Storage Temperatures of Medications: Does it really matter?!?

Helicopter Emergency Medical Services Programs throughout the country all have varying protocols for medications and what to do with the extreme temperatures, but there is not a consistent protocol or accepted policy across the board. The question of whether temperatures affect medications EMS carries is a topic that is only minimally researched.

Most of the medications HEMS and ground EMS carry are intended for storage at "controlled room temperature". In the United States, standards for medicines are set by the United States Pharmacopeial Convention Inc. (USP), a nongovernment entity that establishes standards intended to ensure the quality of medicines and other healthcare technologies. Among other things, the USP prescribes the packaging, storage and distribution of medications. Table I lists some common EMS medications and the temperature-related storage directions on the package label.

Two studies have measured medication storage temperatures in the air-medical setting. The first reported temperatures were recorded inside medication bags kept on two different helicopters in Delaware. Average temperatures ranged from as low as 13.2°C (55.8°F) in winter to as high as 31.2°C (88.2°F) in summer. Roughly half of the winter temperature measurements were below 15°C (59°F) and about 40% of the summer temperature measurements were above 30°C (86°F). The second aeromedical study reported temperatures inside the drug box kept on one air-medical helicopter in northern New Jersey. The helicopter was usually stationed on a rooftop heliport, but it was moved into a hangar during bad weather. Temperatures were recorded for nine weeks during summer and three weeks during winter. More than a third (37%) of the summertime temperature measurements exceeded 25°C (77°F) and 6% exceeded 30°C (86°F); 83% of the wintertime temperature measurements were below 15°C (59°F).

Less than 10 laboratory studies have been designed to test the exposure to out-of-hospital environments and temperatures and then test for changes in medication potency.

The first one was conducted in 1993, when researchers exposed four EMS medications—atropine, lidocaine, epinephrine and naloxone—to temperatures ranging from -20°–70°C (-4° – 158°F). When compared with control samples, none of the tested medications showed significant changes in their chemical makeup.

The following year, researchers from North Carolina, exposed both 1:1,000 and 1:10,000 concentrations of epinephrine to cycles of either heat or cold. Heated samples were warmed to 70°C (158°F) and then allowed to return to room temperature; cooled samples were placed in a freezer until they reached 5°C (41°F) and then removed and allowed to return to room temperature. While the potency of 1:1,000 epinephrine did not diminish, the 1:10,000 epinephrine that was exposed to cyclical heating underwent significant degradation, losing 64% of its potency after the 12-week experiment.

Third a study reported in 1999 compared degradation in diazepam and lorazepam exposed to three different storage arenas: refrigerated at 4°–8°C (39.2°–46.4°F), on an ambulance, and in an oven at 37°C (98.6°F). After 210 days, the concentration of refrigerated diazepam dropped 7%, diazepam stored on the ambulance had a 15% reduction in concentration, and diazepam stored at 37°C (98.6°F) had a 25% loss of concentration. Lorazepam stored in a refrigerator had a 0% drop in concentration, stored on the ambulance a 10% loss of concentration, and stored at 37°C (98.6°F) a 75% reduction in concentration.

Fourth, In 1999, researchers from the Denver, CO, area published a research abstract, but not a complete paper, about epinephrine stored on EMS vehicles there. The recorded temperatures ranged from -7.6°–38.6°C (18.3°–101.5°F) in urban settings and from 0.4°–40.2°C (32.7°–104.4°F) in rural settings. By comparison, medications stored at the EMS office experienced temperatures that met the USP definition of "controlled room temperature." After six months on the ambulances, physiologic activity was determined in a laboratory by injecting the epinephrine into heart tissues and observing the response. When compared with the epinephrine stored in the office, there was significant degradation in both chemical structure and physiologic activity of the epinephrine stored on the EMS vehicles.

In 2007, another study set out to determine the remaining concentration of 23 commonly carried emergency medical services medications used in the United States after they have experienced thermal extremes in the prehospital environment for a period of 1 month. Medications were thermally cycled (−6°C and 54°C) every 12 hours and then assessed by liquid chromatography. Eight (35%) of 23 prehospital pharmaceuticals revealed ending concentrations of less than 90% with strong correlation to thermal exposure time. These included lidocaine, diltiazem, dopamine, nitroglycerin, ipratropium, succinylcholine, haloperidol, and naloxone.

Lastly and the most current study, in 2013, medications when stored at room temperature or in the emergency physician transport vehicle, lorazepam became unstable within 4 weeks. Succinylcholine chloride was stable for 2 months at room temperature and for 1 month in the emergency physician transport vehicle. Epinephrine remained stable for several months, even under room temperature and emergency physician transport vehicle conditions. A drug was considered stable if its content was above 90%.

So, are medications that are kept on helicopters stored in compliance with the standard for "controlled room temperature"? No. If medications are not stored at "controlled room temperature," does that affect their potency? Maybe some drugs including epinephrine, diazepam, succinylcholine and lorazepam. Many medications, though, have never been tested.

In most systems, current EMS medication storage practices are not consistent with USP standards. Exposure to excessive heat and excessive cold are both common. Although the clinical implications of noncompliant storage remain unclear, it's in the best interest of patients to do everything possible to meet the standards. All EMS systems should develop a plan for medication storage that strives to achieve compliance with the USP standards, and reevaluate that plan on a regular basis.

Table I: Common EMS Medications and Their Recommended Storage Temperatures

Medication	Recommended Storage Temperature
Adenosine	15°–30°C (59°–86°F). Do not refrigerate.
Albuterol sulfate	2°–25°C (36°–77°F)
Amiodarone	Controlled room temperature 25°C (77°F)
Atropine	15°–30°C (59°–86°F)
Calcium chloride	15°–30°C (59°–86°F)
Diazepam	At or below 25°C (77°F)
Diltiazem	25°C (77°F); excursions permitted to 15°–30°C (59°–86°F)
Diphenhydramine	15°–30°C (59°–86°F). Protect from freezing.
Dopamine	Controlled room temperature 15°–30°C (59°–86°F)
Epinephrine 1:1,000	15°–30°C (59°–86°F)
Epinephrine 1:10,000	15°–30°C (59°–86°F)
Furosemide	15°–30°C (59°–86°F)
Glucagon*	Controlled room temperature 20°–25°C (68°–77°F)
Ipratropium bromide	2°–25°C (36°–77°F)
Lidocaine 2%	25°C (77°F)
Magnesium sulfate	15°–30°C (59°–86°F). Protect from freezing.
Midazolam	15°–30°C (59°–86°F)
Morphine sulfate	Controlled room temperature 15°–30°C (59°–86°F) Do not freeze.
Naloxone	Controlled room temperature 15°–30°C (59°–86°F)
Sodium bicarbonate	15°–30°C (59°–86°F)

*Glucagon before reconstitution.

Resources:

U.S. Pharmacopeia: 2001 Annual Report. Rockville, MD: United States Pharmacopeial Convention, 2002.

U.S. Pharmacopeia: National Formulary (USP-25/NF-20). Rockville, MD: United States Pharmacopeial Convention, 2000.

Madden JF, O'Connor RE, Evans J. The range of medication storage temperatures in aeromedical emergency medical services. Prehosp Emerg Care 3:27–30, 1999.

Szucs P, Allegra JR, Fields LA, et al. Storage temperatures of medications on an air medical helicopter. Air Med J 19(1):19–21, 2000.

Johansen RB, Schafer NC, Brown PI. Effect of extreme temperatures on drugs for prehospital ACLS. Am J Emerg Med 11:450–452, 1993.

Grant TA, Carroll RG, Church WH, et al. Environmental temperature variations cause degradation in epinephrine concentration and biologic activity. Am J Emerg Med 12:319–322, 1994.

Cairns CB, Cain BS, Honigman B, et al. Prehospital storage degrades the physiological effects of epinephrine in human myocardium (abstract)

Gammon, Dustin CCEMT-P, et al. Alteration in prehospital drug concentration after thermal exposure. Am J Emerg Med 26:566-573, 2008.

Gottenwald MD, Akers LC, Liu PK, et al. Prehospital stability of diazepam and lorazepam. Am J Emerg Med 17:333–337, 1999.

De Winter, Sabrina PharmD, et al. Impact of Temperature Exposure on Stability of Drugs in a Real-World Out-of-Hospital Setting, Annals of Emergency Medicine, 62:380-387, 2013.