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FOCUS ON: PERIOPERATIVE HYPOTHERMIA

Consequences of hypothermia

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KEYWORDS
temperature, body; anesthesia, general; treatment outcome; hypothermia; body temperature regulation

Summary Virtually all anaesthetics render patients poikilothermic and body temperature invariably decreases during surgery. For selected surgical procedures, hypothermia can protect vital organs from ischaemic injury. Hypothermia, however, is not without consequences as hypothermia-related complications are well known. As little as 2°C of core hypothermia impairs coagulation and predisposes to bleeding. Hypothermia slows emergence from general anaesthesia by both pharmacokinetic and pharmacodynamic mechanisms. Thermal discomfort is another commonly recognized perioperative problem. In the postoperative setting, even mild hypothermia exacerbates the stress response by activation of the sympathetic nervous system resulting in increased catecholamines. By this mechanism, hypothermia can precipitate myocardial ischaemia and cardiac morbidity in awake patients. In surgical patients, body temperature should be carefully monitored and controlled with the same level of attention that is given to the other vital signs. By controlling body temperature in the perioperative period, improved outcomes can be achieved. © 2001 Harcourt Publishers Ltd

INTRODUCTION

Although hypothermia may be beneficial in some surgical situations, the risks and side-effects may outweigh the benefits. The following review will cover the physiological effects of cold stress with specific focus on the consequences of intraoperative and postoperative hypothermia. Methods for monitoring and controlling body temperature will also be covered to provide practical information on caring for the surgical patient.

BENEFITS OF HYPOTHERMIA

Neurologic protection

Induced hypothermia is more effective for neurologic protection than any of the pharmacological treatments that have been tested. As little as 2°C of cooling provides significant protection for the brain and spinal cord during periods of interrupted blood flow.[1] Thus, mild hypothermia can be used for brain protection during cerebral aneurysm clipping or procedures with high aortic cross clamps where the spinal cord is at risk from ischaemia. Paraplegia is a well-recognized complication of aortic surgery especially when aortic cross clamps are placed high on the aorta. The incidence of paraplegia is as high as 20–40% in some series where aortic cross clamp is prolonged or the aneurysm is dissecting. In a series of patients cooled to 30°C on partial cardiopulmonary bypass, we found no neurologic deficits in 20 patients.[2] Certainly, there are multiple variables that contribute to spinal cord injury, but even mild hypothermia appears to be protective. Animal studies have shown a twofold prolongation in the duration of aortic cross clamp required to produce paraplegia at 35°C *vs* 37°C,[3] thus supporting the findings in brain protection studies of the benefits of mild hypothermia for neurologic protection.

CONSEQUENCES OF HYPOTHERMIA

Table 1 summarizes the physiological effects of hypothermia and Table 2 gives the results of randomized outcome studies on perioperative thermal management.

Shivering and metabolism

One of the most commonly recognized effects of hypothermia is postoperative shivering. Despite earlier

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Table 1 Physiological effects of hypothermia

System	Effect
Metabolism	Postoperative shivering increases total body oxygen consumption (average increase is $\approx$ 40%, maximum is $=$ 100%)
Respiratory	Blunted ventilatory response to CO_2 5% decrease in tissue oxygen requirements for each °C of cooling Increased oxygen solubility in blood Increased affinity of haemoglobin for oxygen (left shift in Hgb–O_2 curve)
Adrenergic	Activation of sympathetic nervous system 100–500% increase in norepinephrine Little or no adrenomedullary or adrenocortical response (epinephrine and cortisol unchanged)
Cardiovascular	Systemic and pulmonary vasoconstriction Increased arterial blood pressure Increased risk of ventricular dysrhythmias, myocardial ischaemia and cardiac morbidity in awake postoperative hypothermic patients
Coagulation	Impaired platelet function Impaired coagulation cascade Enhanced fibrinolysis
Immune	Impaired neutrophil and macrophage function Decreased tissue partial pressure for oxygen Increased risk of bacterial wound infection
Pharmacokinetics	Increased effect of neuromuscular blockers Prolonged duration of neuromuscular blockers Decreased MAC for inhaled anaesthetics

suggestions that inhalational anaesthetics cause shivering by disassociation of spinal reflexes from cortical centres in the brain, it is now believed that most perioperative shivering (with general or regional anaesthesia) is thermoregulatory in origin.[4]

Based on studies from 20–30 years ago with very small numbers of patients and questionable methods, the myth has been perpetuated that shivering dramatically increases total body oxygen consumption by $\approx$ 400% above baseline. In these earlier studies, there were single patients that reportedly increased their metabolic rates by $>$ 400%,[5,6] but the methods used to measure oxygen consumption were inferior and the average increase with shivering was $\approx$ 100%. In general, these were young patients receiving little or no opioid analgesia. Recent more carefully conducted studies have shown that shivering increases oxygen consumption, but the average increase is $\approx$ 40%, with a maximum increase of $\approx$ 100%.[7] Other predictors of increased oxygen consumption were male gender and increased core temperature (Fig. 1). Although shivering is uncomfortable for most patients, it is unlikely that this relatively small increase in total body oxygen consumption in the average shivering patient is associated with perioperative morbidity.

It is common for patients to complain that their worst memory from the recovery room is the intense cold sensation and uncontrollable shivering. Shivering can be attenuated by relatively small doses of opioids. Although all opioids reduce shivering, meperidine (pethidine) is most effective (12.5–25 mg) due to the increased activity at the kappa receptor. Other drugs that are effective in the treatment of shivering include clonidine, neostigmine, and ketanserine (a serotonin antagonist). Thermal comfort is significantly improved and shivering can be virtually eliminated with the use of cutaneous warming during or following surgery with forced-air warming.[8,9]

Table 2 Summary of randomized trials of thermal management and outcome

Publication	Surgical Procedure	Outcome	Average core temperature (°C)	Outcome difference
Kurz A et al.[20]	Colon resection	Wound infection	34.7	Threefold
Schmeid H et al.[19]	Hip arthroplasty	Bleeding	35.0	20% increase
Frank SM et al.[15]	Abdominal, thoracic with cardiac risk factors, and vascular	Cardiac morbidity	35.3	55% relative risk reduction
Leinhardt R et al.[24]	Major abdominal	PACU length of stay	34.8	40 min increase
Fleisher LA et al.	Gynaecologic	PACU length of stay	35.4	No difference
Kurz A et al.[8]	Major abdominal	Thermal comfort	34.4	40 points on a 100 point scale
Krenzischeck DA et al.[9]	Abdominal, thoracic, vascular	Thermal comfort	35.3	2 points on a 10 point scale

PACU, post-anaesthesia care unit.

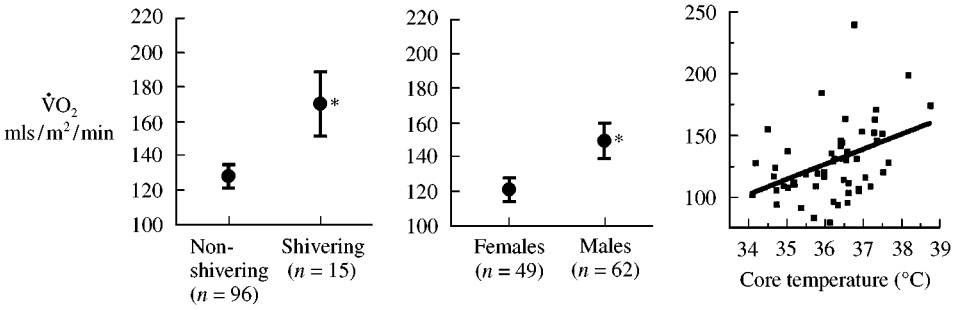

Figure 1 Total body oxygen consumption in the early postoperative period and the effects of shivering, gender, and core temperature. Oxygen consumption was increased in shivering *vs* non-shivering patients but the magnitude of increase was only 40%. Males had a 25% greater metabolic response compared to females due to a greater lean body mass. Core temperature was directly proportional to oxygen consumption. These findings indicate that even when shivering is accounted for, hypothermia is associated with a decrease in metabolism not the increase that one would expect if all hypothermic patients shivered, and all shivering was associated with a large increase in metabolism. $*P < 0.05$ *vs* non-shivering and *vs* females. (Modified from Frank SM et al.[7]).

For every 1°C of core hypothermia, approximately 4°C of skin-surface warming is required to attenuate the shivering response.[10]

Hypothermia and the respiratory system

Hypothermia blunts the ventilatory response to CO_2. The respiratory quotient, or ratio of CO_2 production to oxygen utilization, does not change with hypothermia. Thus oxygen utilization decreases at the same rate as CO_2 production ($\approx$5% per °C).

Hypothermia and sympathetic activation

The adrenergic response to hypothermia in the awake patient is significant. Although this response is not manifested during anaesthesia, norepinephrine is significantly increased postoperatively in awake, mildly hypothermic, patients. A core temperature of < 35.5°C following surgery triggers a twofold increase in norepinephrine, vasoconstriction and increased arterial blood pressure.[11] When young, awake human volunteers are cooled to a core temperature of 35.2°C, a 500% increase in norepinephrine is induced, along with vasoconstriction and increased arterial blood pressure.[12] This response appears to be primarily from the peripheral sympathetic nervous system, with little or no adrenal response, since epinephrine and cortisol are unchanged with core hypothermia (Fig. 2). The adrenergic response is of greater magnitude in younger individuals which may explain the decreased ability for the elderly to protect their core temperature through sympathetically mediated vasoconstriction during cold challenge.[13]

Hypothermia and the cardiovascular system

In high-risk patients (those undergoing peripheral vascular surgery), a core temperature less than 35°C is associated with a two–threefold increase in the incidence of early postoperative myocardial ischaemia (Fig. 3B).[14] This 'cold-induced' myocardial ischaemia is independent of anaesthetic technique (regional or general). In a prospective randomized trial, we demonstrated a 55% reduction of the relative risk for early postoperative cardiac morbidity in patients who were warmed to normothermia during and after surgery.[15] The incidence of postoperative ventricular tachycardia and morbid cardiac events were reduced in the normothermic group (core temperature = 36.7°C) compared with the hypothermic group (core = 35.4°C) (Fig. 3A). Of interest is that intraoperatively, cardiac outcomes occurred with similar frequency in the two groups. This suggests that cold-induced perioperative cardiovascular morbidity is likely to be mediated by the adrenergic response since the effect of temperature on outcome is significant in the postoperative period after emergence, not during anaesthesia when the adrenergic response to hypothermia is attenuated.

Hypothermia and coagulation

The coagulation system is significantly influenced by hypothermia through three different mechanisms: platelet function, the coagulation cascade, and fibrinolysis. The function of platelets is impaired by hypothermia due to reduced levels of thromboxane B2 at the site of tissue injury.[16] There is also reduced activity of coagulation factors in the coagulation cascade since the enzymes involved in the cascade, are temperature dependent.[17] Since the prothrombin time (PT) and partial

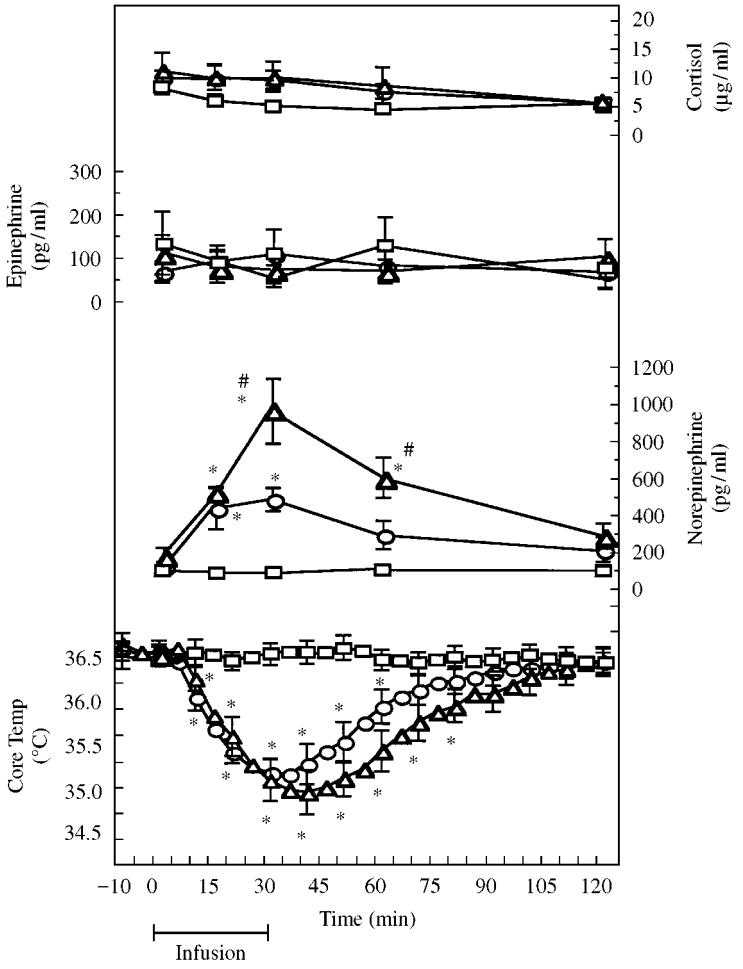

Figure 2 The adrenergic response to core cooling. Mild core hypothermia (35.0–35.5°C) was induced by infusion of cold intravenous (i.v.) fluid. Norepinephrine increased 700% while epinephrine and cortisol were unchanged. Thus, a peripheral sympathetic response is activated by core hypothermia but the adrenal response is absent. The norepinephrine response is associated with increased vasomotor tone and increased arterial blood pressure.*$P < 0.05$ *vs* preinfusion baseline. □, warm infusion (30 ml/kg); ○, cold infusion (30 ml/kg); △, cold infusion (40 ml/kg) (Modified from, Frank SM et al.[12]).

thromboplastin time (PTT) tests are routinely performed at a temperature of 37°C in most laboratories, it is likely that most temperature-related coagulopathies are missed in the clinical setting. Fibrinolysis is enhanced with hypothermia which destabilizes clot and predisposes to increased bleeding.[18] A study in patients undergoing total hip arthroplasty showed a significantly reduction in blood loss (≈20%) and reduced requirements for allogeneic blood transfusion in patients maintained normothermic compared to those with mild hypothermia (35.0°C).[19]

Body temperature, wound healing and infection

There is evidence that wound healing is impaired and that patients are more susceptible to wound infection when hypothermia (core < 35°C) occurs during surgery.[20] Mild hypothermia (34.7°C) increased the incidence of wound infection threefold (19% *vs* 6%) compared with normothermic patients (36.6°C) undergoing colon surgery. This effect is presumably related to impaired macrophage function and reduced tissue oxygen tension secondary to thermoregulatory vasoconstriction. Collagen deposition in the wound has also been shown to be impaired with hypothermia. Increased susceptibility to infection with hypothermia at the time of introduction of bacteria into the skin has also been shown in animal models.[21,22] The 'window of opportunity' for infection to become established is reportedly in the first 3 h following inoculation. If hypothermia occurs at this critical time, then infection occurs more frequently.

Altered pharmacokinetics and pharmacodynamics in hypothermic patients

The minimum alveolar concentration (MAC) for potent inhaled anesthetics is reduced by ≈ 5% for each °C of

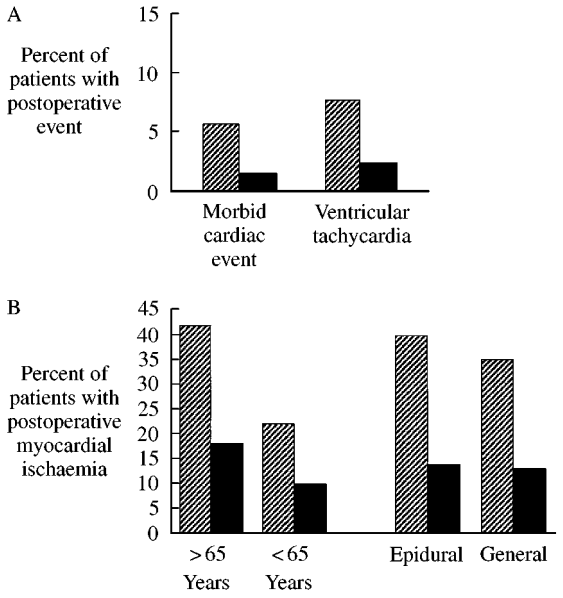

Figure 3 (A) Incidence of early postoperative cardiac morbidity (< 24 h following surgery) in patients who were randomized to receive active warming with a forced-air system (normothermic), or to receive no exogenous warming (hypothermic). Morbid cardiac events (unstable angina, myocardial infarction, or cardiac arrest) occurred more frequently in the hypothermic patients ($P = 0.03$). Ventricular tachycardia (> 5-beat runs) also occurred more frequently in the hypothermic patients ($P = 0.04$). (Modified from Frank et al.[15]). ▨, hypothermic (35.3°C); ■, normothermic (36.7°C). (B) Incidence of myocardial ischaemia in the first 24 h following lower extremity vascular surgery. Patients with core temperature less than 35°C (hypothermic) had a 2.5°-fold greater incidence of Holter-documented ischaemia compared to normothermic patients (≥ 35°C) ($P = 0.008$) regardless of age and anaesthetic subgroups. Older patients had a greater incidence of ischaemia ($P = 0.01$). Epidural and general anaesthetic subgroups had a similar incidence of ischaemia. (Adapted from Frank et al.[14]). ▨, hypothermic (< 35.3°C); ■, normothermic (≥ 35°C).

reduction in body temperature.[23] In addition, the blood/gas solubility for inhaled anaesthetics is increased with hypothermia. In combination, these effects contribute to the slow emergence from general anaesthesia in hypothermic patients. In a recently completed blinded randomized trial, the duration of time in the post-anaesthesia care unit (PACU) required to be ready for discharge was prolonged by an average of 40 min in hypothermic (34.8°C) *vs* normothermic (36.7°C) patients.[24] These findings suggest that substantial cost savings can be achieved by maintaining normothermia and expediting recovery from general anaesthesia.

Mild hypothermia increases the duration of action of non-depolarizing neuromuscular blockers. At 34°C the duration of vecuronium is doubled.[25] Atracurium is also prolonged but somewhat less. When added to the changes in MAC and solubility for inhaled anaesthetics, this prolongation of neuromuscular blockade can delay or prevent emergence from general anaesthesia, especially in the elderly who already have a reduced MAC and are especially susceptible to hypothermia.

Table 3 Accuracy* of temperature monitoring sites

Ability to represent core temperature	Monitoring site
Most accurate	Pulmonary artery
	Oesophagus (distal one-third)
	Tympanic membrane
	Nasopharynx
	Oropharynx
Intermediate	Urinary bladder
	Rectum
	Axilla
Least accurate	Skin-surface

*Accuracy is defined as the ability to reflect changes in blood temperature.

Thermal discomfort

Postoperative patients often suffer from cold thermal discomfort. Even patients with normal core temperatures can experience thermal discomfort since a low skin temperature contributes significantly to thermal sensation. Skin and core temperatures contribute in a 1:1 ratio to thermal sensation.[10] In contrast, the skin : core temperature contribution ratio is 1 : 4 for the physiological thermoregulatory responses — i.e. vasoconstriction and shivering.[10] The elderly exhibit less thermal discomfort at a similar core and skin temperature compared with younger individuals.[13]

BODY TEMPERATURE MONITORING

There are, as Dubois described, 'many different temperatures of the human body and its parts'.[26] In the simplest model, the body is divided into two thermal compartments, the core and the periphery. The core has a relatively constant internal temperature that is protected by the insulation from the peripheral compartment. The chest, abdomen, pelvis and head make up the core compartment. The extremities and skin surface make up the peripheral compartment. Mean body temperature lies somewhere in between the two and is defined as $0.67 \times$ (core temperature) $+ 0.33 \times$ (mean skin surface temperature).[27]

For the purposes of temperature monitoring during anaesthesia and surgery, the best monitoring sites are those that are closest to blood temperature which is considered the 'true' core temperature.[28] The various sites for core temperature monitoring are listed in

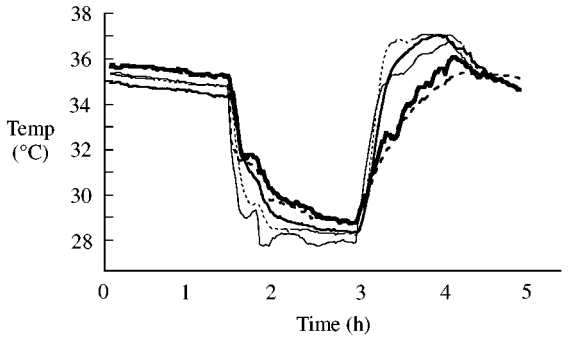

Figure 4 Body temperature monitoring in a patient on cardiopulmonary bypass. The relative ability of each monitoring site to reflect core temperature is shown. Arterial blood temperature coming from the bypass pump into the ascending aorta is shown along with various sites that are used to monitor 'core' temperature. The fastest temperature sites to show change during cooling and warming (other than arterial blood) are those measured at the nasopharynx, tympanic membrane, and oesophagus. Temperature in the urinary bladder and rectum are slower to change and are considered to be 'intermediate' temperatures rather than core temperatures. These sites are helpful in assessing the completeness of cooling and warming during cardiac surgery. Although skin-surface temperature is not shown, changes in skin temperature occur even more slowly than those measured in the rectum or urinary bladder. ——, oesophageal; - - -, tympanic; ——, nasopharynx; ▬▬, bladder; – – –, rectal.

Table 3 in order from most to least accurate for correlation with blood temperature.

Besides blood temperature in the pulmonary artery, nasopharyngeal and oesophageal temperatures are the most accurate estimates of core temperature. Oesophageal measurements, however, must be from the lower one-third of the oesophagus. If the probe is placed in the upper or middle third, then the respiratory gases will heat or cool the temperature probe. The distal third can be reached by going 10 cm beyond the point of maximum heart sounds with an oesophageal stethoscope. Tympanic measurements are an excellent representation of core temperature since the internal carotid artery passes near the tympanic membrane. When body temperature is changing (i.e. during aneasthesia and surgery) bladder and rectal temperatures are the slowest to change, and are likely to underestimate the magnitude of alteration in body temperature. In some clinical situations (i.e. cardiac surgery) these sites are deliberately monitored since the 'slow to change' characteristic is helpful to assess the 'completeness' of cooling and warming on cardiopulmonary bypass.[29] The skin surface is usually 2–3°C lower than core temperature but the core to skin gradient depends on ambient temperature and vasomotor tone.[30] For this reason, skin-surface temperature monitoring can be misleading in the perioperative period by underestimating true core temperature.[31] The relative changes in body temperature from various monitoring sites are shown during cooling and rewarming on cardiopulmonary bypass in Fig. 4.

METHODS OF CONTROLLING BODY TEMPERATURE

Ambient operating room temperature

Anaesthesia induces poikilothermia whereby patients tend to equilibrate body temperature with ambient temperature. At the turn of the century, there were reports of heat stroke during surgery which occurred in anaesthetized patients in hot operating rooms prior to air conditioning.[32] Operating rooms are now maintained at temperatures between 18–21°C (65–70°F) primarily for the comfort of the staff. At these temperatures, patients are predisposed to hypothermia especially with the high rate of air exchange which creates a 'wind-chill' effect. When ambient temperature is > 23°C (≈ 73°F), unintentional hypothermia occurs less frequently during surgery, but this warm environment is not well tolerated by the surgical staff since surgical gowns are now impermeable to fluids and very uncomfortable to wear. It is therefore preferable to warm the patient rather than the entire operating room and the surgical staff therein.

Warming the inspired gases

Active heating and humidification of the inspired gases has little or no effect on core temperature except in neonates where this method may help in maintaining normothermia. Less than 10% of total heat loss during surgery occurs from the respiratory tract in adult patients but this fraction is increased in small children. Earlier studies showing a significant effect on core temperature may have been flawed by measuring core temperature in the oesophagus where direct heating of the temperature probe occurs when airway gases are warmed. Passive humidification with heat-moisture exchangers (HMEs) will increase humidity in the airway but has no effect on the patient's core temperature. Current recommendations are to use an HME for any patient who would benefit from added moisture. Active heating and humidification of the respiratory gases are not necessary unless other methods of warming small children (forced-air warming) are unavailable. Active heater/humidifier systems have been associated with inadvertent disconnections in the breathing circuit and overheating of the inspired gases.

Warming the intravenous fluid

Fluid warming can be used to help reduce the magnitude of hypothermia during surgery but cannot be used to

warm patients since fluids cannot be delivered at temperatures significantly greater than 37°C. For minor procedures requiring minimal fluids (less than 2 l) it is unnecessary to warm the i.v. fluids. For procedures where fluids are given at increased flow rates or in higher volumes, it becomes necessary to warm the fluids in order to maintain normothermia. Either prewarmed fluids can be given or an in-line fluid/blood warmer may be used. When transfusion is likely a fluid/blood warmer should be used since blood is stored at 4°C. When a unit of cold blood or room temperature crystalloid is given to the patient, mean body temperature is reduced by 0.25°C.[33] When this is added to ongoing heat loss from the skin surface, the problem with unwarmed fluids is compounded.

When fluid warmers are used, two factors must be considered in determining the temperature at which the fluid is delivered to the patient (flow rate and length of i.v. tubing).[34] At low flow rates, the fluid returns to ambient room temperature after it leaves the warmer, before it reaches the patient. This heat loss can be eliminated by a warmed fluid-filled jacket around the i.v. tubing, but heat loss during low flow fluid administration is not significant except in paediatric patients. At high flows, fluids pass through the warmer so quickly that the fluids cannot be warmed sufficiently. Newer models of warmers are designed for delivery of warm fluids even at high flow rates.

Passive insulation

A layer of passive insulation reduces heat loss from the skin surface by 30%. The type of insulator is relatively unimportant as there is little difference between materials (plastic, cotton, paper, or reflective 'space blankets').[35] The layer of air between the insulation cover and the patient's skin provides the insulation independent of the material itself. Prewarmed cotton blankets are commonly used in the operating room. Patients feel immediate warmth and comfort, but actual heat flux through the skin over time is identical with both warmed and unwarmed cotton blankets.

Active patient warming

Although passive insulation and intravenous fluid warming can reduce heat loss from the patient, these therapies cannot be used to transfer heat into the patient. Therefore, active warming is required to maintain normothermia during the intraoperative period. One of the most effective methods is forced-air warming. This type of warming became available in the late 1980s and its use has increased dramatically over the last decade. Forced air was initially used to actively warm hypothermic patients in the postoperative period but it was quickly recognized that preventing hypothermia was more desirable than treating hypothermia. The forced-air system consists of two components—the forced-air generator and the blanket. The generator blows air at various flow rates and delivery temperatures into the attached blanket through a hose that inserts into the blanket. The blankets are baffled to fill with warm air with small holes for the air to exit onto the patient's skin-surface. They are designed for covering the upper body, lower body, or full body and the appropriate design is chosen based on the location of the surgical field.

Circulating water mattresses are also designed to actively warm patients during surgery. These mattresses are placed underneath the patient and are connected to a warm water source that circulates flow through the mattress. Heat transfer with this device can be limited since cutaneous blood flow to the patient's back is limited due to pressure on the capillary beds from the body's weight. A recently developed circulating water perfused garment is far superior to traditional mattresses since the surface area contact in greatly increased. In addition, this new system (Allon™, MTRE Inc.) incorporates a temperature feedback loop to regulate core temperature around an adjustable setpoint.

Radiant heat is another type of active warming system. These systems are often used during the intraoperative period and are incorporated into the beds used for neonates. Radiant heaters should be used with a skin-surface thermistor that provides thermostatic feedback to the warmer and reduces the risk of burning. Radiant heaters have also been used in the recovery room for adult patients. By warming the skin surface, shivering is immediately attenuated with radiant warming.

CONCLUSIONS

Hypothermia can be used therapeutically during surgery to protect from ischaemic injury to the vital organs during periods of blood flow interuption. Postoperative hypothermia, in the awake patient, should be considered a significant contributor to perioperative stress through sympathetic activation and should be aggressively avoided and/or treated. As with the other vital signs, body temperature should be carefully monitored and controlled in the perioperative period in order to optimize outcome in the surgical patient.

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