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Complications and Treatment of Mild Hypothermia

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THE combination of anesthetic-induced impairment of thermoregulatory control and exposure to a cool operating room environment makes most surgical patients hypothermic. Several prospective, randomized trials have demonstrated various hypothermia-induced complications. There is no widely accepted definition for the term *mild hypothermia*. Furthermore, the term is not even used consistently in the literature. For the purpose of this review, *mild hypothermia* refers to core temperatures between 34 and 36°C.

Hypothermia-induced Complications

Recent prospective, randomized trials have shown that mild perioperative hypothermia is associated with numerous adverse outcomes. The major ones are listed in table 1. Shivering is an important complication of hypothermia. However, there is increasing evidence that shivering-like tremor is a complicated response that includes at least three different patterns of muscular activity.[1] Furthermore, some shivering-like tremor is not even thermoregulatory.[2,3] Consequently, this topic will be reviewed elsewhere.

Myocardial Ischemia

Myocardial infarctions remains one of the leading causes of perioperative mortality and major morbidity. It has long been suspected that postoperative shivering, which increases oxygen consumption by up to 400%,[4] would cause hypoxemia, myocardial ischemia, and myocardial infarctions in elderly and other high-risk patients.[5] However, there are several difficulties with this logic. The first is that oxygen consumption (*i.e.*, metabolic rate) rarely increases anywhere near 400%. Cold-induced shivering in young, healthy volunteers typically increases oxygen consumption only 200%.[6] Postoperatively, oxygen consumption rarely increases even by a factor of two, and then only during extreme circumstances.[7,8] The second problem is that the elderly rarely shiver because advanced age impairs thermoregulatory responses.[9–11] Shivering appears to be especially rare in the patients at highest risk for cardiac complications.[12] The third difficulty is that shivering does not appear to be an important cause of postoperative hypoxemia. Instead, hypoxemia itself inhibits shivering.[13–16] Finally, several studies indicate that perioperative myocardial ischemia is unrelated to shivering.[17,18] Available evidence thus suggests that shivering, although uncomfortable, does not directly trigger myocardial ischemia or infarction.

Clinical Outcome. Evidence connecting perioperative hypothermia with myocardial complications was initially based on a retrospective analysis of data collected prospectively for a different purpose.[17] Multivariate analysis of these data indicated that patients becoming hypothermic were more likely to experience myocardial ischemia and ventricular arrhythmias. This study suffered from the possibility that older, sicker patients, and those having the largest and longest procedures, may have become most hypothermic.

Fortunately, prospective, randomized data are now available. Frank *et al.*[18] recently demonstrated that high-risk patients assigned to only 1.3°C core hypothermia were three times as likely to experience adverse myocardial outcomes.

The mechanism by which mild hypothermia triggers myocardial events remains unclear. Cold-induced hypertension in the elderly is associated with a threefold increase in plasma norepinephrine concentrations,[19] which may augment cardiac irritability and facilitate development of ventricular arrhythmias. Hypothermia also causes hypertension in elderly patients and those at high risk for cardiac complications.[20]

Coagulopathy

Schmied *et al.*[21] showed that mild hypothermia increases blood loss. In their study, patients were randomly assigned to normothermia or mild hypothermia during elective primary hip arthroplasty. Just 1.6°C core

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Table 1. Major Consequences of Mild Perioperative Hypothermia in Humans

Consequence	Author	N	ΔT_{core} (°C)	Normothermic	Hypothermic	*P*
Surgical wound infection	Kurz *et al.*[52]	200	1.9	6%	19%	< 0.01
Duration of hospitalization	Kurz *et al.*[52]	200	1.9	12.1 ± 4.4 days	14.7 ± 6.5 days	< 0.01
Intraoperative blood loss	Schmied *et al.*[21]	60	1.6	1.7 ± 0.3 l	2.2 ± 0.5 l	< 0.001
Allogeneic transfusion requirement	Schmied *et al.*[21]	60	1.6	1 unit	8 units	< 0.05
Morbid cardiac events	Frank *et al.*[18]	300	1.3	1%	6%	< 0.05
Postoperative ventricular tachycardia	Frank *et al.*[18]	300	1.3	2%	8%	< 0.05
Urinary excretion of nitrogen	Carli *et al.*[55]	12	1.5	982 mmol/day	1,798 mmol/day	< 0.05
Duration of vecuronium	Heier *et al.*[59]	20	2.0	28 ± 4 min	62 ± 8 min	< 0.001
Duration of atracurium	Leslie *et al.*[63]	6	3.0	44 ± 4 min	68 ± 7 min	< 0.05
Postoperative shivering	Just *et al.*[8]	14	2.3	141 ± 9 ml · min^{-1} · m^{-2}	269 ± 60 ml · min^{-1} · m^{-2}	< 0.001
Duration of postanesthetic recovery	Lenhardt *et al.*[144]	150	1.9	53 ± 36 min	94 ± 65 min	< 0.001
Plasma [norepinephrine]	Frank *et al.*[20]	74	1.5	330 ± 30 pg/ml	480 ± 70 pg/ml	< 0.05
Thermal discomfort	Kurz *et al.*[73]	74	2.6	50 ± 10 mm VAS	18 ± 9 mm VAS	< 0.001

Only prospective, randomized human trials are included; subjective responses were evaluated by observers blinded to treatment group and core temperature. Different outcomes of the first three studies are shown on separate lines. VAS is a 100-mm-long visual analog scale (0 mm = intense cold, 100 mm = intense heat). Reprinted with permission.[154]

N = total number of subjects; ΔT_{core} = difference in core temperature between the treatment groups.

hypothermia increased blood loss by 500 ml (30%) and significantly augmented allogeneic transfusion requirement. The same group subsequently confirmed the hemostatic benefits of maintaining intraoperative normothermia in a retrospective analysis.[22] In contrast, another study of blood loss during hip arthroplasty failed to identify a temperature dependence to blood loss.[23] Why the results differed so much in basically similar, and apparently well conducted, studies remains unclear.

Three general mechanisms contribute to temperature-related coagulation disorders: platelet function, clotting factor enzyme function, and fibrinolytic activity. Surgeons have long suspected that hypothermia produces a coagulopathy and increases perioperative blood loss. Other surgeons believed that hypothermia "thickened the blood" and reduced bleeding. Until recently, there were little data on which to base either opinion.

Platelet numbers remains normal during mild hypothermia. However, Valeri *et al.*[24] demonstrated that mild perioperative hypothermia seriously impaired platelet function. Inhibition was a strictly local phenomenon: bleeding time was comparably increased by systemic or local hypothermia. However, wound temperature is largely determined by core temperature and is higher in normothermic than hypothermic patients. Subsequent work indicated that the defect resulted from reduced release of thromboxane A$_2$.[25–27]

One feature of hypothermic coagulopathy is that standard coagulation tests, including the prothrombin time and the partial thromboplastin times, remain normal.[28] The reason is that the tests are normally performed at 37°C, regardless of what the patient's temperature is. These same times are prolonged by hypothermia when they are performed at the patient's actual core temperature.[29,30]

The fibrinolytic system normally regulates the balance between formation of hemostatic plugs and restoration of blood flow after clot formation. Fibrin is a major structural element in formed clots but is subject to degradation by plasmin, the activated enzymatic form of plasminogen. The conversion of plasminogen to plasmin is at the core of the fibrinolytic mechanism. This reaction is enhanced by two types of plasminogen activators, although tissue-type is the most important. Inadequate fibrinolysis predisposes patients to thrombosis, whereas excessive fibrinolysis predisposes to hemorrhage. Preliminary data suggest that fibrinolysis remain normal during mild hypothermia but is significantly increased during hyperthermia, suggesting that hypothermia-induced coagulopathy does not result from excessive clot lysis. The corresponding effects of thermal disturbances on plasminogen activator have yet to be determined, but thromboelastographic data suggest that hypothermia impairs clot formation rather than facilitating clot degeneration.[31]

Wound Infection and Healing

Wound infections are serious complications of anesthesia and surgery. The risk of wound infection in patients undergoing colon surgery ranges from 9 to 27%.[32,33] Surgical wound infections prolong hospitalization by 5–20 days per infection and substantially increase cost.[32,34]

***In Vitro* and Animal Evidence.** Hypothermia may facilitate perioperative wound infections in two ways. First, hypothermia triggers thermoregulatory vasoconstriction.[35,36] Furthermore, vasoconstriction during recovery is universal in hypothermic patients because brain anesthetic concentration decreases rapidly, allowing reemergence of thermoregulatory responses.[1] Thermoregulatory vasoconstriction significantly decreases subcutaneous oxygen tension in humans,[37] and the incidence of wound infections correlates with subcutaneous oxygen tension.[33,38]

Second, considerable evidence indicates that mild core hypothermia directly impairs immune function, including T-cell–mediated antibody production[39,40] and nonspecific oxidative bacterial killing by neutrophils.[41] Bacterial killing by neutrophils is reduced as temperature decreases from 41 to 26°C.[42,43] Decreased killing results, in part, because production of oxygen and nitroso free radicals is oxygen-dependent in the range of oxygen partial pressures found in wounds.[44,45] Thus, hypothermia may directly impair neutrophil function or impair it indirectly by triggering subcutaneous vasoconstriction and tissue hypoxia.

Decisive Period. The first few hours after bacterial contamination constitute a decisive period during which infection is established.[46] The effects of antibiotic administration and of hypoperfusion are especially important during this period. Antibiotics limit infection when given within 3 h of bacterial inoculation but are ineffective when given later.[46,47] Similarly, wound hypoperfusion (achieved by epinephrine infiltration or "dehydration shock") aggravates test infections when induced up to 2.5 h after the inoculation but has no effect when induced later.[46]

Patients having initial postoperative temperature near 34°C—a typical core temperature in unwarmed patients undergoing major surgery[35,36,48]—require nearly 5 h to spontaneously restore core normothermia. Bacterial fixation will thus typically occur while unwarmed patients remain hypothermic.[46] In contrast, it is unlikely that exaggerated bacterial growth aggravates infections in hypothermic patients because the small differences in *in vitro* growth rates within the tested temperature range would decrease bacterial growth during hypothermia.[49]

Clinical Outcomes. Taken together, these data indicate that hypothermia may directly impair neutrophil function or impair it indirectly by triggering subcutaneous vasoconstriction and subsequent tissue hypoxia. Consistent with this theory, mild hypothermia reduces resistance to test infections in animals,[50,51] and only 1.9°C core hypothermia triples the incidence of surgical wound infection after colon resection.[52] A subsequent uncontrolled, retrospective trial failed to identify a correlation between temperature and infection.[53] However, this study suffered such serious methodologic flaws that it is difficult to interpret.[54] Interestingly, hypothermia also increases the duration of hospitalization by 20% even when infected patients are excluded from the analysis, apparently because healing was significantly impaired.[52] This result is consistent with studies by Carli *et al.*[55] showing that mild hypothermia aggravates postoperative protein wasting.

Excluding brain injury, the major causes of morbidity and mortality in trauma patients are bleeding and infection. Both are influenced by hypothermia. It is therefore not surprising that outcome would be improved in normothermic trauma patients.[56] However, the difficulty with this study is that it is a retrospective analysis, and the most seriously injured patients are more likely to become hypothermic. It is therefore difficult to be sure that their adverse outcome results specifically from hypothermia rather than underlying injury.

Pharmacokinetics and Pharmacodynamics

Drug Effects. The enzymes that moderate organ function and metabolize most drugs are highly temperature-sensitive. It is therefore not surprising that drug metabolism is temperature-dependent. Curiously, however, the pharmacokinetics of only a few anesthetic drugs have been evaluated. Hypothermia also alters the pharmacodynamics of various drugs, especially volatile anesthetics.

Muscle Relaxants. In the absence of muscle relaxants, skeletal muscle displays a slight temperature sensitivity.[57] However, the adductor pollicis muscle is the deepest muscle of the palmar arch. Consequently, twitch tension (in the absence of muscle relaxants) depends more on core than local skin-surface temperature.[58] The direct effects of hypothermia on muscle action are probably of limited clinical importance. In contrast, hypothermia markedly alters drug kinetics.

The duration of action of vecuronium is more than doubled in patients with a 2°C reduction in core temperature.[59] This duration of action of vecuronium exceeds that of pancuronium in a normothermic patient. A subsequent study demonstrated that the fist twitch amplitude and train-of-four ratio each decreased approximately 20% per degree Celsius reduction in adductor pollicis temperature.[60] This may be a clinically important reduction because a train-of-four ratio of 0.7 is associated with pharyngeal incoordination.[61] Hypothermic prolongation of vecuronium action results from a pharmacokinetic effect, as pharmacodynamics of muscle relaxants are essentially unchanged by mild hypothermia.[62]

Atracurium duration is less temperature-dependent than vecuronium: a 3°C reduction in core temperature increases the duration of muscle relaxation only by 60%.[63] With both atracurium and vecuronium, the recovery index (time for 25–75% twitch recovery) remains normal during hypothermia. As might be expected from the other muscle relaxants, the duration of action of rocuronium is prolonged during hypothermic bypass.[64]

Volatile Anesthetics. The tissue solubility of volatile anesthetics increases with hypothermia. At a given steady state plasma partial pressure, body anesthetic content thus increases at subnormal temperatures. This does not alter anesthetic potency because potency is determined by partial pressure rather than anesthetic concentration. However, it may slow recovery from anesthesia because larger amounts of anesthetic eventually need to be exhaled. Nonetheless, volatile anesthetic washout rates were comparable in a study that directly compared normothermic and hypothermic individuals.[1]

The minimum alveolar concentration of halothane and isoflurane in rats both decrease roughly 5%/°C reduction

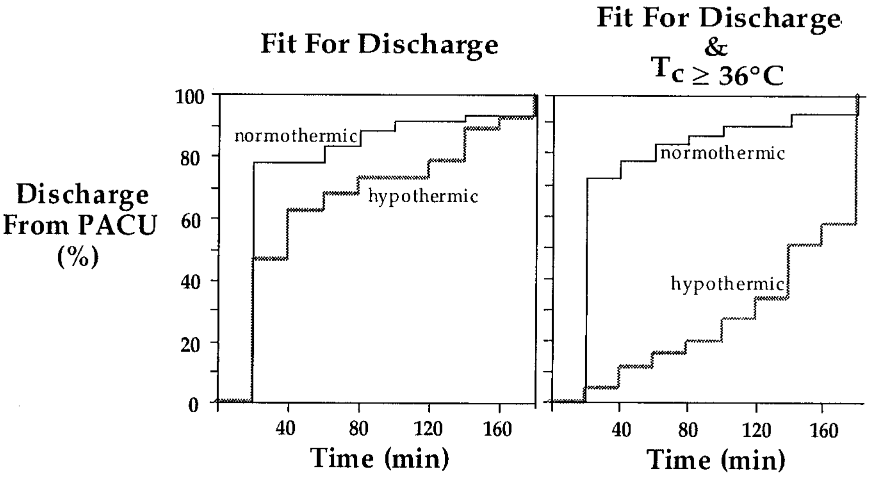

Fig. 1. Mild intraoperative hypothermia prolongs postoperative recovery. One hundred fifty patients were randomly assigned to normothermia or approximately 2.5°C core hypothermia. Fitness for discharge was determined using defined criteria by observers blinded to patient temperature and group assignment. The percentage of patients fit for discharge are plotted against time, using survival curve analysis. Hypothermia significantly delayed discharge by approximately 40 min (*left*). When normothermia (core temperature > 36°C) also was required for discharge, the difference between the groups increased to nearly 2 h (*right*). These data indicate that mild hypothermia significantly prolongs postanesthetic recovery. (Reprinted with permission.[143]) PACU = postanesthesia care unit.

in core body temperature.[65] A brain temperature of 20°C thus obliterates the need for anesthesia (minimum alveolar concentration = 0).[66] Minimum alveolar concentration also varies with a circadian rhythm,[67] a variation that likely results from diurnal temperature fluctuations.[68]

Intravenous Anesthetics. During a constant infusion of propofol, plasma concentration is approximately 30% greater than normal when individuals are 3°C hypothermic. The increase apparently results from a reduced intercompartmental clearance between the central and peripheral compartments. Interestingly, mild hypothermia does not appear to significantly alter hepatic blood flow.[63] Hypothermia also increases steady state plasma concentrations of fentanyl by approximately 5%/°C.[69] The effects of mild hypothermia on the metabolism and pharmacodynamics of most other drugs has yet to be reported. However, the results for muscle relaxants, propofol, and fentanyl suggest that effects are likely. Animal studies are generally consistent with available human data, showing reduced clearance during hypothermia.[70]

Recovery Duration and Thermal Discomfort

Increased solubility of volatile anesthetics and reduced metabolism of intravenous drugs suggests that hypothermia might prolong emergence and recovery from general anesthesia. However, most available studies of this issue have methodologic flaws that preclude accurate interpretation.[71] Typical problems include the following: (1) patients not randomly assigned to normothermia or hypothermia; (2) temperatures measured at inadequate sites (*e.g.*, axilla, mouth); (3) fitness for discharge evaluated by an observer not blinded to intraoperative thermal management and postoperative temperatures; and (4) core temperature being among the discharge criteria.

A recent prospective, randomized trial demonstrated that mild hypothermia significantly delayed discharge of adult patients from the postanesthesia care unit. Recovery duration was prolonged even when core normothermia was not a discharge criteria (fig. 1). Interestingly, similar prolongation of recovery duration was not observed in infants and children.[72] A limitation of that study, however, is that patients were not randomly assigned to specific intraoperative thermal management.

Even mild hypothermia produces marked postoperative thermal discomfort.[1,73] Patients often indicate that feeling cold in the immediate postoperative period is the worst part of their hospitalization, sometimes rating it worse than surgical pain. Given the appropriate efforts to treat surgical pain, it would similarly seem appropriate to prevent and treat thermal discomfort.[20]

Minor Consequences of Perioperative Hypothermia

Hypothermia is associated with mild hypokalemia,[74,75] but the clinical significance of this observation appears trivial. The cardiotoxicity of bupivacaine is markedly increased by mild hypothermia.[76] Hypothermia has a mild effect on somatosensory evoked potentials,[77] but the changes are unlikely to alter clinical management. Neither hypothermia nor hyperthermia significantly alters electroencephalographic values.[78]

Pulse oximeter function is usually well maintained even in vasoconstricted patients.[79] However, sufficient vasoconstriction (usually resulting from the combination of hypothermia and vascular volume depletion) can obliterate the oximeter signal. The signal can be restored by local warming or a finger nerve block.[80] Interestingly, thermoregulatory vasoconstriction slightly increases oxygen saturation, but the increase is not clinically important.[81]

Thermal Manipulations.

Induction of Therapeutic Hypothermia. Hypothermia results initially from core-to-peripheral redistribution.[82] The amount of redistribution is primarily a function of peripheral tissue temperature, which is determined by the patients' previous thermal environment and vasomotor status.[83-86] Cutaneous warming or cooling has relatively little impact during the first hour because redistribution is the primary determinant of core temperature during this period.[87] Subsequently, however, surface cooling facilitates rapid reduction in core temperature by augmenting heat loss and reducing body heat content.[88] It is therefore relatively easy to therapeutically cool anesthetized patients 2–3°C in a couple of hours.

The major impediment to continued intraoperative cooling is reemergence of thermoregulatory vasoconstriction,[35,36] which causes a core-temperature plateau by constraining metabolic heat to the core thermal compartment.[89] Maintaining intraoperative vasodilation thus speeds cooling. Neurosurgery appears to inhibit vasoconstriction in a large fraction of neurosurgical patients.[90] In those who do constrict, however, pharmacologic dilation (*i.e.*, by increasing anesthetic concentration) may speed cooling. This is only likely to be necessary when a core temperature less than 34°C is required. Forced air is probably the most effective currently available cooling system appropriate for intraoperative use.[90,91] Circulating water is also useful but is far more effective when positioned as a covering than a mattress.

Induction of therapeutic hypothermia is far more difficult in unanesthetized patients because skin or core cooling triggers effective thermoregulatory defenses. Hypothermia also triggers shivering and roughly doubles heat production.[92] These effective responses usually prevent core hypothermia even during exposure to moderate-to-severe cold.[6]

Minimizing Redistribution. The extent to which redistribution decreases core temperature depends on two factors. The first is anesthetic-induced inhibition of tonic thermoregulatory vasoconstriction. Surgical doses of all anesthetics profoundly impair thermoregulatory control,[35,36,93–97] decreasing the vasoconstriction threshold 2–4°C; consequently, tonic thermoregulatory vasoconstriction is essentially obliterated by induction of general anesthesia. The peripheral vascular effects of general anesthetics probably contribute relatively little to heat redistribution compared with central thermoregulatory inhibition.

The second major factor is magnitude of the core-to-peripheral tissue temperature gradient. Heat flow is proportional to the temperature gradient; a corollary is that core-to-peripheral flow of heat, and therefore redistribution magnitude, will be directly related to the temperature difference between core and peripheral tissues. Conversely, redistribution magnitude will be restricted when the gradient is small.

Preoperative vasodilation and reduction in the core-to-peripheral tissue temperature gradient form the basis for two methods of restricting redistribution. These are the only techniques that have generally proven effective for reducing intraoperative hypothermia during procedures lasting less than an hour.

Prewarming. Peripheral tissue warming reduces redistribution hypothermia *via* two mechanisms: (1) by decreasing the normal core-to-peripheral temperature gradient; and (2) by eventually provoking vasodilation as the needs of the thermoregulatory system switch from the typical heat-conservation mode to heat dissipation. Subsequent induction of general anesthesia thus has relatively little effect on vasomotion because centrally mediated thermoregulatory vasoconstriction has already been defeated.

Over a very long period, moderate increases in ambient temperature increase peripheral tissue temperature and provoke vasodilation. For example, redistribution hypothermia, which is usually readily apparent,[36,52] was not observed in patients anesthetized during a hot summer in Vienna.[98] The difficulty, however, is that body heat content probably must increase by 210–420 kJ to produce a clinically important reduction in redistribution magnitude.[99] This degree of warming is rare at usual ambient temperatures in modern hospitals.

Far more typically, hospitalized patients are relatively cool. Furthermore, behavioral compensations may be denied or relatively ineffective because of skimpy clothing, old age, infirmity, or underlying illness. It is thus common for surgical patients to enter the operating room with substantial core-to-peripheral temperature gradients. One way to minimize this gradient is by actively warming patients before induction of anesthesia. One to 2 h of forced-air prewarming has been shown to reduce redistribution hypothermia associated with induction of general anesthesia in volunteers[83] (fig. 2) and patients.[84] Prewarming also helps to reduce the initial hypothermia that follows induction of epidural anesthesia.[100] In general, prewarming reduces afterdrop by a factor of two. As a result, most prewarmed patients remain normothermic (core temperature > 36°C), whereas those who were not warmed become hypothermic after 1 h of anesthesia.

Prewarming can be incorporated into the clinical routine without excessive difficulty. The general strategy is to start active cutaneous warming system as soon as patients are admitted to the presurgical holding area. Warming is then continued until patients are transferred to the operating room. One advantage of this approach is that patients are kept comfortably warm and do not remember the operating room as being distressingly cold. An additional advantage is that warming induces vasodilation, which facilitates insertion of intravenous and radial arterial catheters.

Pharmacologic Vasodilation. An alternative to active prewarming is pharmacologic vasodilation. The basis of this method is administration of drugs that defeat normal tonic thermoregulatory vasodilation well before induction of anesthesia. Drug-induced vasodilation facilitates redistribution of core heat to peripheral tissues. Core temperature, however, remains well regulated in the absence of anesthesia. Consequently, thermoregulatory responses generate or conserve sufficient heat to

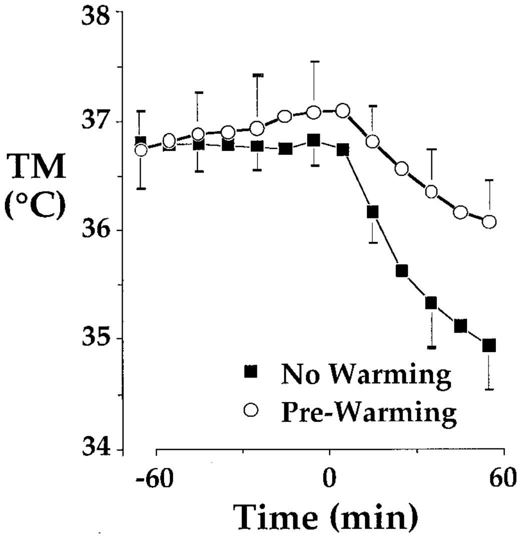

Fig. 2. Prewarming minimizes redistribution hypothermia. During the preinduction period (−120 to 0 min), volunteers were either actively warmed or passively cooled (no warming). At induction of anesthesia (time = 0 min), active warming was discontinued, and volunteers were exposed to the ambient environment. Initial tympanic membrane temperatures (TM) were similar before each preinduction treatment. During the 60 min after induction of anesthesia, core temperature decreased less when volunteers were prewarmed (ΔT = −1.1 ± 0.3°C) compared with when the same volunteers were not warmed (ΔT = −1.9 ± 0.3°C). These data indicate that redistribution hypothermia can be prevented by actively warming peripheral tissues before induction of anesthesia. Data are presented as mean ± SD. (Reprinted with permission.[83])

maintain core temperature. In practice, heat conservation probably results largely from behaviorally mediated increases in insulation (*i.e.*, sleeping with an extra blanket). After equilibration, the patient is left vasodilated, with a small core-to-peripheral tissue temperature gradient. Subsequent induction of general anesthesia then produces minimal redistribution hypothermia because the core-to-peripheral temperature gradient required for heat flow is lacking.

Pharmacologic prevention of redistribution hypothermia has been demonstrated with nifedipine.[86] Patients were given 20 mg long-acting nifedipine orally 12 h before surgery and an additional 10 mg sublingually 1.5 h before surgery. Their core temperatures decreased 0.8°C during the first hour of anesthesia, which was only half the 1.7°C observed in the untreated control patients.

Cutaneous Warming. Roughly 90% of metabolic heat is lost through the skin surface. Therefore, any effective warming system must modulate cutaneous heat loss. Available systems can be categorized as passive insulation or active cutaneous heating.

Passive Insulation. A single layer of most any passive insulator reduces cutaneous heat loss by roughly 30%. This is a clinically important amount and is sometimes sufficient to restore thermal steady state. Efficacy of routinely available insulators are similar. Thus, a plastic bag or single layer of surgical draping retains heat nearly as well as a cotton blanket or metallized plastic cover ("space blanket").[101] The reason is that covers themselves provide relatively little insulation; instead, it is the layer of still air between the covers and the skin that retains most of the heat. Unfortunately, increasing the number of insulating layer only provides a slight further decrement in heat loss. For example, augmenting one blanket with two others decreases heat loss only an additional 20%.[102] The heat capacity of a cotton blanket is trivial. Consequently, cutaneous heat loss is virtually identical with warmed and unwarmed blankets.[102]

The face and upper chest are far more sensitive to temperature than other regions. However, cutaneous heat loss is roughly proportional to surface area over the entire body surface. (Rumors to the contrary, heat loss from the head is very nearly in proportion to its 10% surface area.) The efficacy of applied insulation is thus also directly proportional to the covered surface area.

Active Cutaneous Heating. At best, passive insulation can reduce cutaneous loss nearly to zero. Doing so will increase mean body temperature roughly 1°C/h, depending on the metabolic rate and size of the patient. In practice, however, even the best insulation rarely reduces heat loss even by 50%.[101,102] Active cutaneous warming is often required to compensate for the relatively cool operating room environment and the special heat losses associated with major surgery.[103] Not surprisingly, active warming systems maintain normothermia better than passive insulation.[104-106] As with passive insulation, heat transfer by active warming systems is roughly proportional to treated surface area. With any given system, efficacy will be linearly improved by including additional skin surface within the warmed area.

Circulating Water. Circulating-water mattresses are the classical active intraoperative warming system and have been used for decades. Unfortunately, their efficacy is limited by a number of factors directly related to their position below patients. The back is a relatively small fraction of the total surface area. Furthermore, operating room tables are covered with approximately 5 cm of foam, which is an excellent thermal insulator. The consequence is that approximately 90% of metabolic heat is lost from the anterior surface of the body.[87]

Even effective heat transfer through the back cannot compensate for the typically large anterior losses. Furthermore, flow is restricted in dependent capillaries that are compressed by the patient's own weight. An additional problem with circulating-water warming is that the technique is associated with pressure–heat necrosis.[107,108] Temperature of the circulating water is typically set to 40°C or even 42°C. This is a dangerous practice because temperatures as low as 38°C can cause severe injury in susceptible patients.[109] In contrast to its normal posterior positioning, circulating-water warming is relatively effective when positioned over patients.[110]

It is also much safer because the risk of pressure–heat necrosis is markedly reduced.

Forced Air. Forced-air warming systems consist of a electrically powered heater–blower unit and a patient cover. Most covers consist of some combination of fabric, plastic, or paper, and most are disposable and designed for single-patient use. The blowers are available in various sizes and configurations. Forced-air covers warm *via* two distinct mechanisms: radiant shielding and convection. Radiation is usually the most important source of intraoperative heat loss and results from photon-mediated transfer between two nonadjacent surfaces.[111] One surface is the skin, and the other is usually the ceiling or one of the walls of the room. Forced air reduces radiative loss simply by replacing the cool surfaces of the room with a warm cover.

Convection is the second most important source of intraoperative heat loss; this mechanism is sometimes also referred to as *facilitated conduction*. The reason is that conduction to still air, which is an excellent insulator, can be increased by orders of magnitude when the air moves rapidly over the skin. When the air is colder than skin, convection increases heat loss; this is the familiar wind-chill factor. However, convection similarly increases heat gain when the air is warmer than skin. Forced-air warmers take advantage of this phenomenon by producing a flow of warm air across the skin.

Forced-air heating transfers 30–50 W across the skin surface.[110,112] In contrast, passive insulation reduces normal cutaneous loss from approximately 100 to approximately 70 W.[101,102] It is therefore not surprising that forced air is far more effective than passive insulation.[106,113] Forced-air heating transfers considerably more heat than circulating water.[110] It is therefore also far more effective than circulating-water mattresses in surgical patients.[98]

Surgeons are sometimes concerned that increasing air flow in operating rooms will increase contamination within surgical incisions. All forced-air warming include filters that essentially eliminate bacteria in the heated air. Furthermore, studies have demonstrated that the number of colony-forming units recovered from operating rooms is not increased by forced-air blowers.[114] Finally, use of forced-air heating has been shown to reduce the incidence of surgical wound infection threefold by improving host defense.[52] There is therefore no empirical support for the theory that forced-air heating increases infection risk.

Resistive Heating. Clinical studies suggest that the efficacy of resistive heating (electric) blankets is similar to that of forced air.[115] Resistive heating may be especially helpful for field treatment of accidental hypothermia because they are highly efficient devices,[116] *i.e.*, a large fraction of the heat generated by the device can be transferred to the patient. This becomes a critical factor when current must be supplied by batteries.

Radiant Warmers. Radiant warmers use special incandescent bulbs or heated surfaces to generate infrared radiation. The major advantage of radiant heating is that no contact between the warmer and patient is required because the heat energy is carried by photons and does not depend on the intervening air. In this respect, it differs from all other cutaneous warmers that must be positioned adjacent to the skin surface. Radiant heating is thus ideal for neonatal intensive care units, where it is important that the patients remain visible. It can similarly be helpful during pediatric surgery, where hypothermia is common during anesthetic induction, catheter insertions, skin preparation, and surgical draping. In this setting, radiant heating can substitute for uncomfortably high ambient temperatures.

Radiant warming may be especially useful during trauma resuscitations because many of these patients are already hypothermic on admission and frequently become even colder during multiple diagnostic and therapeutic maneuvers that restrict application of other warming systems. Trauma patients are especially sensitive to hypothermia because coagulopathy[21] and infection[52]—two established consequences of reduced body temperature—are major causes of morbidity and mortality in this population.[117] Therefore, effective heating is critical in these patients.

A major limitation of radiant heating is that convective losses continue unimpeded. Even in hospitals, this is not a trivial concern because nearly as much body heat is lost to convection as radiation.[111] Convection, however, is usually the major source of heat loss outdoors, where air speeds tend to be substantial. Radiant heating is thus unsuitable for search-and-rescue procedures. A second limitation of radiant heating results from the geometry of the warming devices and patients. Radiant heat, like other noncoherent radiation, disperses as a function of distance. Dispersion can be limited somewhat by using parabolically shaped reflectors. Nonetheless, energy transfer decreases rapidly as the distance between the warmer and patient increases. It also decreases markedly when the warming surface and the skin surface are not parallel to each other. In most cases, the limitations of radiant heating combine to make the method relatively ineffective compared with other cutaneous warming systems. Perhaps as a consequence, the method has not become popular outside of neonatal intensive care units.

Negative-pressure Warming. A recently developed device uses a slight vacuum applied to the hand and forearm to facilitate peripheral-to-core heat transfer. The theory is that negative pressure will overcome the isolating effects of thermoregulatory vasoconstriction,[118] thus allowing better transfer of heat from the periphery to the core. Two studies by the inventor report remarkable rates of core warming, up to 10°C/h.[119,120] The investigators' explanation for this rate of rewarming is that the heat is being transferred directly into a core compartment having a mass of only 10 kg and is then retained there. One difficulty with this theory is that the core compartment is actually about half the body mass.[82,89] A second is that the thermoregulatory system can only maintain a limited core-to-peripheral tissue temperature gradient, usually between 2 and 4°C.[121,122]

Because general anesthesia both directly[123] and indirectly[93–96] causes peripheral vasodilation, the maximum effect of negative-pressure heating seems unlikely to exceed the benefits of heating a comparable peripheral surface area intraoperatively. Clinical experience would suggest that warming restricted to a single forearm is unlikely to maintain intraoperative normothermia. Similarly, direct warming of a limited trunk (*i.e.*, core) surface area is insufficient to rapidly rewarm postoperative patients. Consistent with these concerns, two independent studies failed to confirm any significant benefit from negative-pressure rewarming in patients.[124,125]

Hot-Water Containers. Plastic containers of irrigation solution are frequently kept in ovens near operating rooms. The temperature of these ovens often exceeds 45°C. It is tempting to warm patients by positioning these containers in areas of high blood flow, such as the axilla. This practice, however, is both ineffective and dangerous. Lack of efficacy results because the surface area involved is small. As with circulating water, the limit on heat flow is the ability of tissue to absorb and dissipate heat rather than the temperature of the device. Even when the warming bottles are positioned in regions of high blood flow, heat transfer is insufficient to compensate for the small total treatment area. More importantly, failure of tissues to dissipate adequate heat to the remainder of the body means that heat accumulates locally. As a result, local tissue temperatures rapidly approach the temperature of the water bottle. These temperatures reliably cause tissue injury in a swine model,[126] and it is likely that human skin is even more sensitive. Consistent with these data, an analysis of the American Society of Anesthesiologists closed claims database indicated that hot-water bottles were by far the leading cause of perioperative thermal injury.[127] Hot-water bottles should therefore never be used to warm surgical patients.

Fluid Warming and Other Internal Warmers

Fluid Warming. A unit of refrigerated blood or 1 l of crystalloid solution administered at room temperature decreases mean body temperature approximately 0.25°C in adults.[128] Heat loss caused by cold intravenous fluids thus becomes significant when large amounts of crystalloid solution or blood are administered. Fluid warmers minimize these losses and should be used when large amounts of intravenous fluid or blood are administered. In contrast, fluid warming does not warm patients to any important extent because it is unsafe to heat fluids to much above normal body temperature. Fluid warming is therefore not a substitute for cutaneous insulation–warming and alone will not keep patients normothermic. For routine cases, there are no clinically important differences among the available fluid warmers. Special high-volume systems with powerful heaters and little resistance to flow facilitate care of trauma victims and are useful in other cases in which large amount of fluid must be administered quickly.

Airway Heating and Humidification. Simple thermodynamic calculations indicate that less than 10% of metabolic heat production is lost *via* the respiratory tract. The loss results both from heating and humidifying inspiratory gases, but humidification requires two thirds of the heat.[129] It is therefore not surprising that many studies of active airway heating and humidification report that warming of inspiratory gases contributes little to preservation of core temperature in adults undergoing large operations.[87,130] Minimal efficacy of airway heating and humidification is consistent with modest intraoperative respiratory heat loss that is dwarfed by other losses. (The apparent benefit observed clinically and in some studies[131] may result from artifactual warming of a temperature probe positioned in the nasopharynx or upper esophagus.[132])

Respiratory heat transfer theoretically maintains core temperature slightly better than a comparable amount of heat applied to the skin surface because the heat is transferred directly into the core thermal compartment. However, the influence of respiratory gas heating and humidification at steady state remains trivial because the total amount of heat transferred is so small.

Hygroscopic condenser humidifiers and heat- and moisture-exchanging filters (“artificial noses”) retain substantial amounts of moisture and heat within the respiratory system. They are roughly half as effective as active systems in terms of maintaining core temperature[133]; however, they cost only a fraction as much. Heat retention by all clinically available heat-and-moisture exchangers is comparable.[130]

Other Internal Warming Methods. Various invasive internal warming systems are available, including peritoneal dialysis and arteriovenous shunt heating.[134] By far the most powerful of these is cardiopulmonary bypass, which transfers heat at a rate several orders of magnitude faster than any other available system.[122,123] However, none of these methods is used in the prevention and treatment of mild perioperative hypothermia, and they are not reviewed here.

There is, however, one additional internal warming method that deserves consideration: increased metabolic heat production in response to amino acid infusion. In contrast to unanesthetized individuals, amino acid infusions increase metabolic rate by approximately 20 W,[135] mostly in extrasplanchnic tissues.[136] This is a modest but clinically important amount. Consequently, patients given amino acid infusion typically remain approximately 0.5°C warmer than those given crystalloid.[137] An intriguing recent reanalysis of these data suggest that amino acid infusion shortens hospital duration. It is unlikely that such small differences in core temperature would markedly influence duration of hospitalization; consequently, the benefit may result from an effect on wound healing or intestinal function.

Factors Influencing Warming Efficacy. The efficacy of available patient warming systems depends on numerous factors, including the type of heat transfer, device design, and the location and amount of skin available for heat exchange. Almost all commercially available devices are electrically powered; therefore, there is no intrinsic physical limit to the temperature that can be provided. The limitation in each case is the temperature that can be tolerated by human tissues without causing burns. Differences in warmer efficacy results largely from which tissues are contacted by various heaters and the surface area available to each.

Risk of Burns. Cold is well tolerated by human tissues, with very low temperatures or long exposure required to cause freezing (frost bite) or nonfreezing (trench foot) cold injury. In contrast, the tolerance of human skin for high temperatures is relatively low. This is especially so when high temperatures are combined with pressure that reduces regional blood flow. In the absence of pressure, human skin can tolerate temperatures near 45°C indefinitely.[108,138] Adding only a slight component of pressure markedly reduces the safe duration of heating.[138]

The risk of tissue injury is further increased when heat or pressure is combined with chemical irritation such as that produced by many skin-cleaning solutions, especially those containing iodine. Age is another important factor: the elderly often have thin, delicate skin that is especially susceptible to burns or pressure–heat necrosis. The final common limitation of all cutaneous warming systems is the relatively low skin temperature that can be safely maintained. This, in turn, restricts the skin-core gradient and peripheral-to-core transfer of heat. A general strategy for safe and effective warming is to heat as much of the skin surface as possible. This allows a large total amount of heat to be transferred without excessively heating any one region.

Patient Size and Morphology. Infants and children cool more quickly than adults because their high ratio of surface area to weight favors heat loss. For the same reason, pediatric patients can be rewarmed faster than adults.[139] Infants and children should therefore not be denied the putative benefits of therapeutic hypothermia in appropriate cases.

Airway heating and humidification slightly improves core temperature in infants[134] and children[140] but is of little value in adults.[87,131] The reason, presumably, is that pediatric patients maintain a relatively high respiratory rate and thus lose more metabolic heat through ventilation than adults. However, the thermal benefits of conditioning inspired gas are small and by themselves do not justify active airway heating and humidification.

Core-to-peripheral Heat Transfer. The most obvious measure of warmer efficacy is net heat transfer. However, thermoregulatory responses are 80% determined by core temperature,[141,142] and most thermal complications are also largely determined by core temperature.[18,21,52,143] Core temperature is thus the single most important body temperature. When considering warmer efficacy, it is therefore also necessary to consider where heat is delivered, because heat applied peripherally is not instantly transferred to the core.

Roughly speaking, heat flow within the body can be divided into two categories: radial conduction and longitudinal convection.[144] Initial transfer of heat applied to the skin surface is conducted to tissues just under the skin. Subsequently, longitudinal transfer of heat between the core and peripheral thermal compartments is largely mediated by blood-borne convection. Peripheral-to-core heat transfer is thus a function of vasomotor tone that influences both the amount of blood flowing to extremities and the extent to which countercurrent mechanisms reduce heat transfer.

The importance of vasomotor tone is most apparent in hypothermic postoperative patients who are invariably vasoconstricted.[1,20,73] The benefit of cutaneous warming in postoperative patients has been controversial, with some studies identifying a benefit[145,146] and others failing to confirm faster rewarming.[147,148] A recent study confirmed that forced-air warming is more effective than passive insulation in postoperative patients. However, the same study showed that the rewarming rate was slower than might be expected on the basis of cutaneous heat-transfer rates because thermoregulatory vasoconstriction slows transfer of heat from peripheral to core tissues.[119] This same effect was demonstrated in another recent study that showed that postoperative rewarming rates were 1.2 ± 0.1°C/h in patients with residual spinal blocks *versus* 0.7 ± 0.2°C/h in patients recovering from general anesthesia (fig. 3).[149]

Thermoregulatory vasoconstriction somewhat slows core cooling rates during anesthesia.[90] However, a subsequent study failed to demonstrate any important increase in the cooling rate in vasodilated subjects.[88] Intraoperative warming is also relatively rapid, and there is little evidence that applied heat is constrained to the peripheral thermal compartment.[150] Two factors contribute to rapid intraoperative transfer of heat from peripheral tissues to the core. The first is vasodilation induced by central inhibition of thermoregulatory control.[93–96] The second is that general anesthesia itself induces peripherally mediated vasodilation[124] which facilitates intercompartmental heat transfer. Taken together, these studies suggest that intraoperative cutaneous warming is faster than comparable postoperative warming. Because most identified hypothermia-induced

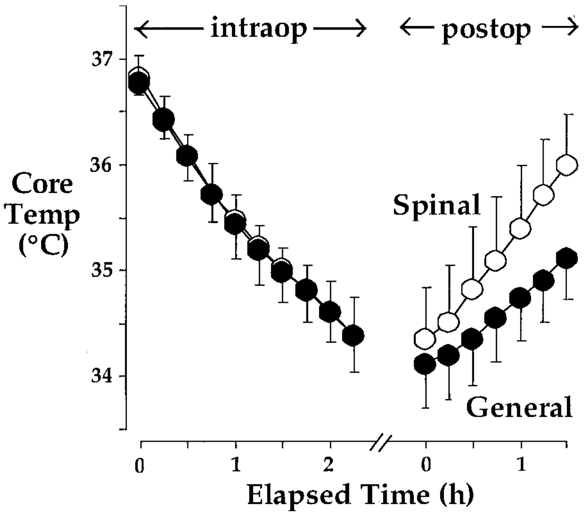

Fig. 3. Residual spinal anesthesia speeds postoperative core rewarming. Intraoperative and postoperative core temperatures in patients assigned to general anesthesia (n = 20) and spinal anesthesia (n = 20). All patients were actively warmed during the postoperative period. Core temperature did not differ significantly during surgery but increased significantly faster postoperatively in patients given spinal anesthesia: 1.2 ± 0.1°C/h *versus* 0.7 ± 0.2°C/h. Data are presented as mean ± SD. (Reprinted with permission.[149])

complications are established intraoperatively, it seems clear that patients should be warmed during surgery rather than allowed to cool and then "rescued" postoperatively.

Thermal Management. Most surgical patients are at risk of at least one proven complications of mild hypothermia, including morbid myocardial outcomes,[18] coagulopathy,[21] wound infection,[52] and prolonged postoperative recovery.[144] The risk is presumably greater in frail, elderly patients undergoing large operations than in young, generally healthy patients undergoing relatively minor procedures. However, the younger patients are also more likely to shiver[151,152] and are also likely to find a given degree of hypothermia more uncomfortable because their behavioral regulation is better preserved.

Available data suggest that there are many surgical patients in whom hypothermia will augment the risk of adverse outcomes or, at the very least, provoke shivering and thermal discomfort. Core temperature normally ranges from 36.5 to 37.5°C and normally always exceeds 36°C.[153] It therefore seems reasonable to maintain core temperature greater than 36°C in surgical patients unless hypothermia is therapeutically indicated. The methods used to maintain normothermia are of little consequence. Clinicians can therefore use whatever combination of techniques they find effective in patients undergoing various types of surgery.

Summary

Perioperative hypothermia triples the incidence of adverse myocardial outcomes. Mild hypothermia significantly increases blood loss and significantly augments allogeneic transfusion requirement. Only 1.9°C core hypothermia triples the incidence of surgical wound infection after colon resection and increases the duration of hospitalization by 20%.

Redistribution hypothermia is the major cause of hypothermia during the first hour of neuraxial or general anesthesia. It can be minimized by actively warming peripheral tissues before induction of general or regional anesthesia. All effective noninvasive warming devices address the anterior skin surface because most heat is lost from this area. Passive insulation reduces cutaneous loss 30% (one layer) to 50% (three layers). However, active warming will be required to maintain normothermia in most patients. Forced-air and resistive heating are currently the most effective noninvasive options, although better systems are being developed.

It is not possible to warm patients to any important extent by administration of heated intravenous fluids. However, each liter of fluid at ambient temperature decreases mean body temperature roughly 0.25°C in adults; each unit of refrigerated blood produces a similar reduction. Intravenous fluids should therefore be warmed when large volumes are required (*i.e.*, several liters per hour) or when forced air alone proves insufficient.

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