Thermoregulation and mild peri-operative hypothermia

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Induced hypothermia (28–32°C) has been indicated for some time for myocardial and cerebral protection in cardiac anaesthesia. However, it has recently been recognised that mild, inadvertent peri-operative hypothermia is associated with a number of adverse postoperative outcomes. Patient outcome can be improved by preventing peri-operative hypothermia. Although there is no clear definition of mild hypothermia, it is generally accepted that it refers to a core body temperature of 34.0–36.5°C. Effective prevention and treatment of peri-operative hypothermia requires an understanding of thermoregulatory physiology and its modulation by general and regional anaesthesia.

Physiology

It is useful to consider thermoregulatory physiology in terms of a two-compartment model. A central core compartment, comprising the major trunk organs and the brain, accounts for two-thirds of body heat content, maintained within a narrow temperature range (36.5–37.5°C) to facilitate cellular enzyme function. The peripheral compartment consists of skin and subcutaneous tissues over the body surface and the limbs. It represents about one-third of total body heat content. In contrast with the core, peripheral tissues undergo a wide variability of temperature, ranging from 2–3°C below to > 20°C below core temperature in extreme conditions.

Maintaining core temperature within a narrow range requires the balancing of heat production and loss. This is achieved by a control system consisting of afferent thermal receptors, central integrating systems and efferent control mechanisms.

Heat balance

Body heat is produced by metabolism, exercise, shivering and non-shivering thermogenesis. Basal metabolic rate (BMR) cannot be manipulated by thermoregulatory mechanisms. It is defined as the energy cost of maintaining homeostasis (40 kcal m⁻² h⁻¹). BMR is increased in children and by hormones such as thyroxine and growth hormone. The principal autonomic mechanisms of preserving body heat and increasing heat production are vasoconstriction and shivering. The latter can increase heat production 6-fold. Non-shivering thermogenesis is particularly important in neonates and can increase heat production 3-fold. Cold stimuli induce norepinephrine release in brown adipose tissue which uncouples oxidative phosphorylation. Therefore, the energy of glucose metabolism is released as heat, rather than stored as energy-releasing compounds, e.g. adenosine triphosphate (ATP). Exercise can increase heat production by as much as 20-fold at maximal intensity.

Peri-operative heat loss occurs predominantly by radiation (60%), convection (25%), and evaporation of body fluids (10%). Radiation and convective heat loss depend on the difference between peripheral body temperature and ambient temperature. Convection also depends on the velocity of air movement around the body. Vasodilatation and sweating are the major autonomic mechanisms of increasing heat loss. Sweating rates can reach > 1 litre h⁻¹ for a short time, resulting in heat loss of up to 15 times BMR.

Effectors

Until the last decade, it was believed that the spinal cord and brain stem were passive conductors of afferent signals to the pre-optic area of the hypothalamus. However, it is now accepted that thermoregulation is a multi-level, multiple-input system with the spinal cord, nucleus raphe magnus and locus subcoeruleus all involved in generating afferent...
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Thermal signals and modulating efferent thermoregulatory responses (Fig. 1).

The spinal cord and a number of brain stem centres integrate afferent thermal signals and attenuate descending efferent responses. In normal adults, the first response to a decrease in core temperature below the normal range (36.5–37.0°C) is peripheral vasoconstriction. If core temperature continues to decrease, shivering commences. Vasoconstriction and shivering are characterised by threshold onset, gain and maximal response intensity. Threshold is the temperature at which the effector is activated. Gain is the rate of response to a given decrease in core temperature. Normally, the threshold temperature for thermoregulatory vasoconstriction is 36.5°C and shivering commences at 36.0–36.2°C. General anaesthesia reduces these thresholds by 2–3°C but gain and maximal response intensity are unaffected.

In physiological conditions, behavioural adaptations have a greater effect in preventing hypothermia in response to a cold environment. In extreme cold, vasoconstriction and shivering are of limited effect compared with behavioural measures such as taking shelter and wearing protective clothing.

Measuring core temperature
Core body temperature can be measured at a number of sites. Measuring blood temperature in the pulmonary circulation using a pulmonary artery catheter is the best estimate of core temperature but this is a very invasive technique. Directly measured tympanic membrane temperature is also an accurate method but the thermometer probe requires careful positioning to avoid damage to the membrane. Indirect measures of tympanic membrane temperature (infra-red thermometers introduced intermittently into the external auditory canal) are increasingly being used. Core temperature may be measured reliably in the nasopharynx and lower oesophagus. Rectal and bladder temperature may lag behind changes in core temperature because these organs are not perfused well enough to reflect rapid changes in body heat content.

Effect of general and regional anaesthesia on thermoregulation
General anaesthesia typically results in mild core hypothermia (1–3°C). This occurs in a characteristic 3-phase pattern (Fig. 2). Phase 1 is a rapid reduction in core temperature of 1.0–1.5°C within the first 30–45 min. This is attributable to vasodilatation and other effects of general anaesthesia. Vasodilatation inhibits normal tonic vasoconstriction resulting in a core-to-peripheral temperature gradient and redistribution of body heat from core to peripheral tissues. General anaesthesia also reduces the threshold for activation of thermoregulatory vasoconstriction. Therefore, core temperature can become much colder before the re-set vasoconstrictor response can occur.

![Thermal receptors (cold & warm)]

- Predominantly skin, some visceral
- Spinal cord
- Brain stem nuclei

![Pre-optic nuclei in the anterior hypothalamus]

Activates heat or cold sensitive neurons

Cold responses: Vasoconstriction, Shivering, Non-shivering thermogenesis, Behaviour
Efferent responses
Warm responses: Sweating, Vasodilation, Behaviour

Fig. 1 A simplified overview of thermoregulatory control. It is now recognised as a multiple-input, multilevel system, with the spinal cord and certain brain stem nuclei processing afferent thermal signals and also modulating efferent thermoregulatory responses.
Phase 2 is a more gradual, linear reduction in core temperature of a further 1°C over the next 2–3 h of anaesthesia. This is due to heat loss by radiation, convection and evaporation exceeding heat gain which is determined by the metabolic rate. Radiation and convective heat losses in this phase are determined by the difference between peripheral and ambient temperature. Evaporation heat loss is exacerbated during major surgery where a greater surface area of tissue may be exposed to the environment.

Phase 3 is a ‘plateau’ phase where heat loss is matched by metabolic heat production. This occurs when anaesthetised patients become sufficiently hypothermic to reach the altered threshold for vasoconstriction which restricts the core-to-peripheral heat gradient.

As with general anaesthesia, redistribution of body heat during spinal or epidural anaesthesia is the main cause of hypothermia. Because redistribution during spinal or epidural anaesthesia is usually confined to the lower half of the body, the initial core hypothermia is not as pronounced as in general anaesthesia (approximately 0.5°C). Otherwise, the pattern of hypothermia during spinal or epidural anaesthesia follows a similar pattern to that of general anaesthesia for the first two phases. The major difference in spinal or epidural anaesthesia is that the plateau phase does not emerge because vasoconstriction is blocked. Therefore, patients undergoing long procedures with combined general and epidural anaesthesia are at risk of a greater degree of hypothermia (Fig. 2).

**Consequences of inadvertent, mild hypothermia**

Recently, a number of prospective, randomised trials have shown that mild peri-operative hypothermia results in a number of adverse outcomes (Table 1). All the adverse outcomes listed in Table 1 resulted from a core hypothermia of 35.0–35.7°C. The mechanism by which mild hypothermia induces myocardial ischaemia and arrhythmias may be increased plasma catecholamine concentrations resulting in hypertension which may aggravate myocardial irritability. Increases in intra-operative blood loss and requirement for blood transfusion are attributable to hypothermia-induced impairment of platelet function. Mild hypothermia also predisposes to surgical wound infection and poor wound healing. The incidence of surgical wound infection is directly related to subcutaneous wound tissue oxygen tension. In turn, this is compromised by hypothermia-induced vasoconstriction. Moreover, mild hypothermia directly impairs neutrophil function. Maintaining normothermia can reduce urinary nitrogen excretion suggesting a decrease in postoperative catabolism.

**Table 1** Major adverse outcome of inadvertent mild peri-operative hypothermia

<table>
<thead>
<tr>
<th>Adverse outcome</th>
<th>Normothermic group</th>
<th>Hypothermic group</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial ischaemia or arrhythmias</td>
<td>1%</td>
<td>6%</td>
<td>Frank SM et al. JAMA 1997; 277: 1127–34</td>
</tr>
<tr>
<td>Intra-operative blood loss</td>
<td>1.7 ± 0.3 litre</td>
<td>2.2 ± 0.5 litre</td>
<td>Schmied H et al. Lancet 1996; 347: 289–92</td>
</tr>
<tr>
<td>Allogenic transfusion requirement</td>
<td>1 unit</td>
<td>8 units</td>
<td>Schmied H et al. Lancet 1996; 347: 289–92</td>
</tr>
<tr>
<td>Urinary nitrogen excretion</td>
<td>982 mmol day⁻¹</td>
<td>1798 mmol day⁻¹</td>
<td>Carli F et al. Br J Anaesth 1989; 63: 276–82</td>
</tr>
<tr>
<td>Duration of action of neuromuscular antagonists</td>
<td>44 ± 4 min</td>
<td>68 ± 7 min</td>
<td>Leslie K et al. Anesth Analg 1995; 80: 1007–14</td>
</tr>
<tr>
<td>Duration of postanaesthetic recovery</td>
<td>53 ± 36 min</td>
<td>94 ± 65 min</td>
<td>Lenhardt R et al. Anesthesiology 1997; 87: 1318–23</td>
</tr>
<tr>
<td>Duration hospitalisation</td>
<td>12.1 ± 4.4 day</td>
<td>14.7 ± 6.5 day</td>
<td>Kurz et al. N Engl J Med 1996; 334: 1209–15</td>
</tr>
</tbody>
</table>

Values shown are mean ± SD.
Because the enzymes which metabolise most drugs are very temperature-sensitive, it is unsurprising that drug metabolism is temperature dependent and that duration of action of neuromuscular antagonists is prolonged. The duration of recovery room stay and overall hospitalisation is reduced by avoidance of mild peri-operative hypothermia. This has significant healthcare cost implications.

Shivering is also an important consequence of hypothermia but the literature suggests that it is not the cause of adverse outcomes per se. Shivering is a complex response with three different patterns of tremor, not all of which are thermoregulatory.

**Prevention and treatment of mild peri-operative hypothermia**

There are three basic strategies for the prevention and treatment of mild peri-operative hypothermia: (i) minimising redistribution of heat; (ii) cutaneous warming during anaesthesia; and (iii) internal warming.

**Minimising redistribution of heat**

This may be achieved by: (i) pre-operative warming of peripheral tissue; and (ii) pre-operative pharmacological vasodilatation.

**Pre-operative warming of peripheral tissue**

This reduces the normal core-to-peripheral temperature gradient so that induction of anaesthesia does not result in the sudden core hypothermia seen in Phase 1. However, to be effective, this would require subjecting patients to over 1 h of exposure to a source of radiated heat pre-operatively which may not be practicable.

**Pre-operative pharmacological vasodilatation**

This facilitates core-to-peripheral redistribution of heat before anaesthesia; it does not compromise core temperature because patients are not anaesthetised and their thermoregulatory responses are intact. Oral nifedipine, taken pre-operatively, has been shown to reduce effectively the extent of the initial redistribution hypothermia by 50%.

**Cutaneous warming during anaesthesia**

**Passive insulation**

A single layer of any insulator (e.g. space blanket) reduces cutaneous heat loss by approximately 30% because it traps a layer of still air between it and the skin. Adding further layers of passive insulation does little or nothing to preserve core temperature.

**Active warming**

Active warming systems maintain normothermia much more effectively than passive insulation. The electrically powered air heater-fan and patient cover is effective because it replaces cool room air with warmed air and also because convection increases heat gain when the forced air is warmer than skin. If being used over the lower body, it should be temporarily switched off during procedures which cut off lower limb blood supply (e.g. aortic clamping) to minimise the effects of distal ischaemia.

Active warming by circulating water mattresses is relatively ineffective because heat is applied only to the patient’s back where relatively little heat is lost. They have been superseded by forced air warming devices. Active warming by resistive heating (electric) blankets is a recent development. It is as effective as the forced air warming technique and may be particularly suitable in preventing hypothermia in the out-of-hospital trauma situation.

**Internal warming**

**Fluid warming**

Fluids should be warmed to body temperature prior to infusion. The administration of one litre of fluid at room temperature decreases core temperature by 0.25°C. Fluid warming devices should be used when large amounts of fluid or blood replacement are anticipated. Fluid warming alone will not prevent core hypothermia.

**Airway humidification**

This contributes little to preservation of core temperature because < 10% of metabolic heat loss occurs via the respiratory tract.

**Invasive internal warming techniques**

Cardiopulmonary bypass transfers heat at a rate and magnitude not seen in any other situation. Peritoneal dialysis is also very effective but neither technique is relevant to mild peri-operative hypothermia.

**Amino acid infusion**

Amino acid infusion during anaesthesia increases metabolic rate and patients are less hypothermic compared with those given the same volume of crystalloid. This technique has not gained wide-spread acceptance because of doubts about the effect on cardiac outcome of increased metabolic rate during anaesthesia.
Conclusions
Mild peri-operative hypothermia is associated with cardiac morbidity, increased blood loss, surgical wound infection and increased duration of hospitalisation. Most surgical patients are at risk of the many adverse outcomes of mild hypothermia, particularly elderly, high-risk patients undergoing major surgery. The particular method of maintaining core temperature above 36.5°C is unimportant but use of forced-air convective warmers probably represent the most efficient, practical strategy of preventing core hypothermia and restoring normal core temperature in current practice.

Key references
Frank SM, Fleisher LA, Breslow MJ et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. JAMA 1997; 277: 1127–34
Sessler DI. Complications and treatment of mild hypothermia. Anesthesiology 2001; 95: 531–43
Sessler DI. Perioperative shivering. Anesthesiology 2002; 96: 467–84

See multiple choice questions 20–22.