Nonpharmacological Prevention of Surgical Wound Infections

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Postoperative wound infection is a common and serious complication of surgery. This review will focus on 2 factors known to modulate perioperative immunity: maintenance of perioperative normothermia and provision of supplemental perioperative oxygen. Hypothermia causes numerous adverse outcomes, including morbid myocardial events, increased blood loss and transfusion requirement, postsurgical wound infections, and prolonged hospitalization. Perioperative normothermia should thus be maintained unless therapeutic hypothermia is specifically indicated. Supplemental perioperative oxygen (inspired fraction of 80% instead of 30%) significantly reduces postoperative nausea and vomiting, diminishes the decrease in phagocytosis and bacterial killing usually associated with anesthesia and surgery, and reduces the rate of postoperative wound infection among patients who undergo colon resection. Available data thus suggest that supplemental perioperative oxygen improves surgical outcome with little or no associated risk.

Maintaining strict asepsis reduces the risk of surgical wound infection. However, some contamination during surgery is inevitable, and many bacteria that cause infections originate within the body. As a consequence, postoperative host defense is probably the major factor that determines whether a surgical patient becomes infected. The present article will focus on 2 factors known to modulate perioperative immunity: maintenance of perioperative normothermia and provision of supplemental perioperative oxygen.

Several nonpharmacological factors obviously influence the risk of infection. For example, avoiding shaving at the surgical site [1] and maintaining careful regulation of the blood glucose level [2] both reduce the rate of infection. The primary defense against surgical pathogens is oxidative killing by neutrophils [3]. Oxygen is a substrate for this process, and the reaction critically depends on tissue oxygen tension throughout the observed physiological range. Therefore, it is unsurprising that subcutaneous tissue oxygen tension is inversely correlated with the risk of surgical wound infection [4, 5]. Factors known to influence tissue oxygenation and perfusion thus have a significant impact on surgical wound infection. Hemoglobin concentration [6], cardiac output [7], local perfusion [8, 9], smoking [10], anemia [6], perioperative fluid management [6, 11, 12], and uncontrolled surgical pain [13] are all known to influence tissue oxygenation and perfusion.

Wound infection is a common and serious complication of surgery; however, it is hardly the only serious complication. Any potential therapy must be considered in the context of all its risks and benefits. We will therefore discuss both the risks and benefits of maintaining normothermia and providing supplemental oxygen.

MAINTAINING NORMOTHERMIA

Body temperature is among the most tightly controlled physiological parameters; it is normally controlled to within 0.2°C. Even small deviations in core body temperature provoke aggressive thermoregulatory defenses. The 3 major autonomic thermoregulatory defenses in humans are sweating, vasoconstriction, and shivering. Each response has a threshold (a triggering core temperature), a gain (an incremental change in
response intensity), and a maximum response intensity. The sweating and vasoconstriction thresholds, which are both \(\sim 37^\circ C\), are separated by only a few tenths of a degree centigrade. This interthreshold range defines the normal range of body temperature. In contrast, the shivering threshold is nearly a full degree centigrade below the vasoconstriction threshold [14].

**Perioperative thermoregulation.** All anesthetic drugs profoundly impair thermoregulatory control. For example, the interthreshold range increases nearly 20-fold with typical doses of volatile anesthetics [15]. A similar increase is observed with the use of the intravenously administered anesthetic propofol [16], but a somewhat smaller increase is noted with the use of opioids [17]. Most sedatives also impair thermoregulatory control. The result is that patients become hypothermic during surgery (figure 1).

Hypothermia develops in 3 characteristic phases. Initially, there is a rapid \(1.0^\circ C–1.5^\circ C\) decrease in core temperature during the first hour of administration of anesthesia. This initial decrease results from a core-to-peripheral redistribution of body heat [19]. Redistribution occurs because anesthetics inhibit thermoregulatory control and therefore disrupt the tonic vasoconstriction that normally maintains a core-to-peripheral temperature gradient. This redistribution is not a net exchange of heat with the environment; rather, heat flows from the core to the periphery, thereby reducing core temperature.

The second phase of the hypothermia curve is a slower, linear decrease in core temperature. It results simply from heat loss exceeding heat production. This phase typically lasts 2–3 h. The slope of this curve depends on the difference between heat loss and metabolic heat production.

Finally, when patients become sufficiently hypothermic, there is a plateau in the core temperature. This plateau results when the reemergence of thermoregulatory vasoconstriction constrains metabolic heat to the core and prevents further hypothermia. Typically, this occurs when the core temperature is \(\sim 34^\circ C\) [20].

**Consequences of mild hypothermia.** Among the most serious consequences of mild hypothermia (core body temperature, \(35^\circ C–36.5^\circ C\)) are adverse myocardial outcomes. Frank et al. [21] demonstrated that a decrease of only \(1.5^\circ C\) in core body temperature triples the risk of morbid myocardial events. Their study, as with all the studies reported in the present article, was a prospective, randomized clinical trial. Their result is of considerable clinical importance because myocardial in-

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**Figure 1.** Anesthetic-induced inhibition of thermoregulatory control is usually the major factor that determines perioperative core temperature. Concentration-dependent thermoregulatory inhibition by desflurane and isoflurane (halogenated volatile anesthetics), propofol (an intravenous anesthetic), and alfentanil (a \(\mu\)-agonist opioid) is shown. The sweating (▲), vasoconstriction (○), and shivering (■) thresholds are expressed in terms of core body temperature at a designated mean skin temperature of \(34^\circ C\). Anesthesia linearly, but slightly, increases the sweating threshold. In contrast, anesthesia produces substantial and comparable linear or nonlinear decreases in the vasoconstriction and shivering thresholds. Typical concentrations of anesthetics thus increase the interthreshold range (the difference between the sweating and vasoconstriction thresholds) \(\sim 20\)-fold from its normal value of \(\sim 0.2^\circ C\). Autonomic thermoregulatory defenses are not activated in patients unless the body temperature exceeds the interthreshold limits; surgical patients are thus poikilothermic over a core temperature range of \(33^\circ C–35^\circ C\). Isoflurane at 1% and desflurane at 6% have comparable anesthetic potency. Data were obtained from [15–18]. Error bars that were smaller than the data markers were deleted from the figure. Reprinted with permission from [14].
The detrimental effects of mild hypothermia were recently demonstrated in a prospective, randomized clinical trial. Patients who had a decrease of nearly 1°C in core temperature were 3 times as likely to develop surgical wound infections as were those in whom a normal body temperature was maintained. These infections were clinically important, with the incidence of surgical wound infection being roughly 10% after colon surgery, a value that has not changed appreciably in several decades. In addition to causing substantial morbidity, surgical wound infections are costly and typically increase the duration of hospitalization by about a week.

Infections are established within 2 h of contamination, with this period known as the decisive period. Treatments such as antibiotics are effective during this decisive period but not subsequently. Similarly, local administration of epinephrine and the development of hypovolemia increase the risk of infection when the drug is given or when the condition occurs within several hours of contamination, but not later.

The primary defense against surgical pathogens is oxidative killing by neutrophils. The key element in this process is the transformation of oxygen to a superoxide radical. This is a nitric oxide–dependent process that is dependent upon the partial pressure of oxygen; the process therefore depends critically on tissue oxygen tension over the entire physiological range.

As one might expect from an oxygen-based defense, the risk of surgical wound infection correlates highly with tissue oxygen tension. For example, infection rates are more or less as predicted when the tissue oxygen tension is near 75 mm Hg. The rate increases markedly as the tissue oxygen tension decreases to 45 mm Hg, and it decreases markedly as the tissue oxygen tension approaches 100 mm Hg.

The primary connection between thermoregulation and postsurgical resistance is that hypothermia triggers thermoregulatory vasoconstriction, which, in turn, decreases tissue oxygenation. In contrast, local warming causes hyperemia and increases tissue oxygenation. There is, however, a second factor: hypothermia reduces the production of superoxide radicals and other oxygen intermediates at a given level of tissue oxygenation. Hypothermia thus reduces neutrophil oxidative killing by decreasing tissue oxygen availability and by impairing the production of reactive oxygen intermediates. Hypothermia may also increase the risk of infection by increasing blood loss and, thus, the transfusion requirement. However, leukocyte-filtered blood (which is usually used now) does not increase the risk of infection.

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the average infected patient staying 1 week longer in the hospital than did an uninfected one [30].

The duration of hospitalization was 20% longer for patients with hypothermia. (The attending surgeons, who were blinded to intraoperative thermal management, determined the duration of hospitalization.) This prolongation remained highly statistically significant even when the analysis was restricted to uninfected patients. Consistent with this observation, collagen deposition (i.e., scar formation) was significantly reduced in the patients with hypothermia. It thus appears that mild hypothermia not only triples the risk of surgical wound infection but, also, prolongs the duration of hospitalization, even for uninfected patients. Table 1 lists the major prospective, randomized trials that have evaluated the adverse effects of mild perioperative hypothermia.

**Thermal manipulation.** There are theoretical reasons to believe that therapeutic hypothermia will be beneficial in certain restricted patient populations. For example, mild hypothermia may improve the outcome associated with cerebral ischemia. However, these putative benefits remain largely unproved in humans. In contrast, there is an enormous amount of prospective, randomized data on outcomes that have indicated that mild hypothermia causes numerous severe adverse outcomes in many patient populations. It thus seems apparent that body temperature should be monitored during nearly every surgical procedure and that patients should be kept in a normothermic state unless hypothermia is being induced therapeutically for a specific indication. Maintaining normothermia during surgery is becoming the community standard of care; however, intraoperative temperature remains unmonitored in many patients, and too many patients are unnecessarily allowed to become hypothermic.

Numerous techniques have been advocated for maintaining normothermia. The easiest technique is simply to cover patients with one of the many passive insulators that are available in every operating room. These include cotton blankets, surgical drapes, plastic bags, and “space blankets.” Each of these interventions decreases cutaneous heat loss by ∼30%, which is a clinically important amount [36]. It is tempting to think that if a single layer of passive insulation decreases heat loss by 30%, then 3 layers would nearly prevent heat loss. Unfortunately, this is not the case: augmenting 1 layer of passive insulation with 2 others decreases heat loss by only an additional 20% [37]. If a single layer of insulation maintains normothermia, then that is sufficient. However, if patients continue to become hypothermic with a single layer of insulation, adding additional layers is unlikely to prove adequate. Instead, it will be necessary to use active warming.

There are several active warming systems available. One of these systems, airway heating and humidification, has been shown numerous times to be ineffective [38]. This is not surprising, because simple thermodynamic calculations demonstrate that heat transfer through the airway is trivial [39]. Another type of active warming system is a circulating-water mattress. Such systems are attractive because they are easy to use and inexpensive; unfortunately, they are also ineffective [40].

Warming of intravenously administered fluids is yet another warming method that is commonly advocated. Warming intravenous fluids will not warm patients, because the temperature of warmed fluid only slightly exceeds body temperature.

### Table 1. Major consequences of mild perioperative hypothermia in humans.

<table>
<thead>
<tr>
<th>Authors [reference]</th>
<th>Consequence</th>
<th>Total no. of subjects</th>
<th>ΔT&lt;sub&gt;core&lt;/sub&gt;, °C</th>
<th>Normothermia&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Hypothermia&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frank et al. [21]</td>
<td>Morbid cardiac events</td>
<td>300</td>
<td>1.3</td>
<td>1%</td>
<td>6%</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Schmied et al. [22]</td>
<td>Intraoperative blood loss</td>
<td>60</td>
<td>1.6</td>
<td>1.7 ± 0.3 L</td>
<td>2.2 ± 0.5 L</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Heier et al. [25]</td>
<td>Duration of vecuronium</td>
<td>20</td>
<td>2.0</td>
<td>28 ± 4 min</td>
<td>62 ± 8 min</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lenhardt et al. [26]</td>
<td>Duration of postanesthetic recovery</td>
<td>150</td>
<td>1.9</td>
<td>53 ± 36 min</td>
<td>94 ± 65 min</td>
<td>&lt;.001</td>
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<tr>
<td>Kurz et al. [30]</td>
<td>Surgical wound infection</td>
<td>200</td>
<td>1.9</td>
<td>12.1 ± 4.4 days</td>
<td>14.7 ± 6.5 days</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Leslie et al. [31]</td>
<td>Urinary excretion of nitrogen</td>
<td>6</td>
<td>3.0</td>
<td>44 ± 4 min</td>
<td>68 ± 7 min</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Just et al. [33]</td>
<td>Postoperative shivering</td>
<td>14</td>
<td>2.3</td>
<td>141 ± 9 mL/min/m²</td>
<td>269 ± 60 mL/min/m²</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Frank et al. [34]</td>
<td>Adrenergic activation</td>
<td>74</td>
<td>1.5</td>
<td>330 ± 30 pg/mL</td>
<td>480 ± 70 pg/mL</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Kurz et al. [35]</td>
<td>Thermal discomfort</td>
<td>74</td>
<td>2.6</td>
<td>50 ± 10 mm VAS</td>
<td>18 ± 9 mm VAS</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**NOTE.** Only prospective, randomized trials involving humans were included; subjective responses were evaluated by observers blinded to treatment group and core temperature. ΔT<sub>core</sub>, difference in core temperature between the treatment groups. Different outcomes of the first 3 studies are shown on separate lines. VAS, a 100-mm-long visual analogue scale (with 0 mm denoting intense cold and 100 mm denoting intense heat). Reprinted with permission from [14].

<sup>a</sup> Data are mean ± SD, unless otherwise indicated.
Warming of fluids also cannot compensate for cutaneous heat loss or for loss from inside incisions. However, the administration of large volumes of unwarmed fluids certainly can produce hypothermia. Each liter of fluid administered at an ambient temperature decreases the mean body temperature of an adult by 0.25°C. Each unit of blood from the refrigerator similarly decreases mean body temperature by 0.25°C [39]. Fluids should thus be warmed if large volumes are being administered. However, it is rarely necessary to warm fluids during small or moderate-sized operations.

Nearly 90% of metabolic heat is lost through the anterior surface of the skin [19, 20]. It is thus apparent that any effective patient-warming system will have to address the anterior skin surface. The most common method of warming surgical patients is forced-air convection [41]. Forced-air convection systems consist of a blower that delivers electrically heated air into a quiltlike cover. The disposable cover disperses the air over the anterior surface of the body, producing a warm microenvironment around the patient. Patients can be warmed equally as well with carbon-fiber electric heating blankets. This system allows for a low-voltage direct current to be passed through a carbon-fiber fabric. The fabric, heated to 42°C, then warms the skin surface. The efficacy of carbon-fiber and forced-air systems is comparable.

Summary. Human body temperature is normally tightly regulated. However, all anesthetics profoundly impair temperature control. The result is that virtually all unwarmed surgical patients become hypothermic. Hypothermia results initially from a core-to-peripheral redistribution of body heat. This is followed by a linear decrease in core temperature that results from heat loss exceeding heat production.

A major adverse effect of mild hypothermia is a tripling of the rate of morbidity myocardial events. Mild hypothermia also significantly increases blood loss in transfusion requirements. There are 3 mechanisms by which mild hypothermia facilitates the development of surgical wound infections. The first is that even mild hypothermia triggers thermoregulatory vasoconstriction, which decreases tissue oxygenation. The second is that hypothermia impairs the production of superoxide radicals and other reactive oxygen intermediates. Third, mild hypothermia decreases scar formation and, therefore, the integrity of the healing wound. The consequence of these impairments is that even mild hypothermia triples the risk of surgical wound infection. Mild hypothermia also significantly prolongs the duration of hospitalization, even among uninfected patients.

Because hypothermia causes so many adverse outcomes, normothermia should be maintained during surgery. Passive insulation can be used if it is sufficient. However, passive insulation alone is rarely enough to keep patients normothermic. Fluid warming should be used when large volumes of fluid are administered. Only active cutaneous warming will routinely maintain normothermia in most surgical patients; forced-air and carbon-fiber warming are the most effective noninvasive systems that are routinely available.

SUPPLEMENTAL OXYGEN

All surgical patients are given at least some oxygen, because anesthetics impair ventilation and oxygenation. Currently, the amount of oxygen given to surgical patients is essentially random. In Europe, most patients are given 30% oxygen during surgery. In the United States, the concentrations administered vary widely, ranging from 30% to 100%. Until recently, there was little basis for choosing one concentration or another. However, recent studies have shown that supplemental oxygen—for example, 80% oxygen—provides substantial benefit and little, if any, risk. Oxygen is remarkably inexpensive; it costs only 0.001 cents/L, which means that it costs 40 times less than tap water. Providing supplemental oxygen for the entire perioperative period thus only costs only a few cents per patient.

Atelectasis and pulmonary function. Very high oxygen concentrations (near 100%) can cause direct pulmonary toxicity. However, toxicity develops only after several days of exposure. There is no reason whatsoever to believe that direct pulmonary toxicity from oxygen develops in the time frame of a surgical procedure.

There is evidence that 100% oxygen promotes atelectasis—that is, collapse of the alveolar air sacs. Atelectasis can develop after just a few breaths of 100% oxygen. However, it is also reversible with just a single sustained positive-pressure breath. Its clinical importance thus remains debatable [42].

A recent study evaluated the sustained administration of 80% oxygen, both during and for 2 h after surgery. Pulmonary function on the first postoperative day was identical in the patients in each group—that is, alveolar-arterial differences in oxygen and oxygen saturations were the same in each group. Furthermore, the rate of atelectasis, as quantified by pulmonary CT, was also similar in each group. This study had a 99% power to detect a 2% difference in the atelectasis rate. It is thus apparent that administration of 80% oxygen in the perioperative period does not cause clinically important atelectasis or impair pulmonary function (figure 2) [43].

Postoperative nausea and vomiting. The overall incidence of postoperative nausea and vomiting is between 20% and 70%, depending on a number of factors [44]. Nausea and vomiting after surgery are not life-threatening complications. However, they are, like thermal discomfort, complications that patients intensely dislike. They are also the leading cause of unexpected admission after planned ambulatory surgery.

Numerous mechanisms contribute to postoperative nausea and vomiting. They can result from stimulation of the central chemoreceptor trigger zone or from vestibulocochlear stimu-
duction of postoperative nausea and vomiting by decreasing the release of dopamine and ameliorating subtle intestinal ischemia. This hypothesis was tested in a study in which patients were randomly assigned to receive 30% or 80% supplemental oxygen. The incidence of postoperative nausea and vomiting was halved in the patients given 80% oxygen [45]. In a subsequent study, 30% oxygen and 80% oxygen were compared, and a third set of patients was given 30% oxygen and a high dose of the antinausea drug ondansetron [46]. In that study, administration of 80% oxygen again halved the incidence of nausea and vomiting. Of interest, 80% oxygen was more effective than was high-dose ondansetron. Ondansetron costs ~$30 (in US$) per dose; this compares unfavorably with oxygen, which costs 3 cents/patient.

Yet another study evaluated the use of supplemental oxygen for treatment of motion sickness. Again, supplemental oxygen markedly reduced the risk of nausea and vomiting in these patients [47]. Only one other study has specifically evaluated the effects of supplemental oxygen on nausea and vomiting. In that study, the benefits of 80% oxygen were evaluated in patients who were undergoing thyroid surgery; there was no benefit whatsoever in these patients [48]. The most likely explanation is that thyroid surgery does not involve the abdominal cavity, whereas the other surgical studies involved colon surgery and laparoscopy, both of which are likely to cause subtle intestinal ischemia. Table 2 shows the results of the 4 prospective, randomized trials that evaluated the effects of administration of supplemental oxygen on postoperative nausea and vomiting.

**Alveolar immune function.** Alveolar macrophages are the primary defense against pulmonary infection, and phagocytosis and oxidative killing are key defense mechanisms. Both are required, because killing cannot occur until the bacteria are ingested, and because ingestion alone is ineffective unless the bacteria are actually killed. Both phagocytosis and oxidative killing are stimulated by proinflammatory cytokines.

Anesthesia administration, surgery, and mechanical venti-
One way to improve tissue oxygenation, as discussed in the “Hypothermia and surgical wound infections” subsection of the Maintaining Normothermia section above, is to maintain perioperative normothermia [30]. An even easier way to increase tissue oxygenation is simply to administer higher concentrations of inspired oxygen. As might be imagined, administration of 80% oxygen markedly increases tissue oxygen tension. This observation was the basis for an outcomes study in which administration of 80% perioperative oxygen was compared with administration of 30% perioperative oxygen.

A total of 500 normothermic patients who were undergoing elective colon resection were randomly assigned to receive supplemental or routinely administered perioperative oxygen. Anesthetic and surgical management was standardized. In the patients given 80% oxygen, the tissue oxygen tension averaged near 100 mm Hg; in contrast, in patients assigned to receive 30% inspired oxygen, the tissue oxygen tension averaged near 50 mm Hg. Supplemental oxygen reduced the risk of infection by a factor of 2 (from 11% to 5%). This reduction was highly statistically significant. Furthermore, the infections were clinically important: infected patients remained in the hospital a full week longer than did uninfected patients [5]. The effects of combining normothermia with supplemental oxygen have not been specifically evaluated. However, it is likely that the benefits are additive.

Supplemental perioperative oxygen is inexpensive and easy to provide. There is no evidence that 80% perioperative oxygen causes atelectasis or any decrement in pulmonary function. Supplemental oxygen does, however, activate alveolar immune defenses. It also reduces the incidence of postoperative nausea and vomiting, and it halves the risk of surgical wound infection. The available data thus suggest that supplemental oxygen improves outcome with little or no associated cost or risk.

References


