Physiology of Thermoregulation

Andrea Kurz* M.D.
Professor and Vice Chair
Department of Outcomes Research, The Cleveland Clinic, 9500 Euclid Avenue, P77 Cleveland, Ohio 44195, USA

Core body temperature is one of the most tightly regulated parameters of human physiology. At any given time, body temperature differs from the expected value by no more than a few tenths of a degree. However, slight daily variations are due to circadian rhythm, and, in women, monthly variations are due to their menstrual cycle. Importantly, both anesthesia and surgery dramatically alter this delicate control, and as a result intraoperative core temperatures 1 to 3 °C below normal are not uncommon.

Consequently, perioperative hypothermia leads to a number of complications including postoperative shivering (which unacceptably increases patients’ metabolic rates), impaired coagulation, prolonged drug action, and negative postoperative nitrogen balance. In this review I will describe how anesthesia and surgery impair thermoregulation, the resulting changes in heat balance, and the physiological responses provoked by perioperative alterations in body temperature.

Key words: anesthesia; core temperature; heat balance; shivering; surgery; sweating; vasoconstriction.

NORMAL THERMOREGULATION

Like many other physiological control systems, thermoregulation uses negative-feedback to minimize perturbations from preset, “normal” values. Early research in 1912 showed that if the hypothalamus was destroyed, animals were unable to adequately regulate body temperature. In the late 1950's experiments showed that mice placed in a cold environment shivered without decreasing their hypothalamic temperatures and thus was recognized the importance of thermal input from the skin surface. Then, in the early 1960's, physiologists reported active thermoregulation in response to isolated warming and cooling at sites other than the hypothalamus or skin surface; these included extra-hypothalamic portions of the brain, deep abdominal tissues, and the spinal cord. Collectively, this research shows that normal
Thermoregulation is based on multiple, redundant signals from nearly every tissue type. It is now understood that the processing of thermoregulatory information occurs in three phases: afferent thermal sensing, central regulation, and efferent responses (Figure 1).

**Afferent input and central control**

Receptors for cold and warm are distributed throughout the body. Cold signals traverse A—delta fibers whereas signals from warmth receptors are conveyed by C fibers. Thermal inputs are integrated at numerous levels within the spinal cord and central nervous system, finally arriving at the hypothalamus which is the dominant thermoregulatory controller in mammals.\(^1\) The skin surface, deep abdominal and thoracic tissues, spinal cord, hypothalamus, and other portions of the brain each contribute very roughly 20 percent to autonomic thermoregulatory control.\(^2,3\) Behavioral responses, in contrast, may depend more on skin temperature.\(^4\)

Threshold, gain, and maximum response intensity describe each thermoregulatory response. Thresholds are defined by the core temperature triggering each thermoregulatory defense (at a given mean skin temperature); this is analogous to the temperature setting on a home thermostat. Gain characterizes the extent to which response intensity increases with further deviation from the triggering threshold; it is analogous to a proportional controller which augments heater output as ambient temperature increases.

**Figure 1.** The hypothalamus is the dominant thermoregulatory controller in mammals, and is shown here as a large square. The skin surface, deep abdominal and thoracic tissues, spinal cord, and non-hypothalamic portions of the brain each contribute very roughly 20 percent to control of autonomic thermoregulatory defenses. These inputs are shown entering the hypothalamus from the left side of the figure. Hypothalamic temperature, per se, also contributes roughly 20 percent to thermoregulatory control. In the hypothalamus, integrated body temperature is compared to thresholds which are the temperatures triggering specific thermoregulatory responses. Temperatures exceeding warm-response thresholds (i.e., sweating) or less than cold-response thresholds (i.e., vasoconstriction and shivering) initiate the corresponding thermoregulatory defense. Temperatures between the sweating and vasoconstriction thresholds define the interthreshold range — temperatures not triggering thermoregulatory defenses. The interthreshold range is normally only 0.2 °C. Because thermoregulatory defenses are effective in most environments, body temperature rarely deviate more than a few tenths of a degree from its time-adjusted target value. The sweating, vasoconstriction, and shivering thresholds are from Lopez et al.,\(^5\) and are shown as means and standard deviations; the nonshivering thermogenesis threshold is estimated.
progressively deviates from the thermostat setting. In this context, the highest possible heat output from the furnace would constitute the maximum response intensity. An approximately 1 °C circadian cycle and an approximately 0.5 °C menstrual cycle are superimposed on the normal human core temperature of 37 °C.

Sweating and active vasodilation, the thresholds for warm responses, normally exceed vasoconstriction, the threshold for the first cold defense, by only 0.2 °C. Temperatures between the initial warm- and cold-response thresholds define the interthreshold range. Temperatures within this range do not trigger autonomic thermoregulatory defenses. Higher or lower temperatures, though, do trigger effective thermoregulatory defenses; consequently, the thermoregulatory system usually maintains core temperature within approximately 0.2 °C of the time-adjusted target value. The precision of thermoregulatory control is similar in men and women, but is diminished in the elderly.

Mean body temperature is used to assess thermoregulatory responses and is defined as a physiologically-weighted average reflecting the thermoregulatory importance of various tissues. In unanesthetized subjects, mean body temperature is \( t_{\text{central}} + 0.15 t_{\text{skin}} \), where average skin temperature can be determined using the formula \( t_{\text{skin}} = 0.3 (t_{\text{chest}} + t_{\text{arm}}) + 0.2 (t_{\text{thigh}} + t_{\text{leg}}) \). The difference between the lowest warm and highest cold thresholds indicates the sensitivity of the system. The interthreshold range (temperature range over which no regulatory responses occur) is typically \( \pm 0.2 \) °C. Central body temperature is frequently substituted for mean body temperature in clinical studies.

Given similar warm and cold threshold temperatures and relatively high response gains, then the regulatory system can also be modeled as a thermostat or “setpoint” (i.e., responses fully activated or completely inactivated at the same temperature). Despite being a simplification of a complex system, the setpoint model often describes thermoregulation remarkably well. However, it is inadequate in anesthetized or sedated patients and cannot explain the consistent order in which effectors are initiated.

Although unknown, the mechanism, which determines absolute threshold temperatures, appears to be mediated by norepinephrine, dopamine, 5-hydroxytryptamine, acetylcholine, prostaglandin E₁, and neuropeptides. The thresholds vary daily in both sexes (circadian rhythm) and monthly in women by \( \pm 0.5 \) °C. Exercise, food intake, infection, hypo- and hyperthyroidism, anesthetic and other drugs (including alcohol, sedatives, and nicotine), and cold- and warm-adaptation alter threshold temperatures. Central regulation is intact in infants, but it may be impaired in the elderly or extremely ill patients.

Efferent responses

Changes in human behavior are the most effective response to changes in body temperature. It is primarily behavioral defenses that allow humans to live and work in extreme environments. Behavioral strategies are mediated by thermal discomfort, which provokes responses such as dressing warmly or adjusting ambient temperature.

Sweating and active cutaneous vasodilation are the major autonomic defenses against heat. Sweating is mediated by post-ganglionic, cholinergic nerves that terminate on widely, but unevenly, distributed glands. Sweat is an ultrafiltrate of plasma whose composition depends on the rate of sweating, hydration status, and a number of other factors. The maximum sweating rate exceeds 0.5 liters/hour in most adults, and is two- or three-fold greater in trained athletes. Each gram of evaporated sweat absorbs 584 cal. Consequently, sweating can easily dissipate many times the basal metabolic
rate in a dry environment. The efficacy of sweating is augmented by pre-capillary thermoregulatory vasodilation. Active thermoregulatory vasodilation is a uniquely human response that is mediated by a yet-to-be-identified factor released from sweat glands. It increases cutaneous blood flow enormously \(^8\), thereby facilitating transfer of heat from the core to the skin for eventual dissipation to the environment.

_Cutaneous vasoconstriction_, the most consistently used effector mechanism, reduces metabolic heat loss from convection and skin surface radiation. Total digital skin blood flow is divided into nutritional (capillary) and thermoregulatory (arterio-venous shunt) components. The arterio-venous shunts are anatomically and functionally distinct from the capillaries supplying nutritional blood to the skin (thus vasoconstriction does not compromise the needs of peripheral tissues). Shunts are typically 100 \(\mu\)m in diameter, which means that one can convey 10,000-fold as much blood as a comparable length of 10 \(\mu\)m-diameter capillary. Blood flow through the arterio-venous shunts tends to be "on" or "off." During heat stress, flow may be 100-fold greater than necessary to supply the nutritional needs of the skin, but thermoregulatory constriction can decrease flow more than 10-fold.

Local alpha-adrenergic sympathetic nerves mediate constriction in the thermoregulatory arterio-venous shunts; flow is minimally affected by circulating catecholamines. Systemic hemodynamic changes are not observed during thermoregulatory vasoconstriction because, except during heat exposure, \(\leq\)10\% of cardiac output traverses these vessels; larger arterioles that control blood pressure are not influenced.

Since thermoregulatory shunts are concentrated in the fingers and toes vasoconstriction reduces flow to a greater extent to the distal extremities than to the central skin. Skin-surface temperature gradients (forearm temperature — finger tip temperature), can therefore be measured to quantify the contribution of vasoconstriction to thermoregulation. Typical skin-temperature gradients are between \(-2\) and \(+2\ ^\circ\)C; gradients \(\geq 4\ ^\circ\)C identify significant vasoconstriction. The relationship between several indices of peripheral cutaneous perfusion is indicated in Figure 1.

Arterio-venous shunts located primarily in fingers and toes are the site of thermoregulatory vasoconstriction. These shunts are controlled by centrally-mediated alpha-1 adrenergic receptors; however, constriction is synergistically augmented by local hypothermia via alpha-2 adrenergic receptors.\(^9\) Diameter of open shunts is approximately 100 \(\mu\)m; consequently, they carry 10,000 times as much blood as a given length of 10-\(\mu\)m capillary.\(^10\)

Nonshivering thermogenesis is an important thermoregulatory defense in infants\(^11\), but contributes little in children and adults.\(^12\) The response is mediated by beta-3 adrenergic nerves that terminate on brown fat.\(^13\) The macroscopic brown coloration of this specialized adipose tissue results from its enormous mitochondrial density. Brown fat is equipped with a unique uncoupling protein that allows direct transformation of substrate into heat.\(^14\) Shivering is an involuntary muscular activity that increases metabolic rate two- to three-fold.\(^15\)

_Shivering_ increases metabolic heat production by \(\approx 200\%\) in adults, but this increase is relatively small and surprisingly ineffective when compared with that produced by exercise (which can increase metabolism by 10-fold). Shivering does not occur in newborn infants, and probably is not fully effective until several years of age. The rapid tremor (\(\approx 50\) Hz) and unsynchronized muscular activity of thermogenic shivering suggests no central oscillator. Superimposed on the fast activity, there may be a very slow (4–8 cycle/minute), synchronous "waxing-and-waning" pattern which is presumably centrally mediated. Because other rhythmic muscular activities may be clinically similar, tremor should be considered normal thermoregulatory shivering only when: 1) mean
body temperature is below the threshold for shivering; 2) tremor is preceded by peripheral cutaneous vasoconstriction and nonshivering thermogenesis; and 3) tremor patterns match those produced by centrally mediated shivering.

Thermoregulatory responses are diminished and the risk of hypothermia is increased by age, infirmity, and medication. For example, decreased muscle mass, neuromuscular diseases, and muscle relaxants all inhibit shivering which will increase the minimum tolerable ambient temperature. Similarly, anti-cholenergic drugs inhibit sweating, decreasing the maximum tolerable temperature.

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**Practice points**

- Core body temperature is tightly regulated around 37°C
- Slight daily variations are due to circadian rhythm
- Processing thermoregulatory information occurs through three pathways:
  - Afferent thermal sensing from cold and warm receptors in the periphery
  - Central regulation in the hypothalamus.
  - Efferent responses

The skin surface, deep abdominal and thoracic tissues, spinal cord, hypothalamus, and other portions of the brain each contribute very roughly 20 percent to autonomic thermoregulatory control

- Thermoregulatory responses are characterized by the threshold, gain and maximum intensity
  - Thresholds are defined by the core temperature triggering each thermoregulatory defense (at a given mean skin temperature)
  - Gain characterizes the extent to which response intensity increases with further deviation from the triggering threshold
    - A small increase in core temperature triggers sweating and active vasodilation (warm response threshold)
    - A small decrease in core temperature triggers active arteriovenous shunt vasoconstriction
    - Further decrease in core temperature triggers shivering

Temperatures between the initial warm- and cold-response thresholds define the interthreshold range

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**THERMOREGULATION DURING ANESTHESIA AND SURGERY**

**General anesthesia**

General anesthesia eliminates behavioral thermoregulatory compensations, leaving only autonomic defenses to environmental perturbations.
**Thermoregulation**

All general anesthetics are known to significantly impair thermoregulatory responses. Anesthetic-induced thermoregulatory inhibition is dose-dependent, and impairs vasoconstriction and shivering about three times as much as sweating. General anesthetics linearly increase the warm-response thresholds. Opioids and the intravenous anesthetic propofol linearly decrease the vasoconstriction and shivering thresholds. In contrast, volatile anesthetics, such as isoflurane and desflurane, decrease cold responses non-linearly (Figure 2). In contrast to other opioids and the anesthetic drugs meperidine possesses additional anti-shivering action and inhibits shivering twice as much as vasoconstriction. It has been hypothesized, that the special anti-shivering effect of meperidine may be primarily related to meperidine’s activity at k-opioid receptors. This theory is supported by the facts that moderate-dose naloxone only partially blocks the anti-shivering effect of meperidine and that butorphanol (also a partial k-opioid receptor agonist) inhibits shivering better than fentanyl. The only drug tested so far, which does not effect thermoregulatory responses is midazolam.

Both halothane and isoflurane impair thermoregulatory vasoconstriction in infants, children, and adults to a comparable extent. On the other hand thermoregulatory

![Figure 2. Anesthetic-induced inhibition of thermoregulatory control is usually the major factor determining perioperative core temperature. Concentration-dependent thermoregulatory inhibition by desflurane (halogenated volatile anesthetics), alfentanil (a µ-agonist opioid), dexmedetomidine (an alpha-2 agonist), and propofol (an intravenous anesthetic). The sweating (triangles), vasoconstriction (circles), and shivering (squares) thresholds are expressed in terms of core temperature at a designated mean skin temperature of 34 °C. Anesthesia linearly, but slightly, increases the sweating threshold. In contrast, anesthesia produces substantial and comparable linear or non-linear decreases in the vasoconstriction and shivering thresholds. Typical anesthetic concentrations thus increase the interthreshold range (difference between the sweating and vasoconstriction thresholds) approximately 20-fold from its normal value near 0.2 °C. Patients do not activate autonomic thermoregulatory defenses unless body temperature exceeds the interthreshold range; surgical patients are thus poikilothermic over a 3 to 5 °C range of core temperatures.](image)
responses are significantly delayed in the elderly subjecting this patient population to intraoperative hypothermia.

Thus, during anesthesia, the interthreshold range (core temperatures not triggering thermoregulatory defenses) increases approximately 20-fold from its normal value near 0.2 °C. As a result, anesthetized patients are poikilothermic over an approximately 4 °C range of core temperatures. Within this range, patients are poikilothermic and body temperature changes are passively determined by the difference between metabolic heat production and heat loss to the environment.

In patients receiving volatile anesthetics both gain and maximum response intensity of sweating and active vasodilation are well preserved. Desflurane, however, reduces the gain of arterio-venous shunt vasoconstriction three-fold, without altering the maximum intensity (Figure 3). It seems likely that the thermoregulatory effects of general anesthetics are primarily central since anesthetics of widely different types produce similar thermoregulatory inhibition. However, the possibility of peripheral inhibition has not been eliminated.

Higher vasoconstriction thresholds are observed in anesthetized individuals who are subject to rapid core temperature perturbations, but the magnitude of the increase has yet to be quantified. Similarly, the extent to which intraoperative thermoregulatory responses depend on the direction of temperature change remains unclear. The ratio of cutaneous to core thermal input to autonomic thermoregulatory

![Figure 3. Gain of vasoconstriction: Finger blood flow, as determined using volume plethysmography, without (open circles) and with (filled squares) desflurane administration. Values were computed relative to the thresholds (finger flow = 1.0 ml/min) in each subject. Flows of exactly 1.0 ml/min are not shown because flows in each individual were averaged over 0.1 or 0.05 °C increments; each data point thus includes both higher and lower flows. The horizontal standard deviation bars indicate variability in the thresholds among the volunteers; although errors bars are shown only at a flow near 1.0 ml/min, the same temperature variability applies to each data point. The slopes of the flow vs. core temperature relationships (1.0 to ≈0.15 ml/min) were determined using linear regression. These slopes defined the gain of vasoconstriction with and without desflurane anesthesia. Gain was reduced by a factor of three, from 2.4 to 0.8 ml min⁻¹ °C⁻¹ (P < 0.01).](image)
responses ranges from 5–20%, and it is unknown if the ratio remains similar in anesthetized individuals. But once triggered, the intensity of arterio-venous shunt vasoconstriction during anesthesia is similar to that in unanesthetized individuals.

Both core and skin temperatures contribute to steady-state thermoregulatory control. Skin and core temperatures contribute linearly to control of vasoconstriction and shivering in men, and the cutaneous contributions average \( \approx 20\% \) in both men and women. The same coefficients can thus be \( \approx 20\% \) used to compensate for experimental skin temperature manipulations in men and women (Figure 4).\(^{25} \) However, there is also a dynamic component that provokes especially aggressive defenses against rapid thermal perturbations. The dynamic component potentially complicates interpretation of thermoregulatory studies and slow induction of therapeutic hypothermia. Onset of vasoconstriction and shivering occurred at similar mean-skin temperatures when the skin was cooled at between 2 and 6 °C/h. Surface cooling at a rate of \( \leq 6 \) °C/h can thus be used in thermoregulatory studies and for induction of therapeutic hypothermia without provoking dynamic thermoregulatory defenses.

In anesthetized, hypothermic adults total body oxygen consumption does not increase significantly, indicating that nonshivering thermogenesis is not functional during general anesthesia. Since nonshivering thermogenesis is of little importance in normal humans, it is not surprising that its influence during anesthesia is also minimal. When anesthetized infants undergo vasoconstriction, oxygen consumption increases

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**Figure 4.** Skin core contribution: Core and skin temperatures at the vasoconstriction and shivering thresholds were linearly related in men. The correlation coefficients \( (r^2) \) averaged 0.90 ± 0.06 for vasoconstriction, and 0.94 ± 0.07 for shivering. The extent to which mean skin temperature contributed to central thermoregulatory control \( (B) \) was calculated from the slopes \( (S) \) of the skin temperature vs. the core temperature regressions, using the formula: \( B = S/(S - 1) \). Cutaneous contribution to vasoconstriction averaged 20 ± 6%, which did not differ significantly from the contribution to shivering: 19 ± 8%.
simultaneously, indicating that nonshivering thermogenesis remains intact, and that its gain is approximately normal.

Temperature variation within surgical incisions has an unknown clinical effect. All formulas for determining mean body and average skin-surface temperature were developed in normal subjects; consequently, no equations for mean body temperature include compensation for surgical incisions of different sizes, in different locations. Since thermal receptors are widely distributed, it is likely that the afferent input from tissues exposed to cold by large incisions contributes significantly to total central (hypothalamic) input and alters thermoregulatory thresholds. Patients having small incisions (at a given anesthetic concentration) require lower mean body temperatures to trigger thermoregulatory vasoconstriction than those requiring large incisions.

Collectively, these studies indicate that general anesthetics increase the interthreshold range from a normal value <0.6 °C to approximately 4 °C. It remains possible that body temperature remains accurately sensed during anesthesia, but that temperatures within the interthreshold range simply are not integrated to initiate regulatory responses. However, once body temperature deviates sufficiently from normal to trigger thermoregulatory responses, the gain and maximum intensity of these effector responses remains nearly normal. Markedly altered thermoregulatory thresholds with relatively well preserved gain and maximum intensities contrasts starkly with anesthetic effects on several other homeostatic systems.

Heat balance

Thermal steady state is defined by heat loss to the environment equaling metabolic heat production. Thus, over the long term, heat loss must equal heat production to maintain body temperature. However, body temperature and tissue heat content is not uniformly distributed: thermoregulation keeps core temperature nearly constant, whereas peripheral tissues usually are maintained at a lower temperatures by tonic vasoconstriction.

In practice, vasomotion alters the heat content of peripheral tissues, yet the temperature of vital organs remains unchanged, because the periphery acts as a thermal buffer. This allows individuals to lose heat in a cold environment or absorb heat in a warm environment. This strategy minimizes the need for other autonomic responses which may be costly in terms of metabolic needs, use of resources, or behavioral requirements. Because of their large mass, the legs probably constitute most of the peripheral thermal buffer. The capacity of the peripheral compartment is approximately 150 kcal (i.e., body heat content can change this amount without altering core temperature).

Usually a 2–4 °C core-to-peripheral temperature gradient is maintained by tonic thermoregulatory vasoconstriction, resulting in the uneven distribution of body heat. Induction of general anesthesia reduces the vasoconstriction threshold to below body temperature, thus opening arterio-venous shunts. The resulting core-to-peripheral redistribution of body heat decreases core temperature 1–1.5 °C during the first hour of general anesthesia. Net loss of heat to the environment contributes little to this initial decrease (Figure 5).

Redistribution hypothermia is difficult to treat, but can be prevented by cutaneous warming before induction of anesthesia. Pre-induction warming only slightly increases core temperature (which remains well regulated), but markedly increases peripheral compartment temperature. Because heat only flows down a temperature gradient, redistribution is prevented in proportion to the reduction in the core-to-peripheral temperature gradient.
In the subsequent few hours, core temperature usually decreases at a slower rate. This decrease is nearly linear and results simply from heat loss exceeding metabolic heat production. It has been attributed to undressing patients in a cool environment, anesthetic-induced vasodilation (which increases skin temperature), evaporation of surgical skin preparation solution, loss of heat from surgical incisions, and anesthetic-induced reduction in metabolic rate. Approximately 90 percent of all heat is lost via the skin surface, with radiation and convection usually contributing far more than evaporative or conductive losses.

After 3 to 5 hours of anesthesia, core temperature often stops decreasing. This core-temperature plateau may be a simple thermal steady-state, with heat loss equaling heat production. It has been attributed to undressing patients in a cool environment, anesthetic-induced vasodilation (which increases skin temperature), evaporation of surgical skin preparation solution, loss of heat from surgical incisions, and anesthetic-induced reduction in metabolic rate. Approximately 90 percent of all heat is lost via the skin surface, with radiation and convection usually contributing far more than evaporative or conductive losses.

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After 3 to 5 hours of anesthesia, core temperature often stops decreasing. This core-temperature plateau may be a simple thermal steady-state, with heat loss equaling heat production. This sort of steady-state plateau is especially likely in patients who are well insulated or effectively warmed. In patients becoming sufficiently hypothermic, however, the plateau results from re-activation of thermoregulatory vasoconstriction which decreases cutaneous heat loss and constrains metabolic heat to the core thermal compartment. Intraoperative vasoconstriction thus re-establishes the normal core-to-peripheral temperature gradient by preventing loss of centrally-generated metabolic heat to peripheral tissues. From a clinical point of view, an active core-temperature plateau is potentially dangerous because mean body temperature and body heat content continues to decrease, although core temperature remains

Figure 5. Changes in body heat content and distribution of heat within the body during induction of general anesthesia (at elapsed time zero). The change in mean body temperature was subtracted from the change in core (tympanic membrane) temperature, leaving the core hypothermia specifically resulting from redistribution. Redistribution hypothermia was thus not a measured value; instead, it is defined by the decrease in core temperature not explained by the relatively small decrease in systemic heat content. After one hour of anesthesia, core temperature had decreased $1.6 \pm 0.3 \ ^\circ\text{C}$, with redistribution contributing 81 percent to the decrease. Even after three hours of anesthesia, redistribution contributed 65 percent to the entire $2.8 \pm 0.5 \ ^\circ\text{C}$ decrease in core temperature. Data obtained from Matsukawa et al.\textsuperscript{26}
constant. Because vasoconstriction is effective, intraoperative core temperature rarely decreases the additional 1 °C necessary to trigger shivering.

BMI substantially influences intraoperative core temperature changes, and this effect depends on the phase of hypothermia. During the initial phase, the amount of redistribution hypothermia is inversely proportional to the percentage body fat ($\Delta T_C = 0.034 \cdot BF - 2.2, r^2 = 0.63$) and the weight-to-surface area (Wt/SA) ratio ($\Delta T_C = 0.052 \cdot Wt/SA - 3.35, r^2 = 0.66$). During the second phase, the core cools linearly, and the cooling rate is inversely proportional to the weight-to-surface area ratio ($\text{Rate} = 0.035 \cdot (Wt/SA) - 2.2, r^2 = 0.29$). And, during the final phase, thermoregulatory vasoconstriction is effective in virtually all patients independent of their morphology, and produces a four-fold reduction in the core cooling rate. (Figures 6–9)

Taken together, these studies suggest that intraoperative hypothermia develops in three phases. Initially, core temperature decreases rapidly when anesthetic-induced inhibition of tonic thermoregulatory vasoconstriction allows core-to-peripheral redistribution of body heat. Although difficult to treat, redistribution hypothermia can be prevented by warming peripheral tissues before induction of anesthesia. Secondly, a slower, linear decrease in body temperature results from heat loss exceeding metabolic heat production. Because nearly all heat is lost from the skin surface, adding cutaneous insulation will decrease the rate of cooling; similarly, sufficient active warming will increase body temperature during this phase. And in the final phase, core

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**Figure 6.** Plateau phase: Vasoconstriction decreased cutaneous heat loss (adjusted for evaporative and respiratory loss) ≈ 25 kcal/h. However, heat loss always exceeded heat production. Consequently, mean body temperature, which decreased at a rate of ≈ 0.6 °C/h before vasoconstriction, subsequently decreased at a rate of ≈ 0.2 °C/h. Core temperature also decreased at a rate of ≈ 0.6 °C before vasoconstriction, but remained virtually constant during the subsequent three h. Since mean body temperature and body heat content continued to decrease, constraint of metabolic heat to the core thermal compartment contributed to the core-temperature plateau. That is, vasoconstriction re-establishing the normal core-to-peripheral temperature gradient by preventing metabolic heat (which is largely generated in the core) from escaping to peripheral tissues. Constrained heat is presented cumulatively, referenced to vasoconstriction at elapsed time zero; asterisks (*) indicate values significantly different from those obtained at elapsed time zero.
temperature stops changing after 3–4 h of anesthesia. This plateau can be passive in patients remaining relatively warm, or may be accompanied by thermoregulatory vasoconstriction which decreases cutaneous heat loss and sequesters metabolic heat to the core.

### Practice points
- Hypothermia is common during anesthesia and surgery
- Most anesthetics and narcotics effect central and peripheral thermoregulatory responses
- Anesthetics increase the sweating threshold and markedly decrease the vasoconstriction and shivering threshold thus increasing the interthreshold range
- An increased interthreshold range makes patients poikilothermic and thus susceptible to hypothermia
- Intraoperative hypothermia develops in a very characteristic pattern:
  - During induction of anesthesia heat redistributes from the body to the periphery causing an initial drop in core temperature of 1–1.5 °C
  - During the following 3 hours core temperature linearly decreases due to heat loss exceeding metabolic heat production
  - After 3–5 hours of anesthesia core temperature stops dropping. This core temperature plateau is due to peripheral vasoconstriction preventing loss of centrally generated metabolic heat to peripheral tissues.

### Research agenda
- Test drugs, which might impair thermoregulatory control without having anesthesia-related side effects. This is especially important if hypothermia is needed for therapeutic reasons.
- Evaluate and quantify the effect of operating room environment perioperative heat loss.
- Quantify heat loss from the wound during different types of surgery.

### Regional anesthesia
Regional anesthesia impairs both central and peripheral thermoregulatory control. As a result, hypothermia is common in patients given spinal or epidural anesthesia. In patients becoming sufficiently hypothermic, shivering may again appear — and is often disturbing to both patients and medical staff.

### Thermoregulation
Neural mediation affects all thermoregulatory responses (except during fever, circulating factors normally contribute little to thermoregulatory control). Consequently,
Nerve blocks prevent regional manifestation of the major thermoregulatory defenses including sweating, vasoconstriction, and shivering. Spinal and epidural anesthesia disrupt nerve conduction to more than half the body. This peripheral inhibition of thermoregulatory defenses is a major cause of hypothermia during regional anesthesia.

Regional anesthesia, however, also impairs central thermoregulatory control. That spinal or epidural anesthesia would inhibit central control was surprising because regional anesthesia has no direct central effect. Inhibition is similar with spinal and epidural anesthesia, and does not result simply from recirculation of local anesthetic to the brain. Instead, it appears that the regulatory system misinterprets skin temperature in blocked areas as being abnormally elevated.\(^{29,30}\) This apparent (as opposed to actual) elevation in leg skin temperature fools the regulatory system into tolerating lower-than-normal core temperatures before triggering cold defenses.

Typically, the vasoconstriction and shivering thresholds are reduced approximately \(0.5\,^\circ\text{C}/\text{C}^{\circ}\) whereas the sweating threshold is elevated approximately \(-0.3\,^\circ\text{C}/\text{C}^{\circ}\).\(^{30,31}\) The

\[\Delta T_C = 0.034 \cdot \text{BF} - 2.2, \quad R^2 = 0.63.\]

The 95% confidence interval for the slope was 0.025 to 0.043 \(^\circ\text{C}/\text{C}\%\).

**Figure 7.** Effect of body mass on redistribution: The amount of redistribution hypothermia [reduction in core temperature during the first hour of anesthesia \((\Delta T_C)\)] was inversely proportional to the percentage body fat (BF): \(\Delta T_C = 0.034 \cdot \text{BF} - 2.2, \quad R^2 = 0.63.\) The 95% confidence interval for the slope was 0.025 to 0.043 \(^\circ\text{C}/\text{C}\%\).

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\[\text{Rate} = 0.035 \cdot (\text{Wt/SA}) - 2.2, \quad R^2 = 0.29.\]

The 95% confidence interval for the slope was 0.017 to 0.053 \(^\circ\text{C}/\text{C}\%\).

**Figure 8.** Effect of body mass on linear phase: The core cooling rate during the second (linear decrease) phase was inversely proportional to the weight-to-surface area (Wt/SA) ratio, although the relationship was weak: Rate = 0.035 \cdot (\text{Wt/SA}) - 2.2; \(R^2 = 0.29.\) The 95% confidence interval for the slope was 0.017 to 0.053 \(^\circ\text{C}/\text{C}\%\).
result is a 3-fold increase in the normal inter-threshold range. Spinal anesthesia reduces the shivering threshold in direct relation to the number of dermatomes blocked. Thus extensive spinal blocks impair central thermoregulatory control more than less extensive ones. Clinicians can thus anticipate more core hypothermia during extensive than during restricted blocks. 32

Heat flow and distribution during regional anesthesia is comparable to general anesthesia. Core hypothermia during the first hour after induction of epidural anesthesia results largely from redistribution of body heat from the core thermal compartment to the distal legs. Even after three hours of anesthesia, redistribution remains the major cause of core hypothermia. Redistribution contributes proportionately more to core hypothermia than previously reported during general anesthesia because metabolic rate was maintained during epidural anesthesia. Despite the greater fractional contribution of redistribution, epidural anesthesia decreases core temperature half as much as general anesthesia because metabolic rate was maintained and the arms remained vasoconstricted. 31

Furthermore thermoregulatory responses during regional anesthesia are delayed even further in the elderly patient population. Not only do regional anesthetics delay the vasoconstriction and shivering threshold, but they also decrease the gain and maximum intensity of shivering. Clinically, regional anesthetic-induced thermoregulatory inhibition is frequently compounded by concomitant administration of sedatives and/or general anesthesia (Table 1). 16

Although regional anesthesia typically causes core hypothermia, patients often feel warmer after induction of anesthesia. 33,34 Increased thermal comfort, like inhibition of autonomic defenses, presumably results from the thermoregulatory system

Figure 9. Redistribution hypothermia during induction of regional anesthesia: To separate the contributions of decreased overall heat balance and internal redistribution of body heat to the decrease in core temperature, we divided the change in overall heat balance by body weight and the specific heat of humans. The resulting change in mean body temperature (“heat balance”) was subtracted from the change in core temperature (“measured”), leaving the core hypothermia specifically resulting from redistribution (“redistribution”). After one h of anesthesia, core temperature had decreased 0.8 ± 0.3 °C, with redistribution contributing 89% to the decrease. During the subsequent two h of anesthesia, core temperature decreased an additional 0.4 ± 0.3 °C, with redistribution contributing 62%. Redistribution thus contributed 80% to the entire 1.2 ± 0.3 °C decrease in core temperature during the three h of anesthesia. The increase in the “redistribution” curve before induction of anesthesia indicates that thermoregulatory vasoconstriction was constraining metabolic heat to the core thermal compartment. Such constraint is, of course, the only way in which core temperature could increase while body heat content decreased. Induction of epidural anesthesia is identified as elapsed time zero. Asterisks (*) identify values differing significantly from time zero.
misinterpreting skin temperature as being elevated in the blocked area. Because core-temperature monitoring remains rare during spinal and epidural anesthesia, and because patients often fail to recognize that they are cold, undetected hypothermia is common during regional anesthesia.

**Heat balance**

Core hypothermia is comparable during regional and general anesthesia. As during general anesthesia, the initial hypothermia results from a core-to-peripheral redistribution of body heat. In this case, however, redistribution results primarily from peripheral rather than central inhibition of tonic thermoregulatory vasoconstriction. Although arterio-venous shunt vasodilation is restricted to the lower body, mass of the legs is sufficient to produce substantial core hypothermia. Subsequent hypothermia results simply from heat loss exceeding heat production. Patients given spinal or epidural anesthesia cannot, however, develop a regulated core-temperature plateau because vasoconstriction remains peripherally impaired. Consequently, hypothermia tends to progress throughout surgery.

Patients becoming sufficiently hypothermic during spinal or epidural anesthesia shiver. Shivering is disturbing to patients and caregivers, but produces relatively little heat because it is restricted to the small muscle mass cephalad to the block. Shivering can be treated by skin-surface warming, or administration of clonidine (75 µg intravenously) or meperidine (25 mg intravenously). Meperidine is considerably more effective than equianalgesic doses of other opioids; its special anti-shivering action may be mediated by kappa opioid receptors.

Taken together, these studies indicate that normal thermoregulatory shivering is induced by core hypothermia during regional anesthesia. Hypothermia results when sympathetic nerve block obliterates tonic thermoregulatory vasoconstriction, allowing redistribution of heat from the warm core to cooler peripheral tissues. Despite the core hypothermia and shivering, many patients feel warmer after induction of regional anesthesia, apparently because perceived skin temperature is elevated. Shivering can be prevented by maintaining normothermia; as during general anesthesia, redistribution hypothermia is difficult to treat, but can be prevented by peripheral tissue warming before induction of anesthesia.

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The sweating, vasoconstriction, and shivering thresholds under three different conditions: no anesthesia, epidural anesthesia, and spinal anesthesia. Also shown are the sweating-to-vasoconstriction (interthreshold) range, the vasoconstriction-to-shivering range, and the sweating-to-shivering range. All values are expressed in °C. Asterisks (*) indicate statistically significant differences vs. no anesthesia.
Summary

Temperatures throughout the body are integrated by a thermoregulatory system that coordinates cold- and warm-defenses. These effective responses usually keep core temperature within 0.2 °C of time-adjusted normal values. General anesthesia produces marked and dose-dependent inhibition of thermoregulatory control, typically increasing the sweating and vasodilation thresholds approximately 1 °C and reducing the vasoconstriction and shivering thresholds approximately 3 °C. As a result, the interthreshold range increases roughly 20-fold, leaving patients poikilothermic over an approximately 4 °C range of core temperatures. Regional anesthesia also impairs thermoregulatory control, producing both peripheral and central inhibition.

The combination of anesthetic-induced thermoregulatory impairment and exposure to cold operating room environments makes most surgical patients hypothermic. Hypothermia results initially from a core-to-peripheral redistribution of body heat, and subsequently from heat loss exceeding metabolic heat production. Patients becoming sufficiently hypothermic during general anesthesia develop a core-temperature plateau when arterio-venous shunt tone is reestablished.

REFERENCES

1. Satinoff E. Neural organization and evolution of thermal regulation in mammals — several hierarchically arranged integrating systems may have evolved to achieve precise thermoregulation. Science 1978; 201: 16–22.

Practice points

- Hypothermia is common during regional anesthesia
- Neuraxial anesthesia causes central, peripheral and behavioral impairment of thermoregulatory responses
- Neuraxial anesthetics slightly increases the sweating threshold and decreases the vasoconstriction and shivering threshold thus increasing the interthreshold range
- Intraoperative hypothermia develops in a very characteristic pattern:
  - During induction of neuraxial anesthesia heat redistributes from the body to the periphery causing an initial drop in core temperature of 1–1.5 °C
  - During the following 3 hours core temperature linearly decreases due to heat loss exceeding metabolic heat production
  - Sympathectomy prevents the core temperature plateau making patients under regional anesthesia even more prone to perioperative hypothermia.


