

## Conclusion

Most temperature-measuring devices are accurate and precise within a range. The problems are 1) the site where they are used and 2) the relationship between the site and the body's core temperature. Based on current knowledge, the tympanic membrane using the thermocouple technology would seem to be the present gold standard.

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# Pathophysiology and Consequences of Hypothermia

**Steven M. Frank, MD**

*Department of Anesthesiology/Critical Care Medicine  
The Johns Hopkins Medical Institutions  
600 N. Wolfe Street  
Baltimore, MD 21287 USA  
stevefrank37@comcast.net*

**Learning Objectives:** 1) to review the importance of body temperature in the perioperative period, with a focus on the effects of anesthesia on thermoregulation, and the physiologic effects of hypothermia, and 2) to review the various outcome studies that correlate body temperature and clinical outcomes.

### Abstract

The role of anesthesiologists is to maintain physiologic homeostasis during the perioperative period, a time when alteration in body temperature is common, especially in patients with traumatic injuries. Anesthetics create a state of poikilothermia in which body temperature tends to equilibrate with ambient temperature. Body temperature should be managed in a similar fashion as the other vital signs, with efforts made to maintain normothermia.

Patients suffering traumatic injuries are subjected to dramatic alterations in body temperature during both the intraoperative and postoperative periods. Patients often arrive at the hospital with hypothermia that has developed in the field, or they develop hypothermia in the operating room during surgery. For many years, body temperature has been considered to be the vital sign of least importance during the perioperative period.

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Despite the common occurrence of hypothermia during surgery,<sup>1,2</sup> few studies have examined the relationship between body temperature and outcome, and only recently have such studies been performed.

Virtually all anesthetics that have been tested impair thermoregulation. Patients are thus rendered poikilothermic, and body temperature decreases in the typically cool operating room environment. Opioids, inhalational anesthetics, propofol, spinal, and epidural anesthetics have all been shown to impair thermoregulatory mechanisms either through the central effects on the brain and the hypothalamus, or through impairment of the vasoconstriction and shivering responses. Patients receiving regional anesthesia are at similar risk for developing hypothermia as are those receiving general anesthesia.<sup>1</sup> The elderly and the very young are at greatest risk for developing perioperative hypothermia, as are those patients anesthetized in cold operating rooms, less than  $\approx 21^{\circ}\text{C}$  ( $70^{\circ}\text{F}$ ).<sup>1</sup>

## Shivering and Metabolism

One of the most commonly recognized effects of hypothermia is postoperative shivering. Despite earlier suggestions that inhalational anesthetics cause shivering by disassociation of spinal reflexes from cortical centers in the brain, it is now believed that virtually all perioperative shivering (with general or regional anesthesia) is thermoregulatory in origin.

Based on studies from 20 to 30 years ago with very small numbers of patients and questionable methods, the myth has been perpetuated that shivering dramatically increases total body oxygen consumption by 400% above baseline.<sup>4,5</sup> In these earlier studies, there were single patients who reportedly increased their metabolic rates by more than 400%, but the methods used to measure oxygen consumption were inferior, and the average increase with shivering was 100%.<sup>5</sup> In general, these were young patients receiving little or no opioid analgesia. More carefully conducted studies have shown that shivering increases oxygen consumption, but the average increase is  $\approx 40\%$ , with a maximum increase of  $\approx 100\%$ .<sup>6</sup> Evidence shows that predictors of increased total body oxygen consumption in the early postoperative period are 1) the presence of shivering, 2) male gender, and 3) increased core temperature (Fig. 1).<sup>6</sup> Although shivering is uncomfortable for most patients, it is unlikely that this relatively small increase in total body oxygen consumption in the average shivering patient is associated with perioperative morbidity.

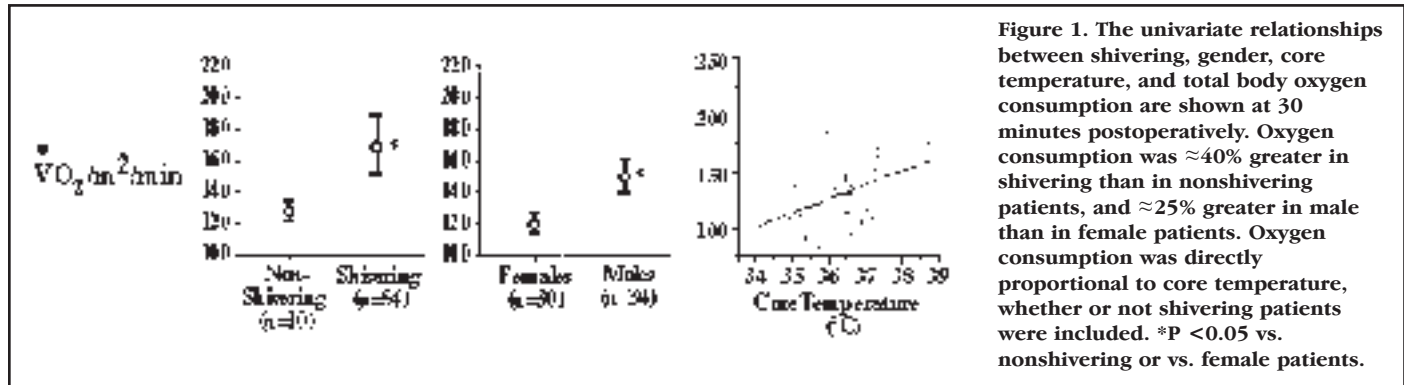


Figure 1. The univariate relationships between shivering, gender, core temperature, and total body oxygen consumption are shown at 30 minutes postoperatively. Oxygen consumption was  $\approx 40\%$  greater in shivering than in nonshivering patients, and  $\approx 25\%$  greater in male than in female patients. Oxygen consumption was directly proportional to core temperature, whether or not shivering patients were included. \*P < 0.05 vs. nonshivering or vs. female patients.

Shivering can be attenuated by relatively small doses of opioids. Although all opioids reduce shivering, meperidine (12.5–25 mg) is most effective because of the increased activity at the kappa receptor.<sup>4,7</sup> Other drugs that are effective in the treatment of shivering include clonidine, dexmedetomidine, neostigmine, and ketanserin (a serotonin antagonist). Thermal comfort is significantly improved and shivering can be virtually eliminated during or following surgery by skin-surface warming with a forced-air system.<sup>8</sup> For every 1°C of core hypothermia, approximately 4°C of cutaneous warming is required to attenuate the shivering response.<sup>9</sup>

### Respiratory

Whole-body oxygen consumption and carbon dioxide production decrease with hypothermia by 5% for each degree Celsius of core cooling. The magnitude of this decrease reflects the behavior of most enzyme-controlled biologic phenomena, that is, a halving of activity with a fall in temperature of 10°C. This halving is formally expressed as a  $Q_{10}$ , or quotient of measured activities at two temperatures 10°C apart. Initially, cooling increases respiratory rate by central stimulation; ventilatory depression supervenes. Decreases in both tidal volume and respiratory rate contribute to the decreased minute ventilation. Body  $CO_2$  content remains constant at hypothermia. One might expect the magnitude of decrease in minute ventilation to parallel that of  $CO_2$  production. However, ventilatory dead space increases with hypothermia, thus blunting the decrease in minute ventilation.<sup>10</sup>

### Adrenergic

The adrenergic response to hypothermia is significant. Although this response is not manifested during anesthesia, norepinephrine is significantly increased postoperatively in mildly hypothermic patients. A core temperature of less than 35.5°C following surgery will trigger a twofold increase in norepinephrine, vasoconstriction, and increased arterial blood pressure (Fig. 2).<sup>11</sup> When human volunteers are cooled to a core temperature of 35.5°C, a 700% increase in norepinephrine is induced, along with vasoconstriction and increased arterial blood pressure. Venous levels of epinephrine and cortisol are unchanged.<sup>12</sup> However, arterial concentrations of both epinephrine and norepinephrine increase significantly.<sup>13,14</sup> Local hemodynamic effects of cold increase extraction of circulating catecholamines and underestimate the arterial epinephrine response.<sup>15</sup> Thus, cold evokes both an adrenomedullary and a sympathoneural response. The adrenergic response is of greater

magnitude in younger individuals, which may explain the decreased ability for the elderly to protect their core temperature during cold challenge.

### Cardiovascular

It is well recognized that cold stress adversely affects the cardiovascular system by triggering myocardial ischemia. For several decades, a seasonal variation in death rate from myocardial infarction has been recognized with increased morbidity during the winter months.<sup>16,17</sup> This effect appears to be temperature-related and is independent of climate changes such as snowfall. The classic model of cold stress that is used to precipitate myocardial ischemia is the cold pressor test. The test was described over 50 years ago and involves a brief period of immersion of the hand and forearm into an ice bath. The stimulus triggers a significant increase in both norepinephrine and epinephrine, along with alpha-adrenergically mediated coronary vasoconstriction.<sup>18</sup> In human volunteers, mild core hypothermia constitutes a catecholamine-mediated cardiovascular stress test with beta-adrenoceptor-mediated increased cardiac work, sympathoadrenal activation, increased myocardial

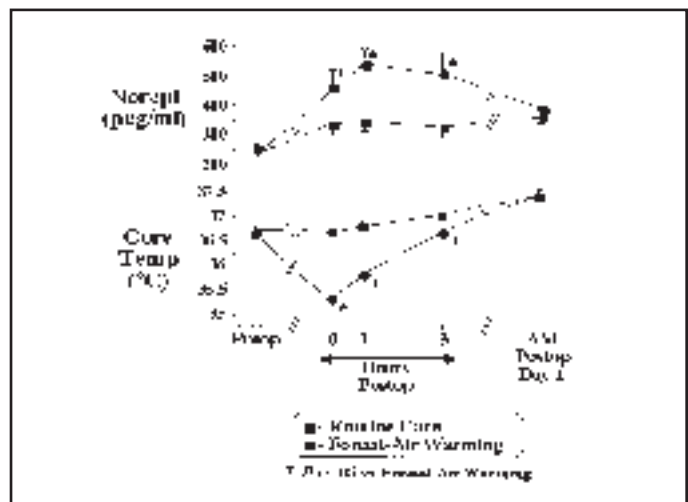


Figure 2. In patients randomly assigned to receive routine care (n = 37) or forced-air warming (n = 37), core temperature differed by 1.4°C at the end of surgery, which was associated with a significantly increased norepinephrine (Norepi) response in the mildly hypothermic patients during the early postoperative period.

perfusion, increased cardiac output, and increased rate-pressure product.<sup>13,14</sup> However, coronary vascular resistance is unchanged.<sup>13</sup> In high-risk surgical patients, a core temperature less than 35°C is associated with a two- to threefold increase in the incidence of early postoperative myocardial ischemia.<sup>19</sup> This “cold-induced” myocardial ischemia is independent of anesthetic technique (regional or general) and age (median age = 65 years). In a randomized trial, we demonstrated a reduced incidence of early postoperative cardiac morbidity in patients who were aggressively warmed during surgery. The incidence of ventricular tachycardia and morbid cardiac events were reduced in the normothermic group (36.7°C) compared with the hypothermic group (35.4°C) (Fig. 3).<sup>20</sup> It is of interest that, intraoperatively, the incidence of cardiac outcomes was not different in the two groups. This suggests that cold-induced perioperative cardiovascular morbidity is likely to be mediated by the adrenergic response since the effect is more prominent in the postoperative period after emergence, not during anesthesia, when the adrenergic response to hypothermia is attenuated.

Conduction velocity decreases throughout the hypothermic heart, yielding prolonged PR and QT intervals as well as a widening of the QRS complex on the electrocardiogram. Both J-point elevations, termed “Osborne waves,” and T-wave flattening or inversions occur with hypothermia. Atrial fibrillation is common when core temperature approaches 30°C. This is especially true when the atrium has been traumatized by cannulation for cardiopulmonary bypass. Ventricular fibrillation develops between 24 and 28°C. Hypothermia-induced ventricular fibrillation is refractory to pharmacologic therapy.

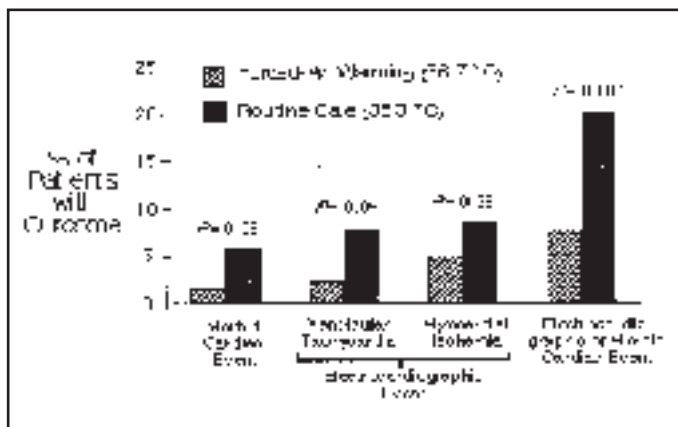


Figure 3. Cardiac morbidity was increased in patients who were mildly hypothermic following surgery. Three hundred patients having vascular, thoracic, or major abdominal surgery with documented coronary artery disease (CAD) or risk factors for CAD were randomly assigned to receive forced-air warming or routine thermal care during surgery. Morbid cardiac events included cardiac arrest, myocardial infarction, and unstable angina or ischemia.

## Coagulation and Bleeding

The coagulation system is significantly influenced by hypothermia through three different mechanisms: platelet function, the coagulation cascade, and fibrinolysis. The function of platelets is impaired by hypothermia because of reduced levels of thromboxane B2 at the site of tissue injury.<sup>21</sup> There is also reduced activity of coagulation factors in the coagulation cascade because the enzymes involved in the cascade, like all enzymes, are temperature-dependent.<sup>22</sup> Since the PT and PTT tests are routinely performed at a temperature of 37°C in most laboratories, it is likely that most temperature-related coagulopathies are missed in the clinical setting.<sup>22</sup> Fibrinolysis is enhanced by hypothermia, which destabilizes clot and predisposes to increased bleeding.<sup>23</sup> Platelet sequestration is also thought to contribute to hypothermia-related coagulopathy.<sup>24</sup> Sequestration, however, has only been shown in severely hypothermic dogs (20°C) and is unlikely to be significant in the perioperative setting. In patients undergoing total hip arthroplasty, there was a significant reduction in blood loss and reduced requirements for allogeneic blood transfusion in patients who were maintained normothermic, compared with those with mild hypothermia (35°C).<sup>25</sup>

## Wound Healing and Infection

There is evidence that wound healing is impaired and that patients are more susceptible to wound infection when hypothermia (<35°C) occurs during surgery.<sup>26</sup> Mild hypothermia (34.7°C) increased the incidence of wound infection threefold (19% versus 6%) compared with normothermic patients (36.6°C) undergoing colon surgery. This effect is thought to be related to impaired macrophage function and reduced tissue oxygen tension secondary to thermoregulatory vasoconstriction. Collagen deposition in the wound has also been shown to be impaired with hypothermia.<sup>26</sup> Increased susceptibility to infection with hypothermia at the time of introduction of bacteria into the skin has also been shown in animal models.<sup>27</sup> The “window of opportunity” for infection to become established is reportedly in the first 3 hours following inoculation. If hypothermia occurs at this critical time, infection occurs more frequently.

## Altered Pharmacokinetics and Pharmacodynamics

The minimum alveolar concentration (MAC) for potent, inhaled anesthetics is reduced by less than 5% for each degree Celsius of reduction in body temperature.<sup>28</sup> In addition, blood/gas solubility for inhaled anesthetics is increased with hypothermia. In combination, these effects contribute to the slow emergence from general anesthesia in hypothermic patients. In a randomized prospective trial, the duration of time in the postanesthetic care unit required to be ready for discharge was prolonged by an average of 40 minutes in hypothermic (34.7°C) as opposed to normothermic (36.6°C) patients.<sup>29</sup> These findings suggest that substantial cost savings may be achieved by maintaining normothermia and expediting recovery from general anesthesia.

Mild hypothermia increases the duration of action of nondepolarizing neuromuscular blockers. At 34°C, the duration of vecuronium is doubled.<sup>30</sup> Atracurium is also prolonged, but somewhat less. A 60% increase in duration occurs at 34°C. This effect, when added to the changes in MAC and solubility for inhaled anesthetics, can delay or prevent emergence from general anesthesia, especially in the elderly, who already have a reduced MAC and are especially susceptible to hypothermia.

## Conclusions

Alteration in body temperature is common during anesthesia, especially in patients with traumatic injuries. Anesthetics create a state of poikilothermia in which body temperature tends to equilibrate with ambient temperature. The role of the anesthesiologist is to maintain physiologic homeostasis during the perioperative period, a time during which anesthesia and surgery create an abnormal physiologic state. Body temperature should be managed in a similar fashion as the other vital signs, and efforts should be made to maintain normothermia.

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