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Hypothermia Evidence, Afterdrop, and Practical Experience

To the Editor:

We congratulate Zafren et al[1] for their recent publication "Wilderness Medical Society practice guidelines for the out-of-hospital evaluation and treatment of accidental hypothermia." In particular, we commend them for identifying clinically important questions and attempting to answer these using an evidence-based approach. We would like to share our opinion that much remains unknown about the optimal management of accidental hypothermia patients and that significant controversies remain. Our intention is to underline that the evidence supporting some of the Wilderness Medical Society (WMS) recommendations may not be as robust as suggested by their evidence grades. We are particularly concerned by the prominence of afterdrop and the WMS guideline's recommendation for patients with mild hypothermia to avoid standing or walking for 30 minutes. Strict adherence to this part of the WMS guideline has the potential to cause harm, particularly in the mountain environment. Even in organized mountain rescue, shelter and rewarming resources are usually limited and "staying put" can trap subjects and rescuers into a protracted rescue and unnecessary cooling.

The authors of this WMS guideline[1] state they "considered only peer-reviewed randomized controlled trials (RCTs), observational studies, case series, and case reports related to evaluation and treatment of accidental hypothermia." One hundred and twenty references are listed: 3 are clinical RCTs (representing approximately 182 mild and 19 moderate or severe hypothermia patients),[2–4] approximately 14 are case series, 33 are single case reports, and 30 are experimental physiology studies. In the supplemental materials, the authors of the guideline refer to experimental physiology studies as RCTs, without reference to their important limitations for clinical practice (especially for moderately and severely hypothermic patients) and without balancing the findings against the evidence from clinical studies. Cooling experiments in humans are ethically limited to normothermia or mild hypothermia (body core temperature $>32^\circ$C). In these experimental studies, the subjects are generally healthy, mildly hypothermic, and no adverse events are triggered.[5,6] It is, therefore, difficult to understand how such studies could provide adequate evidence to justify Grade 1 recommendations for real patients.

Organ failure (eg, cardiac, pulmonary) is an important early complication of accidental hypothermia. It can be caused in whole or in part by hypothermia, by comorbid illness (eg, trauma, intoxication, preexisting disease) or by patient management (eg, rewarming, resuscitation). The incidence of organ failure as it relates to various management strategies remains largely unknown.[7] Older or more comorbid patients tend to have higher morbidity and mortality rates.[8] During the prehospital phase, malignant arrhythmias causing cardiac arrest are the most feared complication, but we do not know why some patients continue to perfuse at temperatures less than 24°C whereas others have cardiac arrest. Even more intriguingly, some patients will rewarm unscathed whereas others will have fatal complications.[8]

The lack of RCTs and our inability to ethically study moderate and severe hypothermia ($<32^\circ$C) has led some experts to rely on surrogate markers for potential morbidity. Given that colder patients have higher morbidity, it might seem reasonable to use core temperature as a surrogate for potential morbidity. Extending this logic further, it might seem reasonable to recommend rewarming techniques that minimize core temperature drop after rescue and during rewarming—the "afterdrop." This word appears more than 20 times in the WMS guideline[1] and seems to have critical importance. In our opinion, the clinical significance of afterdrop in the clinical management of accidental hypothermia patients is unknown. A small drop in core temperature after the start of rewarming is a thermodynamic fact for any simple solid that has a warmer core and a colder exterior. The heat from the warm core will continue to be conducted to the colder parts, until such time as the outer portions of the solid equilibrate with the core. Once this happens, the core temperature will stabilize and then start to climb. Humans are more complex because circulation can cause convective heat transfer and various tissues can generate heat. Careful physiology experiments involving mild hypothermia using active rewarming have consistently demonstrated an afterdrop of approximately 0.5°C in controls and approximately 1°C in subjects who are exercised or in whom shivering is chemically impaired.[5,6] However, one clinical RCT and several clinical case series have failed to demonstrate any afterdrop in patients during rewarming.[4,9,10] The choice of the WMS guideline[1] to highlight that afterdrop "can be as much as 5°C to 6°C" is questionable as it is based on 1 case report and 2 case series that measured rectal temperatures (not recommended by the WMS guideline,[1] as rectal temperatures "can give the false impression that the patient is still cooling") and likely provided suboptimal prehospital insulation. In one of these series, the investigator (Fox et al. *Aviat Space Environ Med.* 1988) admits that as "the severity of hypothermia increased, less prehospital rewarming was done." This highlights the difficulty of assessing the cause and relevance of afterdrop in the prehospital environment where patients may be exposed to further cold stress or have altered thermoregulatory function or comorbid illness.

Rescue collapse is not uncommon in terrestrial rescue of severely or profoundly hypothermic patients.[7] No reports exist of collapse of mild hypothermic patients in the absence of comorbidities such as asphyxia or medical conditions that predispose to cardiac instability. Therefore, in a terrestrial rescue environment, after the patient has been assessed as having mild hypothermia, and given calories and improved insulation, a good strategy is often to walk the patient to safety. That becomes more important when resources such as insulating bags, stretchers, personnel, and transport facilities are limited, or there are other patients requiring many rescuers to effect an evacuation.

The vast majority of patients with mild hypothermia will rewarm during the evacuation phase, and there are no data to indicate that allowing these patients to stand or walk is dangerous. It is our opinion that the recommendation to limit physical effort of all hypothermic patients in the initial stages of rescue be revised to only include moderately, severely, and nonambulatory hypothermic patients. We further suggest lowering the grade of recommendations for situations in which clinically oriented data are lacking.

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Hypothermia Evidence, Afterdrop, and Guidelines

To the Editor:

We thank Brown et al for their response[1] to our article "Wilderness Medical Society practice guidelines for the out-of-hospital evaluation and treatment of accidental hypothermia."[2] We did our best to use the available evidence to provide useful guidelines. Although we agree that some aspects regarding management of accidental hypothermia are controversial, the basics of hypothermia pathophysiology are well established. We disagree with the assessment of Brown et al that the evidence is not sufficiently robust to guide treatment.

The basis of our recommendation to delay standing or walking a mildly hypothermic patient for 30 minutes is related to the potential for afterdrop as well as hypotension with clinical deterioration.[3,4] We should have been more explicit that this recommendation does not apply to a mildly hypothermic patient who is already walking, and may not be advisable when rescuers have limited resources to provide shelter and rewarming. We advise practical and sensible application of the guidelines rather than strict adherence. Rescue personnel should do the best they can under the circumstances.

Brown et al counted the types of studies in our list of references. We reviewed all the relevant studies we could identify. In the supplemental materials,[2] we mentioned that the experimental physiology randomized clinical trials we cited were limited to studying nonhypothermic or mildly hypothermic subjects. The subjects were generally young and healthy. It is probable that afterdrop would be greater and adverse effects more likely in older, less healthy, and more severely hypothermic patients, especially when hypothermia is combined with volume depletion and exhaustion under field conditions.

Brown et al suggest that it would be better to wait for stronger evidence to make Grade 1 recommendations. We used the classification system of the American College of Chest Physicians in which recommendations are Grade 1 (strong) or Grade 2 (weak).[5] The strength of evidence is rated separately by a letter. For example, Grade 1A is a strong recommendation based on strong evidence. Providers of medical care often must act with incomplete information, especially in the prehospital setting. We attempted to be conservative in our recommendations to avoid harm to patients. It is appropriate to make strong recommendations based on low-quality evidence when potential benefits clearly seem to outweigh risks. Guidelines that make mainly Grade 2 (weak) recommendations do not provide much guidance to those who use them.

We agree with Brown et al that organ failure, particularly ventricular fibrillation causing circulatory arrest, is important. It is the main cause of death due to hypothermia. We also remind our readers that "there is great variation among individuals in response to core temperature, as with any other physiologic parameter."

There is good evidence to suggest that afterdrop and peripheral vasodilation are clinically important and should be minimized in moderate and severe hypothermia to decrease morbidity and mortality.[3,6–8] Experimental evidence in humans demonstrates that circulation contributes more to afterdrop than conduction.[9] It is not possible to decrease the conductive component of afterdrop, but it is possible to limit the contribution of circulation.

We do not state or imply that rewarming causes afterdrop. Any intervention that increases blood flow to cold extremities, including some rewarming methods, increases afterdrop. The studies that Brown et al cite in which hypothermic patients were rewarmed without afterdrop were in-hospital studies. The patients likely had already experienced afterdrop in the prehospital phase. Our recommendations are to avoid movement or warming of extremities initially to limit afterdrop caused by return of cold peripheral blood to the core.

Brown et al are correct that rescue collapse occurs in terrestrial rescue. It is usually impractical to measure core temperature before rescue collapse. A patient who has had rescue collapse is assumed to have been moderately or severely hypothermic. For this reason, there is unlikely to be a report of rescue collapse of a mildly hypothermic patient without comorbidities. Like Brown et al, we recommend giving a mildly hypothermic patient additional insulation and calories. For the source of calories, we recommend high carbohydrate liquids and food.[2] If adequate resources are not available, the patient might need to walk to safety, with an