Temperature Control of Prehospital Medications:

“Who’s Burning Who??”
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Reality Check

• "Instead of getting married again, I'm going to find a partner I really don't like and just give her a house."  Steven Seagal

• "The problem with the designated driver program, it's not a desirable job. But if you ever get sucked into doing it, have fun with it. At the end of the night, drop them off at the wrong house."  Jeff Foxworthy

• "Why does Sea World have a seafood restaurant? I'm halfway through my fish burger and I realize, "Oh, my Goodness... I could be eating a slow learner."  Lynda Montgomery

• "Relationships are hard. It's like a full time job, and we should treat it like one. If your boyfriend or girlfriend wants to leave you, they should give you two weeks' notice. There should be severance pay, and before they leave you, they should have to find you a temp."  Bob Ettinger

• "My Mom said she learned how to swim when someone took her out in the lake and threw her off the boat. I said, 'Mom, they weren't trying to teach you how to swim.'  Paula Poundstone"
The use of medications in the out-of-hospital environment may benefit certain patients:

- Asthma
- Seizures
- Hypoglycemia
- Cardiac Arrest
- Arrhythmia
What is clear is that the environment that medications are being taken into is different from an in-house pharmacy.
DOES IT MATTER???
DOES IT MATTER???
Revisions in the standards of the United States Pharmacopeia (USP) related to product dating, packaging, and temperature monitoring are discussed. USP has revised product dating specifications as they relate to pharmacy practice.

“Revised USP standards for product dating, packaging, and temperature monitoring.”
Okeke CC, Bailey L, Medwick T, Grady LT
“A drug is deemed to be adulterated if the methods used in or the facilities or controls used for the drug’s manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with good manufacturing practice to assure that such drug has the identity and strength, and meets the quality and purity characteristics which such drug purports or is represented to possess…”

21 USCA 351(a)(2)(b) – 351 (c)
The United States Pharmacopeia and National Formulary (USP 24/NF19, 2000)
USP requires that the pharmacy facility where dispensing or repackaging occurs be maintained at a controlled room temperature such that the calculated mean kinetic temperature does not exceed 25 degrees C.
Controlled Room Temperature – A temperature maintained thermostatically that encompasses the usual and customary working environment of 20 – 25 degrees C (68 – 77 degrees) that results in a mean kinetic temperature calculated to be not more than 25 degrees, and that allows for excursions between 15 and 30 degrees C (59 and 86 degrees F) that are experienced in pharmacies, hospitals, and warehouses.
\[ \text{MKT} = T_k - 273.2 \]

\[-10,000 \]

\[ \ln \left( e^{-10,000} + e^{-10,000} + \ldots + e^{-10,000} + e^{-10,000} \right) \]

\[ \frac{\text{T1H} + \text{T1L} + \ldots + \text{TnH} + \text{TnL}}{2n} \]
Drug Adulteration

In Prehospital Emergency Medical Services

A Report of Findings in Science, Practice, Law and Government

Robert C. Kellow
Carter L. Ferguson, JD
Wade N. Spruill, Jr.

October 1994
Concern over the de-stabilizing effects of temperature extremes on prehospital drugs was first reported in 1985. The Palmer study found that temperatures encountered in the prehospital setting are far more extreme than those required for safe drug storage. Further, excessive medication temperatures are sustained, disproportionate to their ambient environment. The study did not report the effects of extreme cold conditions or prehospital exposure to sunlight and humidity. It did suggest that drugs used in the prehospital setting are being chemically altered as a result of the uncontrolled storage conditions that are indigenous to the EMS setting.

Subsequent studies reported results that appear to be associated with the length of exposure to temperature extremes. One study reported an 11 percent loss of parent isoproterenol and changes in the ionized state of epinephrine after four weeks of exposure to extreme heat. Another showed no changes in the drugs tested when subjected to 16 hours of variable temperature extremes. No studies conducted to date have attempted to determine the remaining bioactivity in drugs subjected to temperature extremes.

Investigation into the effects of excessive temperatures on drugs is not limited to the United States. In 1991, Horderzen, et al. reported the effect of temperature extremes on a consignment of drugs that was shipped from the Netherlands to the Nile Province Essential Drugs Project in Sudan. They were subsequently transferred to the Central Medical Stores in Khartoum. An analysis of their potency
“Prehospital storage degrades the physiological effects of epinephrine in human myocardium”

Cairns CB, Cain BS et al
Annals of Emergency Medicine
[ACEP Research Forum Abstracts],
1999, Oct, Part 2, 34(4)
Constant (169 total hours of heat exposure) heating resulted in complete degradation of both compounds (epinephrine) and dark brown discoloration of the solution. Cyclical heating (672 total hours of heat exposure) resulted in a 31% reduction in EPI concentration and a 225% increase in EPI-SA concentration with no discoloration of the solution.


Thermal degradation of injectable epinephrine.
Church WH, Hu SS, Henry AJ
Department of Chemistry, East Carolina University, Greenville, NC 27858.
Prehospital Stability of Diazepam and Lorazepam

Gottwald, PharmD, Akers, MS, and Liu, MD
American Journal of Emergency Medicine, Volume 17, #4; 333-337

Department of Clinical Pharmacy, University of California
San Francisco, CA
Prehospital Stability of Diazepam and Lorazepam

Subjected samples of Valium and Ativan to temperatures ranging from refrigeration to 37 degrees centigrade (98.6 farenheit) for periods up to 210 days.

Samples were analyzed at 30 day intervals using HPLC analysis.
The degradation of Valium is accompanied by the appearance of a yellow color produced by a "benzophenone derivative"
“When the ambient storage temperature is 30 degrees or less, ambulances carrying Ativan and Valium should be restocked every 30 to 60 days. When drug storage temperatures exceed 30 degrees C, more frequent stocking or refrigeration is required.”

Gottwald et al “Stability of Diazepan and Lorazepam”
The degradation of drugs carried in EMS drug boxes produces breakdown products the effects of which cannot be predicted.
“The results indicate that drug storage temperatures in some prehospital rescue vehicles exceed USP guidelines. Mechanical cooling of the storage compartment results in drug storage temperatures within the USP guidelines. Mechanical cooling of drug storage compartments on vehicles is technologically and financially possible.”


Drug storage temperatures in rescue vehicles.
DuBois WC
“This study demonstrates that out-of-hospital medications are subject to temperatures both above and below recommended storage temperatures. Time-temperature indicator labels can reliably monitor exposure to elevated temperatures.”

Acad Emerg Med 1999 Nov;6(11):1098-103

Storage temperatures of out-of-hospital medications.
Allegra JR, Brennan J, Lanier V, Lavery R, MacKenzie B
Bay Temperatures Showed a Steady Rise During the Summer Texas Heat
Drug box temperatures showed a more gradual and less extreme rise.
Comparison shows the greater temperature change on the Bay.
At all times, and in all measurements...

...temperatures exceeded recommended storage temperatures
Average Temperatures Exceeded the safe range at all times
75% degradation of Ativan in the ambient temperatures of Texas
Almost no degradation of Ativan in the ambient temps of San Francisco.
15% degradation of Valium in the ambient temperatures of San Francisco
25% degradation of Valium in the ambient temperatures of Texas.
The Simple Reality:

It has been shown time and again that EMS drugs are regularly subjected to temperatures outside of recommended storage recommendations.

EMS Drugs are adulterated!!
Do it really make a difference?
Does receiving only a half milligram of Ativan, or only three milligrams of Valium make a potential difference in the seizure patient?
Does receiving only a half milligram or even a fourth of a milligram of epinephrine instead of a whole milligram make a difference in the setting of cardiac arrest?
Does receiving dosages of butyrophenones and epinephrine-sulfonic acid cause toxic effects in the human?
Are we not administering unprescribed chemicals when we give drugs that have, or may have, breakdown products in the fluid?
Even if we change out drug boxes once a week –

OR EVEN DAILY –

THE MEDICATIONS ARE STILL ADULTERATED!!
Reality Check, continued

• "The day I worry about cleaning my house is the day Sears comes out with a riding vacuum cleaner." Roseanne

• "I think that's how Chicago got started. A bunch of people in New York said, 'Gee, I'm enjoying the crime and the poverty, but it just isn't cold enough. Let's go west.'" Richard Jeni

• "If life was fair, Elvis would be alive and all the impersonators would be dead." Johnny Carson

• "Sometimes I think war is God's way of teaching us geography." Paul Rodriguez

• "My parents didn't want to move to Florida, but they turned sixty, and that's the law." Jerry Seinfeld

• "In elementary school, in case of fire you have to line up quietly in a single file line from smallest to tallest. What is the logic? Do tall people burn slower?" Warren Hutcherson

• "Bigamy is having one wife/husband too many. Monogamy is the same." Oscar Wilde
Organized Medicine in General

NO POSITION
...CAN YOU CALL BACK AFTER LUNCH??
Dry **Cool'Em**/Heat'Em

Hydrated **Cool'Em**/Heat'Em

Use **Em** Cold

0 - 10°F

Flexible

Adaptable

Reusable

Use **Em** Hot

140 - 160°F
CFE Medical Products
Laramie Wyoming
fcylvick@drugcase.com

$495 - $715

17 x 16 x 7H
21 x 16 x 16H
21 x 16 x 21H
Very reliable sensors and electronics control the thermoelectric heat pump to assure the MC-2000 drug case will keep medications in the recommended storage temperature range of 59 - 86 degrees F (15 - 30 degrees C) in ambient temperatures ranging from 20 - 120 degrees F (-8.7 - 48.9 degrees C).

- Solid state controls - no moving parts
- Very quiet brushless fan
- Adjustable temperature set point
- Operates with any 12 VDC vehicle power
- or 110 VAC with optional power adapter
- Internal storage temperature displayed on digital panel
MC-2000 has FDA approval to market. (according to the manufacturer)
“No demand”
“Very new”
“No orders for them”
“One person has called”
“It was too big for the unit”
WHAT

REALLY

IS

THE

FUTURE?!?!
Synthesis
Can we resolve this medications temperature problem??
Immediate Issues

1. Drug boxes have to be changed out more often if the boxes are not kept refrigerated. How often?
2. Ativan needs to be refrigerated.
3. Little is published about the other drugs
4. Epinephrine is known to break down also, which should mean that Levophed does also
5. Pills in a solid matrix are known to be temperature stable
“William Moore" <wmoore@etmc.org>
Solution from Carrollton, Texas

Backpack Cooler
(from Costco, I think)
That wasn't chicken.
Future Issues and Dilemmas

1. Future ambulances should be equipped with chambers that maintain temperature.
2. Problem is, the technology is not commonplace at this time.
3. Optional temperature control devices are available from ambulance makers, but at what cost?
Are ambulance services prepared to spend costs approaching $1,500 per rig to adequately equip EMS units - ANY VEHICLE CARRYING MEDS - for temperature control of medications?
The Texas Department of Health has issued a warning to all providers of Emergency Medical Services that the operators of the vehicles will be responsible for the proper storage of medications and devices, or face possible state action against their license and operation.
...thank you for your kind attention