Liqiong MD; Yuan, Zhihao MD; L, Jianfei MD; Shen, Haoliang MD; Hou, Peter C. MD; Kang, Hongjun MD, PhD. Outcome and risk factors associated with extent of central nervous system injury due to exertional heat stroke. Medicine 2017; 96(44):p e8417. doi: 10.1097/MD.0000000000008417

Rudd, R., Prasad, A., Weston, D., & Wietholter, K. (2015, July). Functional assessment of unattended child reminder systems. (Report No. DOT HS 812 18). Washington, DC: National Highway Traffic Safety Administration.

Ozcetin M, Arslan M, Yilmaz R, Yildirim A. Rare Cause of Cerebral Damage: Child with Heatstroke Found inside an Enclosed Vehicle. Hong Kong Journal of Emergency Medicine. 2012;19(2):126-129. doi:10.1177/102490791201900208

(2023) Worrying spike in number of kids and pets locked in cars as summer heats up. Royal Automobile Association of South Australia. Available at: https://daily.raa.com.au/worrying-spike-in-number-of-kids-and-pets-locked-in-cars-as-summer-heats-up/

(2024) For the Greater Good Report. Royal Automobile Club of Queensland. Available at: https://www.racq.com.au/-/media/project/racqgroup/racq/pdf/about-us/annual-reports/fy24-for-the-greater-good-report-racq.pdf?rev=5f39bd0a393b42e487382f096a481393&hash=A830EC89E5A8AEEF552CFD15F17F6CE9

J. Romero, F. Clement, C. Beiden, Neuropsychological Sequelae of Heat Stroke: Report of Three Cases and Discussion, Military Medicine 200; 165(6). Pp. 500–503. doi: https://doi.org/10.1093/milmed/165.6.500

Sartin, E., Metzger, K., Maheshwari, J. US caregivers' attitudes and risk perceptions towards pediatric vehicular heatstroke: A national survey. Accident Analysis & Prevention 2023; 190. Pp.107147. doi: https://doi.org/10.1016/j.aap.2023.107147

Schlader ZJ, Davis MS, Bouchama A. Biomarkers of heatstroke-induced organ injury and repair. Exp Physiol. 2022 Oct;107(10):1159-1171. doi: 10.1113/EP090142. Epub 2022 Jun 14. PMID: 35654394; PMCID: PMC9529995.

Shimada, T., Miyamoto, N., Shimada, Y., Watanabe, M., Shimura, H., Ueno, Y., Yamashiro, K., Hattori, N., Urabe, T. Analysis of Clinical Symptoms and Brain MRI of Heat Stroke: 2 Case Reports and a Literature Review. Journal of Stroke and Cerebrovascular Diseases 2020; 29(2). pp. 104511. doi: 10.1016/j.jstrokecerebrovasdis.2019.104511.

Singh AK, Jhalani M, Shahi SK, Christopher R, Kumar B, Das MK. Acute Encephalopathy in Children From Muzaffarpur, Bihar, India, and the Potential Role of Ambient Heat Stress-Induced Mitochondrial Dysfunction. Cureus. 2023 Apr 3;15(4):e37073. doi: 10.7759/cureus.37073. PMID: 37153288; PMCID: PMC10156069.

Torrico, T., Munakomi, S. Neuroanatomy, Thalamus. StatPeals. PMID: 31194341

Uibel D, Sharma R, Piontkowski D, Sheffield PE, Clougherty JE. Association of ambient extreme heat with pediatric morbidity: a scoping review. Int J Biometeorol. 2022 Aug;66(8):1683-1698. doi: 10.1007/s00484-022-02310-5. Epub 2022 Jun 25. PMID: 35751701; PMCID: PMC10019589.

Ishmine, P. Heat stroke in children. Available at: https://www.uptodate.com/contents/heat-stroke-in-children#references

Xu, Z., Sheffield, P.E., Su, H. Wang, X., Bi, Y., Tong, S. The impact of heat waves on children's health: a systematic review. Int J Biometeorol 58, 239–247 (2014). https://doi.org/10.1007/s00484-013-0655-x

Xuhao, L., Wenchao, H., Liang, L. Analysis of Hyperthermia of Children in Enclosed Vehicle. IOP Conf. Series: Earth and Environmental Science 2020; 714. pp. 042073. doi: 10.1088/1755-1315/714/4/042073

Yeo TP. Heat stroke: a comprehensive review. AACN Clin Issues. 2004 Apr-Jun;15(2):280-93. doi: 10.1097/00044067-200404000-00013. PMID: 15461044.