

# Prevention and Treatment of Hypothermia in Trauma Patients

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**Learning Objectives:** 1) to review the risk factors for hypothermia in the trauma patient; 2) to discuss the use of therapeutic hypothermia in trauma; and 3) to become familiar with strategies for preventing and treating hypothermia.

## Abstract

Hypothermia occurs in trauma patients because of decreased heat production, impaired thermoregulation, exposure, transfusion of cold fluids and blood, opening of body cavities, and associated medical conditions. Although hypothermia may be beneficial in selected patients with neurologic injury and after out-of-hospital cardiac arrest, hypothermia may be associated with increased morbidity and mortality due to impaired coagulation, cardiovascular abnormalities, and infections. Treatment of hypothermia begins with prevention of further heat loss, increasing ambient temperature, use of efficient fluid-warming devices, and convective warming. Newer warming techniques such as use of garments with circulating water may prove to be useful because of the greater energy transfer compared with convective warming. Active core rewarming techniques increase core temperature by 1.5°C to 2.5°C per hour and can be life-saving in the hypothermic trauma patient with adequate perfusing rhythm.

Hypothermia is a commonly encountered problem in patients sustaining traumatic injuries. Although hypothermia decreases metabolic function of the body and is cerebroprotective, hypothermia most often results in deleterious effects in traumatized individuals. The adverse effects of hypothermia in the trauma patient include major coagulation derangements, cardiac arrhythmias, peripheral vasoconstriction, metabolic acidosis, compensatory increased oxygen requirements during rewarming, and impaired immune response. Collectively, these adverse effects have been associated with an increased morbidity and mortality in

hypothermic trauma patients. This article focuses on the etiology and risk factors of hypothermia in the trauma patient. The article also reviews methods to prevent and treat hypothermia in the trauma population. Mention is made of therapeutic hypothermia in trauma.

## Incidence and Risk Factors

Hypothermia is a well-recognized consequence of injury.<sup>1</sup> Mortality data from the National Center for Health Statistics show that, during the 13-year period from 1968 to 1980, 6,460 deaths were attributed to the effects of environmental or exposure hypothermia.<sup>2</sup> There were 411 deaths from hypothermia, frostbite, and other cold-induced injuries between 1992 and 1996 in Canada.<sup>3</sup> Each year, approximately 780 persons die in the United States from exposure to cold. The age-adjusted death rates for hypothermia in the absence of trauma range from 2.2 to 4.3 per million US population.<sup>4</sup> The highest mortality rates occur in the elderly, possibly because physiologic and behavioral components of thermoregulation such as vasoconstriction, shivering, and the ability to discriminate temperatures with precision are impaired.<sup>5,6</sup> Other persons at risk for exposure hypothermia include the very young and the homeless. Alcohol intoxication, psychiatric illness, and motor vehicle accident or breakdown are known risk factors for hypothermia-related injuries and death.<sup>7-9</sup> Medical conditions predisposing to hypothermia include spinal cord injuries, basilar skull fractures, subdural hematomas, hypothalamic injuries, brain tumors, hypothyroidism, hypoglycemia, autonomic neuropathy, adrenal insufficiency, exhaustion, and malnutrition.<sup>10</sup>

In the trauma population, Luna et al<sup>11</sup> analyzed the frequency and risk factors for hypothermia in 94 tracheally intubated injured patients at a regional trauma center in a temperate climate. Thirty-two percent of patients had a core temperature of more than 36°C, 43% had a core temperature between 34°C and 36°C, and 23% had a core temperature less than 34°C, with a range between 27°C and 33.8°C. In normothermic patients, mortality rate was 22%, compared with 59% in the hypothermic group. In a retrospective study of 71 patients with truncal injury and injury severity scores more than 25, 42% of the patients had core temperatures less than 34°C, 23% had a temperature less than 33°C, and 13% had a temperature less than 32°C.<sup>12</sup> In a prospective observational study of blunt and penetrating trauma patients requiring surgery within 24 hours of admission, 14% were hypothermic (<36°C) upon admission to the emergency department, 61% were hypothermic at one point during surgery, and 36% were hypothermic at the end of the operation.<sup>13</sup>

In trauma patients, hypothermia has been associated with increased mortality and morbidity. For example, Jurkovich et al<sup>12</sup> demonstrated that survival, independent of severity of injury, depended on the core temperatures, such that at core temperatures of 34°C, 33°C, and 32°C, mortality rates were 40%, 69%, and 100%, respectively.

Factors that may contribute to the high incidence of hypothermia in the trauma population include prolonged exposure in the field, alcohol intoxication, head injury, shock, associated medical conditions, and administration of cold intravenous fluids (Table 1).<sup>1,14-18</sup>

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**Table 1.****Risk Factors for Hypothermia in Trauma Patients****Impaired thermoregulation and decreased heat production**

- Head injury
- Spinal cord injury
- Extremes of age
- Shock
- General anesthesia
- Epidural and spinal anesthesia
- Associated medical conditions
  - Thyroid disease, adrenal disease, diabetes, cardiac dysfunction, hepatic disease, malnutrition, autonomic nervous system dysfunction
- Drugs
  - Alcohol, tricyclic antidepressants, phenothiazines, antipyretics, neuromuscular relaxants
- Bacterial toxins

**Increased heat loss**

- Exposure
- Cold IV fluids and blood products
- Burns
- General anesthesia
- Epidural and spinal anesthesia

Patients requiring emergency surgical intervention may suffer additional hypothermic insults from cold surgical preparation solutions, heat loss to the cold operating room environment, and the infusion of inadequately warmed intravenous fluids.<sup>18-20</sup> Administration of anesthetic agents impairs the ability to maintain thermal homeostasis and causes internal redistribution of body heat from the warmer core to the cooler peripheral tissue, thereby further reducing core temperature in the exposed patient.<sup>21,22</sup> General anesthesia also alters the threshold for thermoregulatory vasoconstriction and shivering.<sup>23</sup>

## Morbidity

Adverse effects of hypothermia in the trauma patient are shown in Table 2. Intense shivering may occur between 34°C and 36°C with resultant increase in oxygen demand and metabolic rate. During rewarming, there may be release of sequestered cold blood and acid metabolites from peripheral vascular beds, dilation of the systemic vasculature, with resultant cardiac instability. Hemodynamic instability due to “rewarming shock” is characterized by hypotension, myocardial depression, and release of metabolic acids.<sup>24</sup>

Hypothermia exerts a negative inotropic effect on the myocardium, and depression of left ventricular contractility occurs with moderate hypothermia.<sup>25</sup> Hypothermia is also associated with atrial and ventricular arrhythmias. The initial electrocardiographic (ECG) change seen in cases of hypothermia is sinus tachycardia. As the core temperature decreases, progressive bradycardia ensues. Major ECG manifestations of hypothermia include decreased myocardial conduction velocity with prolongation of the PR and QT

intervals and QRS complex duration. J waves may appear. ECG changes may partly be due to alterations in the electrophysiologic properties of the cardiac Purkinje fibers or serum potassium reductions induced by the hypothermia.<sup>26</sup> Below core temperatures of 30°C, ectopic atrial rhythms, atrial flutter, and atrial fibrillation commonly occur. Once the temperature decreases to 28°C, ventricular tachycardia and ventricular fibrillation are seen.<sup>27</sup> Asystole occurs at a core temperature of less than 15°C. Hemodynamically significant arrhythmias are difficult to treat in cases of hypothermia because the hypothermic myocardium is relatively unresponsive to defibrillation and drugs such as lidocaine. The cardiac response to catecholamines may also be blunted in hypothermic hearts, and cold cardiac tissue poorly tolerates hypervolemia and hypovolemia.<sup>28-30</sup>

**Table 2.****Adverse Effects of Hypothermia in Trauma****Impaired cardiorespiratory function**

- Cardiac depression
- Myocardial ischemia
- Arrhythmias
- Peripheral vasoconstriction
- Impaired tissue oxygen delivery
- Elevated oxygen consumption during rewarming
- Blunted response to catecholamines
- Increased blood viscosity
- Metabolic acidosis

**Bleeding diathesis**

- Decreased kinetics of coagulation factors
- Reduced platelet function

**Reduced clearance of drugs**

- Decreased hepatic blood flow
- Decreased hepatic metabolism of drugs
- Decreased renal blood flow

**Increased risk of infection**

- Decreased white blood cell number and function
- Impaired cellular immune response
- Wound infection
  - Thermoregulatory vasoconstriction
  - Decreased subcutaneous oxygen tension
  - Impaired oxidative killing by neutrophils
  - Decreased collagen deposition
- Pneumonia
- Sepsis

In a randomized trial of normothermia versus mild hypothermia (35.4°C),<sup>31</sup> maintenance of intraoperative normothermia reduced the incidence of morbid cardiac events such as myocardial ischemia, unstable angina, and ventricular tachycardia in patients with cardiac risk factors undergoing abdominal, thoracic, or vascular surgery. Hypothermia was an independent predictor of morbid cardiac events, with a relative risk of 2.2 (95% confidence interval [1.1, 4.7]). Increased cardiovascular morbidity may partly be due to a greater degree of peripheral vasoconstriction, increased norepinephrine levels, and altered alpha-adrenoceptor tone in response to cold.<sup>32</sup>

Hypothermia may promote surgical wound infection because of thermoregulatory vasoconstriction, decreased subcutaneous oxygen tension, impaired oxidative killing by neutrophils, and decreased collagen deposition.<sup>33</sup> In a randomized trial of normothermia versus mild hypothermia (34.7°C),<sup>34</sup> maintenance of intraoperative normothermia reduced the incidence of infectious complications and shortened duration of hospitalization in patients undergoing colorectal resection.

Hypothermia may lead to a bleeding diathesis as a result of impaired platelet function, inhibition of clotting enzyme kinetics, and activation of the fibrinolytic cascade.<sup>35</sup> Life-threatening coagulopathy in patients with severe injury who required massive transfusion was predicted by a temperature below 34°C and progressive metabolic acidosis.<sup>36</sup>

Moderate hypothermia (28–32.1°C) impairs respiratory drive and is associated with hypoventilation and loss of protective airway reflexes.<sup>1</sup> Aspiration pneumonia, atelectasis, acidosis, and hypoxia may ensue. Hypothermia has also been shown to inhibit hypoxic pulmonary vasoconstriction<sup>37</sup> and to shift the oxygen-hemoglobin saturation curve to the left so that oxygen is bound more avidly to the hemoglobin molecule. With further reductions in core temperature (<28°C), pulmonary congestion and edema may occur.<sup>1</sup> There is a risk of pneumonia in patients undergoing induced hypothermia for prolonged periods.<sup>38,39</sup>

Renal blood flow and glomerular filtration rates decline progressively with hypothermia. There is also impaired renal tubular function, which leads to increased urinary loss of sodium, potassium, and water and a “cold-induced” diuresis. Renal clearance of water-soluble drugs is diminished. Phosphate concentrations decrease. Potassium may shift into the cells during induced hypothermia, and potassium administration may lead to hyperkalemia during rewarming.<sup>40,41</sup> Blood glucose concentrations increase, which may require intensive insulin therapy to reduce mortality.<sup>42,43</sup> With core temperature <28°C for a prolonged period, rhabdomyolysis and disseminated intravascular coagulation may occur.<sup>10</sup> Controversy exists regarding temperature correction of blood gases during hypothermia. At issue is the maintenance of electrochemical neutrality during hypothermia. Much experience with hypothermia during cardiopulmonary bypass has shown that maintaining intracellular pH near pN, where  $[H^+] = [OH^-]$ , results in preservation of the ionization state of histidine imidazole.<sup>44</sup> This alpha-stat management of blood gases requires that the arterial pH is maintained at 7.40 and PaCO<sub>2</sub> at 40 mm Hg as measured with a 37°C blood-gas electrode, regardless of actual body temperature. Because the solubility of CO<sub>2</sub> in blood increases with hypothermia, actual in vivo PaCO<sub>2</sub> is much less than 40 mm Hg, resulting in an apparent respiratory alkalosis. However, this apparent alkalosis is physiologically appropriate because it maintains the proper ionization state of histidine.<sup>44</sup>

## Mechanisms of Heat Loss

Heat loss from the human body can be explained by four mechanisms: radiation, evaporation, conduction, and convection (Table 3). Radiant heat loss occurs whenever exposed skin and viscera are warmer than the surrounding environment. Radiant heat loss may be as high as 50 kcal/hr in a fully exposed adult patient, or as low as 10 kcal/hr in a fully draped patient in the surgical suite.

**Table 3. Mechanisms of Heat Loss in the Adult Trauma Patient**

### Radiation

Transfer of heat from warmer objects to cooler objects in the absence of direct contact

### Conduction

Transfer of heat due to direct contact of skin and viscera with colder objects

- Operating room table or spine backboard
- Skin-preparation solutions
- Irrigating fluids
- Surrounding air

Transfer of heat from circulating blood volume to colder IV fluids

- Crystalloid, 21°C: 16 kcal/L
- Blood, 4°C: 30 kcal/L

### Convection

Removal of air warmed by skin or viscera

- Increases conductive heat loss by 10 kcal/hr

### Evaporation<sup>a</sup>

Transfer of heat from skin, respiratory tract, and viscera because each gram of water that vaporizes consumes 0.6 kcal

<sup>a</sup>Note that the normal 600 to 75-kcal/hr heat loss in a 70-kg adult patient is offset by 60–75 kcal/hr of metabolic heat production to maintain normothermia. For every 60- to 75-kcal/hr heat loss in excess of production, a 1°C decrease in core temperature may result. When heat production is diminished (e.g., anesthesia, severe injury, advanced age), greater decreases in core temperature may occur.

Evaporation of a liquid from the skin surface occurs because the warmer molecules tend to move into the ambient atmosphere, resulting in a net reduction of heat content at skin tissue.<sup>45</sup> Heat loss from evaporation also occurs from the airway and from exposed thoracic and abdominal viscera. Evaporative heat losses account for between 12 and 16 kcal/hr, but may be as high as 160 to 400 kcal/hr from exposed viscera (e.g., during liver or bowel surgery).<sup>46,47</sup>

Conductive heat loss occurs between skin or tissue and direct contact with colder objects, such as the operating room table. Conductive heat loss is accelerated or increased whenever air currents are present because of the continual removal of warmed air (i.e., convective heat loss).

Conductive heat loss also occurs between the patient's circulating blood volume and intravenously administered cold fluids and blood products. It is known that 1 kcal of heat is required to raise the temperature of 1 kg of water by 1°C. Assuming that 1 liter of crystalloid weighs 1 kg, and that its specific heat is the same as water, one would need 16 kcal of energy to raise the temperature of 1 liter of crystalloid infused at 21°C to 37°C.<sup>48–51</sup> Similarly, infusion of 4.3 liters of crystalloid at room temperature to an adult trauma patient would require 71 kcal, the equivalent of 1 hour of heat production in an awake adult, or 1.5 hour of heat production in an anesthetized male adult. The negative thermal balance of 4.3 liters of room temperature fluids is thus equivalent to a decrease of 1°C body temperature in an awake individual and a 1.5°C body temperature decrease in an anesthetized patient. Conversely, 30 kcal are required to raise the temperature of

cold (4°C) blood to 37°C, so that infusion of 2.3 liters could result in a core temperature decrease of between 1 and 1.5°C.

General anesthesia produces cutaneous vasodilation with increased heat loss and redistribution hypothermia. The most likely explanation for redistribution hypothermia is loss of heat content due to increased distal extremity skin blood flow through capillary and arteriovenous shunts and conduction of heat away from the core, toward the periphery.<sup>52</sup>

## Therapeutic Hypothermia in Trauma

Hypothermia may prevent the initiation of the cascade of events after injury that lead to cell death<sup>53,54</sup>; for this reason it was the focus of an advisory statement by the Advanced Life Support Task Force of the International Liaison Committee. The task force recommended that unconscious adults with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was ventricular fibrillation.<sup>55</sup> Hypothermia increases the tolerance time for cardiac arrest and reduced blood flow during cardiopulmonary resuscitation because of reduced cerebral metabolism and inhibition of deleterious effects of hypoxia such as free radical reactions, excitotoxicity, and changes in membrane permeability.<sup>56</sup>

Studies have focused on the use of hypothermia as a therapy for clinical situations such as cardiac arrest, traumatic head injury, shock, stroke, and spinal cord ischemia.<sup>57-70</sup> In two prospective, randomized controlled studies, induced hypothermia of 33°C to 34°C for 12 to 24 hours in patients with anoxic brain injury following resuscitation from prehospital cardiac arrest improved outcome.<sup>71-73</sup> Therapeutic hypothermia has also been advocated for the treatment of head injuries.<sup>74-80</sup> A total of 12 randomized controlled trials with 812 participants was reviewed in a meta-analysis.<sup>81</sup> There was no evidence that hypothermia is beneficial in the treatment of head injury. Active immediate hypothermia (34–35°C for at least 12 hours) was associated with an odds ratio for death of 0.88, and 0.75 for being dead or severely disabled. Moreover, hypothermia treatment was associated with an increased risk of pneumonia (odds ratio 1.95). Possible reasons that hypothermia was not found to be beneficial after head injury include methodologic issues such as excluding patients with hypoxia or hypotension after resuscitation, timing of the hypothermic intervention, and duration of therapeutic hypothermia. It is possible that longer periods of hypothermia (>48 hours) may be beneficial, especially when the patient is already hypothermic or when intracranial hypertension requires additional therapy.<sup>71</sup>

## Prevention and Treatment of Hypothermia

To prevent or treat hypothermia, airway, breathing, and circulation must be maintained. Rewarming methods for the hypothermic trauma patient include passive rewarming, active external rewarming, and active internal rewarming (Table 4).

**Passive Methods.** Heat loss can be minimized by reducing the velocity of air around the patient and draping the patient. Evaporative heat loss from skin can be reduced by avoiding cold preparation solutions and drying the skin quickly. Reduction of heat loss can also be achieved by reducing the temperature gradient between the ambient environment and the patient; i.e., by warming the room.<sup>82</sup> Since radiation and convection account for 65% to 85% of

**Table 4. Methods to Rewarm Trauma Patients**

### Passive

- Higher ambient room temperatures  
Reduces heat loss by several mechanisms, but relies on patient's internal heat production for rewarming.
- Warm blankets, insulating blankets, dry off wet skin  
Reduces heat loss but relies on patient's internal heat production for rewarming

### Active External

- Convective warming  
Intraoperative (vasodilated): provides 90 kcal/3 hr in a 70-kg patient (1.5°C gain)  
Postoperative (vasoconstricted): rewarmed patients at rate of 0.86°C per hour
- Heated humidified gases  
Provides 7–13 kcal/hr
- Conductive warmers  
Efficacy depends on amount of surface area covered and degree of vasoconstriction
- Radiant warmers  
Provides 17.7 kcal/hr  
Reduces shivering postoperatively regardless of effect on core temperature
- Warmed IV fluids  
Effective at preventing heat loss  
1 liter crystalloid at 20°C corresponds to 17-kcal loss and 0.29°C fall in core temperature  
1 liter 4°C blood corresponds to 30-kcal loss and 0.42°C fall in core temperature  
Effective fluid warmers can deliver fluids at 39°C, which can rewarm patients requiring massive fluid resuscitation

### Active Internal

- Continuous arteriovenous rewarming (CAVR)  
Provides 90–165 kcal/hr and rewarms core by 1.3–2.2°C per hour  
Does not require heparinization
- Cardiopulmonary bypass  
Most effective heat exchange device but requires heparinization and perfusionist
- Hemodialysis or body cavity lavage with warmed fluids  
Can increase core temperature by 1.5–2.0°C per hour

the intraoperative heat loss, and both of these mechanisms are directly related to the ambient room temperature, it follows that increasing the operating room temperature to more than 26°C could help prevent hypothermia.

**Active Methods. Radiant Warmers.** Radiant heat lamps have been used to prevent hypothermia and to reduce shivering in the postanesthesia care unit.<sup>83,84</sup> In order for radiant heat lamps to be effective, the patient should be unclothed so as large a surface area as possible is exposed to the radiant heat.

**Heated Water Mattresses.** Use of heated conductive water mattresses placed under the patient has not been shown to be

**Table 5. Convective (Forced-Air) Warmers**

Name/Manufacturer	Description	Special Features
Bair Hugger 750 (Arizant Healthcare Inc., Eden Prairie, MN)	Convective air delivered to variety of blankets (upper, lower, full, torso, surgical access, pediatric, cardiac) at three settings: high (43°C), medium (38°C), low (32°C)	Increased airflow, hose-end temperature sensing, compatible with 241 blood/fluid warming set
Bair Hugger 505 (Arizant Healthcare)	Same as above	Compatible with 241 blood/fluid warming set
Equator (Smiths Medical ASD, Rockland, MA)	Convective air delivered to variety of adult and pediatric blankets. Three settings: high (44°C), medium (40°C), low (36°C)	Thermistor with temperature sensors at end of air-delivery hose. Elapsed time display. Even distribution of air throughout blanket. Disconnect indicator
Snuggle Warm (Smiths Medical ASD)	Same as above	Thermistor with temperature sensors at end of air-delivery hose
Thermacare TC3000 series (Gaymar Industries, Inc., Orchard Park, NY)	Convective air delivered at four temperature settings to adult and pediatric quilts: low (90°F [32°C]), medium (100°F [38°C]), high (110°F [43°C]), maximum (115°F [46°C])	
WarmTouch 5200 (Nellcor, Pleasanton, CA)	Convective air delivered at three temperature settings to adult and pediatric blankets: high (42–46°C), medium (36–40°C), and low (30–34°C)	
CSZ WarmAir 135 (Cincinnati Sub-Zero Products, Cincinnati, OH )	Convective air delivered at three temperature settings: low (90°F [32.2°C]), medium (100°F [37.8°C]), high (110°F [43.3°C])	

*Note: All units can deliver forced air at ambient temperature (fan only).*

effective for rewarming.<sup>85</sup> This method is ineffective because only a limited amount of body surface area actually comes into contact with the water mattress. Trauma patients with hypoperfused peripheral tissues may be particularly vulnerable to water mattress burn injury because heat remains locally in compressed anoxic tissue. Thermal injury from a heated water mattress has been previously described,<sup>85,86</sup> and was responsible for 5 of 28 burns resulting from materials and devices used for warming patients, according to a closed claims study analysis.<sup>87</sup>

*Convective (Forced-Air) Warming.* Considerable evidence exists demonstrating the safety and efficacy of forced-air warming devices in both preventing and treating hypothermia and preventing shivering during the perioperative period.<sup>22,88,89</sup> These devices (Table 5; Figs. 1–3) not only transfer heat across cutaneous surfaces but, if a large enough surface area can be covered, they also create a thermoneutral microenvironment so that all heat production goes to restoring body temperature.<sup>90</sup> In a randomized controlled trial of hypothermic patients (with average core temperature of 28.8°C),<sup>91</sup> forced-air warming increased core temperature by about 2.4°C per hour versus 1.4°C per hour in control patients. Both groups of patients received IV fluids warmed to 38°C as well as warmed, humidified oxygen at 40°C by inhalation. Koller et al<sup>92</sup> reported the use of forced-air warming in five patients with core temperature <30°C. The outcome of all five patients was good without neurologic sequelae. Core temperature

increased by approximately 1°C per hour without any cardiac arrhythmias or core temperature afterdrop.

Thermoregulatory vasoconstriction, which separates and limits heat transfer between peripheral skin and central thermal compartments, has been shown to limit the rate of



**Figure 1. Bair Hugger 750 convective warmer (Arizant Healthcare, Eden Prairie, MN). The device delivers forced air to a wide variety of disposable blankets (upper, lower, full, torso, surgical access, pediatric, cardiac) at three settings: high, 43°C; medium, 38°C; low, 32°C.**



**Figure 2. (left) Bair Hugger 750 convective warmer and blanket prior to thoracic surgery.**

**Figure 3. (right) The hypothermia station (Smiths Medical ASD, Rockland, MA). The convective warming unit (Snuggle Warm) sits at the base. The temperature monitor and IV fluid warmer (Hotline) are attached to an IV pole. There is a four-outlet power strip to eliminate loose cords and an adjustable tree arm to hold the hose.**

rewarming using forced air in hypothermic patients recovering from surgery.<sup>93</sup> Although it may be difficult to apply forced-air warming to the trauma patient in the emergency department or operating room setting because of the requirement for patient exposure, an upper, lower, or whole-body forced air blanket should be used whenever possible to reduce heat loss, maintain a thermoneutral environment, and restore heat to the body.<sup>94,95</sup>

*Warm-Water Garment.* A system has been developed that circulates warm water through a whole-body garment,

transferring heat to the patient via conduction (Table 6). It is likely that heat transfer via conduction is more effective than convective warming.<sup>96</sup> The warm-water garment allows more body area to be covered (and warmed) than does the forced-air warming system. In a prospective, randomized trial involving patients undergoing liver transplantation, the warm-water garment provided more consistent maintenance of normothermia compared with upper- and lower-body forced-air warming.<sup>97</sup> Similar results were reported in studies of adult patients undergoing open abdominal surgery, pediatric

**Table 6. Conductive Warmers**

Name/Manufacturer	Description	Special Features
Medi-Therm III (Gaymar Industries, Orchard Park, NY)	Conductive warming and cooling. Circulates water from the control unit to polymer hyper/hypothermia blankets. Manual settings: 4–42°C; automatic: 30–39°C.	Automatic mode to achieve desired patient temperature. Single use and “heavy-duty” reusable disposables. Wrap-around blankets to optimize body surface coverage.
Blanketrol II Hyper – Hypothermia Water System (Cincinnati Sub-Zero Products, Cincinnati, OH )	Conductive warming and cooling. Circulates water from the control unit to specialized blankets (adult and pediatric). Temperature range, 4–42°C	Reuseable as well as disposable blankets available. Microprocessor controlled. Consistent water temperature at the blanket.
Norm-O-Temp Hyperthermia System (Cincinnati Sub-Zero Products)	As above. Temperature range, 20–42°C	As above
Cool/Heat (Advanced Surfaces/ Pedigo Products, Vancouver, WA)	Conductive system. Circulates a heated element through a pressure-reducing table pad using fiber optics and carbon technology. Four settings: high (39°C), average (38°C), low-average (37°C), low (36°C)	Special pressure-reduction pads designed to fit multiple surgical beds and positioners. Radiolucent. Wipes clean easily. Reusable.
Arctic Sun 100 (Medivance, Louisville, CO)	Conductive system. Circulates water via negative pressure from the control unit to energy-transfer pads (disposable gel pads usually placed on back). Temperature range, 4–42°C	Automatic mode to achieve desired patient temperature: 33–37°C. Adhesive gel interfaces well with patient's skin to provide consistent energy exchange.

Table 7. Fluid and Blood Warmers

Name/Manufacturer	Description	Special Features
Level 1 System H-1200 (Smiths Medical ASD, Rockland, MA)	Aluminum heat exchanger with counter-current 42°C circulating water bath. Air detector/clamp.	Rapid pressurized infusion; ultrasonic air sensor automatically stops flow of solution and alarms when air is detected.
Level 1 System H-1000, H-1025 (Smiths Medical ASD)	Same as above without air detector/clamp.	Same as above without air detection.
Level 1 H-525, H-500, H-275, H-250 (Smiths Medical ASD)	Same as above without air detector/clamp.	Same as above without air detector/clamp. No longer being serviced or sold by manufacturer
Hotline (Smiths Medical ASD)	Water bath heat exchange. Surrounds patient line with layer of 42°C circulating fluid.	Effective at low and moderate flow rates. Patient line cool down eliminated. Not recommended for rapid infusion.
FMS 2000 (Belmont Instrument Corp., Billerica, MA)	Magnetic induction heat exchange. Volumetric pump with flow rate to 500 ml/min. Ultrasonic air detection.	Rapid infusion without pressurization of bag; ultrasonic air sensor to stop flow of blood and crystalloid with automatic repriming.
Buddy Fluid Warmer (Belmont Instrument Corp.)	Dry heat exchange. Outlet temperature = $38 \pm 3^\circ\text{C}$ at flow rates up to 100 ml/min. Heating unit placed near infusion site to minimize IV line cool down.	Effective at low and moderate flow rates. Internal microporous membrane to vent out-gassed air. Not recommended for rapid infusion
Ranger (Arizant Healthcare, Eden Prairie, MN)	Dry heat exchange. Plastic disposable with aluminum heating plates (set point, 41°C).	High flow disposable has autoventing bubble trap.
241 Set (Arizant Healthcare)	Convective heat exchange. Coiled plastic fits inside hose of Bair Hugger 500 and 700 series units.	Liquid crystal temperature display on outlet tubing; not recommended for rapid infusion.
FW600 Medi Temp III (Gaymar Industries, Inc., Orchard Park, NY)	Dry heat exchange. Plastic disposable with aluminum heating plates (set point, 41°C).	Can adjust set points between 38 and 43°C. Bubble trap with manual air vent.
Thermal Angel TA-200 (Estill Medical Technologies, Dallas, TX)	Battery-powered, portable in-line warmer. Outlet temperature, $38 \pm 3^\circ\text{C}$ at flow rate 2–150 ml/min	Can be used in the field, ambulances, helicopters, and military. Compatible with any tubing set that uses a standard luer fitting.
Warmflo FW538 (Nellcor, Pleasanton, CA)	Dry heat exchange. Single-use metal cassette. Maximum flow rate, 500 ml/min	Warming set points can be altered from 28–42°C.
Animec AM-2S (Futuremed America, Granada Hills, CA)	Dry heat exchange for pediatrics: low flow rates, ranging from 1–12 ml/min.	Uses standard IV tubing instead of special disposable sets.
Biegler Protherm II (Central Medical Supplies Ltd, Leek, Staffordshire, UK)	Dry heat exchange.	Selector that allows the operator to set the warmer to a temperature between 37 and 41°C in increments of 0.5°C.
Fluid Warming Cabinet EC230L (Enthermics Medical Systems, Menomonee Falls, WI)	Temperature can be set from 32–43° C for injection mode or 32–65.5° C for irrigation mode. Set-point accuracy, +3°F	Danger of overheating fluids. May violate fluid manufacturer storage recommendations. Not recommended for blood.
Blickman Warming Cabinet 7925 (Millennium Surgical Corp, Haverford, PA)	Temperature can be set from 32–71° C within 1°F increments.	Danger of overheating fluids. May violate fluid manufacturer storage recommendations. Not recommended for blood.

patients, and cardiac surgery patients.<sup>98–102</sup> In a study of patients undergoing abdominal surgery and who were anesthetized with continuous epidural and general anesthesia, the circulating-water garment often caused hyperemia.<sup>103</sup> However, cutaneous perfusion returned to normal soon after surgery. The authors noted that hyperemia is a normal response to aggressive local heating and caution against the

use of circulating-water garments in patients with fragile skin.

**Warmed Intravenous Fluids.** The ideal fluid warmer should be capable of safely delivering fluids and blood products at normothermia at both high and moderate flow rates. The ability of blood warmers to safely deliver normothermic fluids over a wide range of flow rates is limited by several factors, including limited heat-transfer capability of

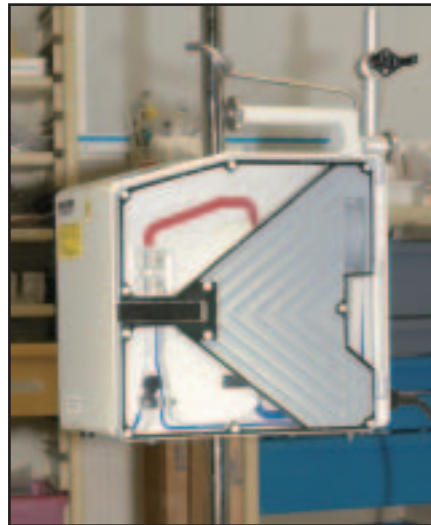


Figure 4. (left) The Level 1 System H-1000 (Smiths Medical ASD) device uses an aluminum heat exchanger with counter-current 42°C circulating water bath. The two pressure chambers accommodate standard blood and solution bags for pressurized infusion, if necessary.

Figure 5. (middle) The FMS 2000 warming system (Belmont Instrument Corp., Billerica, MA) system consists of an integrated volumetric infusion pump coupled with a high-capacity magnetic induction heater. There are two ultrasonic air detectors, one at the fluid inlet and the other at the outflow to the patient, coupled to an automatic shut-off valve.

Figure 6. (right) The Ranger blood/fluid warming unit (Arizant Healthcare, Eden Prairie, MN) device uses dry heat exchange technology. A plastic disposable is inserted between the aluminum heating plates, which have a set point of 41°C.

materials, limited surface area of the heat-exchange mechanism, inadequate heat transfer of the exchange mechanism at high flow rates, erythrocyte damage caused by microwaving, and heat loss after the IV tubing exits the warmer.<sup>104-111</sup> Table 7 and Figures 3 through 6 describe and show, respectively, some of these fluid-warming systems.

Table 8 summarizes the implications of using five fluid warmers during commonly encountered clinical situations: pressure-driven infusion and gravity-driven infusion with the roller clamp wide open.<sup>112,113</sup> It can be seen from the calculations in Table 8 that the thermal stress of infusing cold

fluids may result in considerable changes in mean body temperature, especially if the patient was unable to increase heat production or to prevent further heat loss (e.g., general anesthesia with neuromuscular blockade). The larger the gradient between the temperature of the infused fluid and the core temperature, the greater the drop in mean body temperature. Also, the greater the fluid requirement relative to body weight, the greater the potential drop in body temperature.

Because the thermal stress of infusing fluids at normothermia is essentially zero, it follows that use of

**Table 8. Implications of Using Warming Devices for Crystalloid Fluid Resuscitation (5 and 10 Liters) in Anesthetized Trauma Patients\***

Pressure Gravity	Flow Rate (ml/min)	Outlet Temperature (°C)	Decrease in MBT* (5-liter infusion) (°C)	Decrease in MBT* (10-liter infusion) (°C)
Flotem IIe	260	24	-1.12	-2.24
	90	27	-1.03	-2.06
Astotherm	260	25	-1.03	-2.06
	90	30	-0.60	-1.20
Bair Hugger 2.4.1	360	24.2	-1.10	-2.20
	80	29.6	-0.64	-1.27
Level 1 H-250	600	33	-0.34	-0.69
	290	36	-0.09	-0.17
Level 1 H-1000	470	39.5	+0.22	+0.43
	150	39.4	+0.21	+0.41

\*Change in mean body temperature (MBT) was calculated as  $(T_F - T_p) \times S_F / Wt \times S_p$  where  $T_F$  = temperature of fluid delivered to the patient (outlet temperature of the warmer),  $T_p$  = temperature of the patient (assumed to be 37°C),  $S_F$  = specific heat of infused fluid (1 kcal/1°C crystalloid),  $S_p$  = specific heat of the patient (0.83 kcal/1°C). Fluids were infused during two conditions: pressure-driven infusion and gravity-driven infusion with the roller clamp wide open.<sup>112,113</sup>

Table 9. Other Hypothermia/Hyperthermia Devices

Name/Manufacturer	Description	Special Features
AV-300: CAVR – Continuous Arteriovenous Rewarming (Smiths Medical ASD, Rockland, MA)	Rapid core rewarming. Circulates colder blood of patient through Level 1 heat exchanger and returns it to patient at normothermia.	Uses patient's own blood pressure as driving force. Requires large-bore venous and arterial cannulation. Does not require heparinization.
CairCooler (Pentatherm Ltd, Wakefield, England)	Forced-air cooling system. Connects to forced-air blanket to deliver 10°C air.	Noninvasive cooling method. Modular design, easy maintenance. Uses BairHugger blankets.
Arctic Sun 2000 (Medivance, Louisville, CO)	Circulating water temperature is controlled between 4°C (39.2°F) and 42°C (107.6°F) to achieve a preset target patient temperature.	Patient temperature control range 33–37°C (91.4–98.6°F)
CoolGard 3000 System: CoolLine, Icy, or Fortius Catheter (Alsius, Irvine, CA)	Rapid cooling. Circulates temperature-controlled saline through a heat exchanger incorporated into a venous catheter to cool patient's blood.	Automatic mode to achieve desired patient temperature: closed-loop design. Requires central line insertion.

effective fluid-warming devices permits more efficient rewarming of hypothermic trauma patients than the use of other methods, such as the patient's own metabolically generated heat or externally provided heat.

**Humidified Gases.** Evaporative heat loss from the airway can be prevented by using warm, humidified gases. Delivery of warm, humidified gas has also been shown to increase core temperature by 0.5°C to 0.65°C per hour in injured, hypothermic patients.<sup>114,115</sup> The effectiveness of airway humidifiers has been questioned,<sup>116</sup> and the use of these devices has resulted in airway injury.<sup>117</sup> Another method to conserve airway moisture and heat is the use of passive heat and moisture exchangers (high surface area hygroscopic membrane filters). This method of heat conservation helps prevent hypothermia.

**Hot Packs.** Watts et al<sup>118</sup> assessed the utility of traditional prehospital interventions in maintaining thermal homeostasis in 134 trauma patients who required transport to a hospital. Patients who received hot pack rewarming had a mean increase in body temperature of 1.4°C during transport, compared with a mean decrease of 0.3°C to 0.6°C in controls.

**Carbon Fiber Blankets.** Kober et al<sup>119</sup> studied the effects of actively warming critically ill trauma patients during intrahospital transport. They found that resistive heating using carbon fiber blankets (set point 42°C), compared with wool blankets, increased core temperature and ensured normothermia in all actively warmed patients.

**Heated Surgical Pads.** Conductive warming can be applied to the patient through reusable operating room table pads such as Cool/Heat (Pedigo Products, Vancouver, WA). The material becomes warm when an electrical charge is applied (fiberoptics and carbon technology). To the author's knowledge, no studies have been published comparing the efficacy of these pads with that of conventional warming systems.

**Active Internal Rewarming.** Active core rewarming refers to the use of various techniques such as peritoneal and hemodialysis, venovenous hemofiltration, body cavity lavage (such as pleural, gastric, mediastinal, abdominal, bladder, colonic lavage), and cardiopulmonary bypass (CPB). Active or internal rewarming restores normothermia at a faster rate than surface methods and has been associated with more rapid normalization of cardiac output and the electrocardiogram,

and a decreased risk of rewarming shock.<sup>120</sup> These methods of core rewarming are generally appropriate for severely hypothermic patients (<28°C) but may also be useful for moderately hypothermic patients (28–32.1°C) with cardiovascular instability. Surface rewarming following severe hypothermia may worsen an already precarious clinical situation by release of sequestered cold fluids from peripheral vascular beds, dilation of the systemic vasculature with resultant hypotension, and myocardial depression and release of metabolites. Moreover, the hypothermic heart may not respond appropriately to the metabolic demands of rewarming.

Peritoneal or mediastinal lavage with heated crystalloid at an exchange rate of 6 liters/minute may increase core temperature at a rate of 2°C to 3°C per hour and has been shown to be beneficial in patients sustaining environmental or exposure hypothermia.<sup>1</sup> However, peritoneal and mediastinal lavage may be inappropriate in patients with abdominal or thoracic injuries. Because of the limited surface areas available for heat exchange, continuous gastric, colonic, or bladder lavage is not usually done.

CPB is the most effective means of rewarming severely hypothermic patients but requires systemic heparinization. Relative contraindications to CPB include asphyxia, severe traumatic injury (risk of bleeding), and greatly elevated potassium levels (>10 mmol/L).

Another technique involves the connection of a percutaneously placed femoral arterial line to a countercurrent fluid warmer.<sup>50</sup> The patient's blood volume flows through the warmer and returns to the patient by large-bore venous tubing so a fistula is created through the heating warmer. This technique, known as continuous arteriovenous rewarming (CAVR), has been shown to rapidly rewarm mildly hypothermic patients. In the initial experience of 16 patients treated with CAVR, core rewarming to 35°C was accomplished in 39 minutes, and to 36°C in 66 minutes.<sup>51</sup> Advantages of CAVR include no requirement for heparinization, rapid reversal of hypothermia, decreased total fluid requirements, decreased organ failure, and decreased length of stay in the intensive care unit. The CAVR technique provides a continuous transfusion of heat to the patient as long as systolic blood pressure was more than 80 mm Hg. Risks of CAVR consist mainly of those related to percutaneous

cannulation of the femoral vessels. Table 9 lists the CAVR and other related rewarming methods.

Gentilello et al<sup>121</sup> compared CAVR with standard rewarming in a randomized, prospective trial of 57 hypothermic trauma patients. Although there was a marked decrease in early mortality in patients receiving CAVR (7% with CAVR versus 43% with standard rewarming), survival to discharge was not significantly different between groups (66% versus 50%, respectively).

**Subatmospheric Pressure Rewarming.** This technique is based on the principle that thermoregulatory blood flow to discrete skin areas is regulated by arteriovenous anastomoses. Subatmospheric pressure is used to manipulate regional blood flow and to open up constricted arteriovenous anastomoses, thus overcoming peripheral vasoconstriction, which limits the transfer of cutaneously applied heat. A thermal load is then applied to transfer heat directly to the dilated arteriovenous anastomoses.<sup>122</sup>

To accomplish subatmospheric pressure rewarming, the patient's forearm is fitted through acrylic tubing with a neoprene collar to create an airtight seal around the arm. Vacuum pressure of -40 mm Hg is then established and the thermal load is applied (water perfusion blanket or heat from a controlled exothermic chemical reaction).

In the initial experience with this technique, rewarming was associated with normalization of tympanic membrane temperature within 10 minutes.<sup>123</sup> Core temperature remained normal afterward without an afterdrop. The maximum rewarming rate in the study was from a core temperature of 34.2°C to 36.2°C over 10 minutes. Subsequent studies, however, have not been able to duplicate these results.<sup>124</sup>

## Summary

Hypothermia often complicates the management of severely injured patients and has been associated with increased morbidity and mortality. The increased morbidity and mortality is likely due to impaired coagulation, metabolic acidosis from poorly perfused tissues, hemodynamic instability, respiratory problems, and infections. Therapeutic hypothermia may be beneficial in selected patients with neurologic injury and after out-of-hospital cardiac arrest. Hypothermia occurs in trauma patients because of ongoing thermal insults such as exposure, transfusion of cold fluids and blood, opening of body cavities, associated medical and surgical conditions, and decreased heat production and impaired thermoregulation.

Treatment of hypothermia in the trauma patient should begin with prevention of further heat loss, which can be achieved by maintaining the patient in a thermoneutral environment at high ambient temperature. The thermal stress from fluid resuscitation can result in substantial core temperature decreases, mandating the use of efficient fluid-warming devices. Of the various noninvasive treatment modalities, convective warming is effective in restoring heat to the core, although radiant heat may be easier to apply to the multiply injured trauma patient. Newer warming techniques such as use of garments with circulating water may prove to be useful because of the greater energy transfer compared with convective warming. Active core rewarming techniques such as CAVR increase core temperature by 1.5°C to 2.5°C per hour and can be life-saving in the hypothermic trauma patient with adequate perfusing rhythm.

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## Therapeutic Hypothermia

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**Learning Objectives:** 1) to familiarize the reader with contemporary studies on the application of resuscitative hypothermia in the treatment of traumatic brain injury and hemorrhagic shock, 2) to describe the potential mechanisms for the beneficial effects of hypothermia in these settings, 3) to present some recent findings from both laboratory and clinical studies of resuscitative hypothermia conducted at the University of Pittsburgh, 4) to discuss possible side effects and limitations of the application of therapeutic hypothermia, and 5) to discuss future directions for novel applications of hypothermia.

### Abstract

There have been some exciting advancements in the field of therapeutic hypothermia during the past 7 years. Studies have shown the beneficial effects of mild hypothermia after ventricular fibrillation cardiac arrest and its use has been recommended by two leading medical groups. Ongoing work in the areas of the therapeutic efficacy of mild cooling and methods for rapid reduction and use during field resuscitation have been presented. The importance of mild cooling during CPR—a subject of intense investigation by the late Dr. Peter Safar near the end of his career—is beginning to become evident in laboratory studies. Mild hypothermia is also under additional investigation for use as treatment of severe traumatic brain injury. Further work is needed in this area in both children and adults because of controversial findings in the recent adult multicenter clinical trial. There also have been developments in the area of the potential applications of hypothermia in resuscitation from hemorrhagic shock. The studies of this controversial use are still in the experimental stage. Finally, we discuss a novel approach to treatment of exsanguination cardiac arrest by application of suspended animation with delayed resuscitation.

In 1997, our group at the Safar Center for Resuscitation Research consulted on an article for the ITACCS-sponsored monograph on hypothermia in trauma that was entitled *Therapeutic Hypothermia After Traumatic Brain Injury or Hemorrhagic Shock: From Mild Cooling to Suspended Animation*.<sup>1</sup> Having been asked to update that article for *TraumaCare* in 2004, we take a look back and a glimpse forward on the topic of therapeutic hypothermia in the collective field of resuscitation medicine.

### From 1997 to 2004

Unquestionably, the most exciting and important development in the field of therapeutic hypothermia for resuscitation medicine came in February 2002. In that month, two separate studies were reported in the *New England Journal of Medicine* demonstrating beneficial effects of mild hypothermia (~33°C) after ventricular fibrillation (VF) cardiac arrest (CA) in adults.<sup>2,4</sup> Sterz and his multicenter group in Europe<sup>2</sup> and Bernard et al<sup>3</sup> in Australia reported significant beneficial effects on outcome when hypothermia was initiated after restoration of spontaneous circulation. In the study by Sterz and colleagues,<sup>2</sup> to prevent one unfavorable outcome, six patients would need to be treated with hypothermia. Cooling was continued for either 12 hours in the study by Sterz and colleagues<sup>2</sup> or 24 hours in the study by Bernard and colleagues.<sup>3</sup> Even more surprising to our group in Pittsburgh was the fact that cooling was effective even though the time to target temperature was about 12 hours in the study by Sterz and colleagues.<sup>2</sup> This suggests benefit of hypothermia after cardiac arrest even with delayed application. One mechanism that may be involved is the ability of mild cooling to block delayed neuronal death, which is likely to develop as part of an activated apoptosis cascade after CNS injury.<sup>5,7</sup> Blockade of the release of the key initiator of the mitochondrial intrinsic pathway of apoptosis—cytochrome C—by mild hypothermia was recently shown in experimental brain ischemia.<sup>7</sup> Of interest, successful delayed application of mild hypothermia has been shown in experimental animal models.<sup>8</sup> These two clinical studies prompted a recent Level I recommendation of the American Heart Association (AHA) and the International Liaison Committee on Resuscitation (ILCOR) for the use of mild hypothermia after VFCA in adults.<sup>9</sup>

It is, however, widely recognized that therapeutic hypothermia is most efficacious when applied either before or early after CNS insults. In this regard, there have been two important studies that we believe will further expand the therapeutic efficacy of mild cooling. In 2003, in a study of 22 adults, Bernard et al<sup>10</sup> reported that 30 mL/kg bolus over 30 min of an ice cold (4°C) lactated Ringer's solution is safe and reduces core temperature by ~2°C when administered after establishing stable restoration of spontaneous circulation (ROSC) in CA victims. This is a simple, inexpensive, and very feasible approach to rapid induction of mild hypothermia. Ambulances should develop systems to have several liters of ice cold fluid readily available. More recently, in an experimental laboratory model of CA in dogs simulating field resuscitation, Nozari et al<sup>11</sup> carried this concept further and