

To the Editor: We are concerned about the report by Kurz et al. (May 9 issue) of a randomized clinical study in which intraoperative hypothermia was shown to increase the incidence of surgical-wound infection and prolong hospitalization as compared with normothermia.

The authors imply that only negative effects of unintended intraoperative hypothermia have been observed to date. In previous studies in animals, the same group showed that mild hypothermia significantly impairs resistance to dermal infection.[2,3] With the exception of its effects in cardiac surgery and neurosurgery, we, too, know of no positive effects of intraoperative hypothermia on postoperative outcome. Nevertheless, in the study by Kurz et al., a preventable pathological condition (hypothermia) was intentionally induced in 50 percent of the patients. This almost necessarily had to cause a poorer outcome.

This paper raises the following questions: Were the patients informed in detail before surgery of the study hypothesis "that mild core hypothermia increases both the incidence of surgical-wound infection and the length of hospitalization"? Were the patients fully informed that there was a 50 percent possibility that they would not receive the optimal treatment? Why were the patients not informed postoperatively that they had been assigned to the hypothermia group and that hypothermia was the probable cause of their infection and the reason for their prolonged hospitalization?

We were unable to verify the authors' statement that "mild perioperative hypothermia (approximately 2°C below the normal core body temperature) is common in colon surgery," with reference to an article by Frank et al.[4]

It is questionable whether the results of the study by Kurz et al. make an important contribution to the large body of knowledge regarding the negative effects of intraoperative hypothermia. It is not without good reason that every anesthesiology textbook describes measures to prevent and treat intraoperative hypothermia.

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To the Editor: In the study by Kurz et al., patients in the hypothermia group were actively cooled. They were not subjected to "routine intraoperative thermal care" or merely allowed to cool, as was suggested in the abstract. Air at room temperature is typically 20°C, but no measures to insulate the lower body in either group were mentioned. Whereas most patients are routinely covered by blankets to create an envelope of warm, stagnant air, the patients in the hypothermia group appear to have been not only minimally insulated but also exposed to cool air at high convective rates from the forced-air blower, causing substantial convective and evaporative cooling.

Even with this increased active cooling of the hypothermia group, significant differences between groups in core temperature began to occur only after about 60 minutes (as shown in Fig. 1 of the article), suggesting that the "protective" effects of normothermia developed only after 1 hour. Although the study design does have the semblance of blinding the surgeons to the temperature treatment (by covering the warming devices and applying them at 20°C as compared with 37°C), it is doubtful that blinding truly occurred. There is no evidence that the core temperature readouts were shielded from view, and the surgeons were described as "unaware" of the treatment groups rather than "blinded." These sham blinding measures served only to increase cooling over that produced by standard procedures and served no valid purpose in the study.

This study demonstrated that forced-air products should not be used to cool patients undergoing colon surgery; conclusions regarding the use of normothermia as compared with standard care (cotton blankets) are not possible. The use of forced-air products has become necessary to combat the cool temperatures required to keep gowned surgeons comfortable in the operating room. The additional expense of the warming blanket may be relatively little (purchase price of \$18 to hospitals) or significant (cost of \$100 on the patient's bill), but the need for such devices can be reduced considerably by maintaining temperatures in operating rooms and patient-holding areas at higher levels or simply by maintaining an envelope of warm air around the patient through the use of hospital blankets and sheets.[1,3] Upper-body warming is not of benefit in short procedures, as evidenced in this study.

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To the Editor: Kurz et al. report a statistically significant reduction in infection rates in patients undergoing colorectal surgery when an attempt is made to maintain intraoperative normothermia. However, it is troubling that the difference detected in infection rates seems to be due to a greater than usual number of infections in the control (unwarmed) group (18 of 96, or 19 percent) rather than a reduced number of infections in the treated (warmed) group (6 of 104, or 6 percent). Moreover, we are never told how many of these infections are of clinical significance. The authors suggest that "most infections were substantial" but base this observation on the longer average hospital stay among patients with infections. A single outlier could produce this result, and there are a number of other causes for prolonged hospital stays. The actual data would be more helpful.

A second difficulty is the intention-to-treat approach to the data analysis. We are told only that patients treated without warming blankets had more wound infections. We are not told whether the intraoperative temperatures of patients who went on to have infections were actually lower.

A still more troubling problem is the small number of patients in this study. If two more wound infections had occurred in the experimental (warmed) group, the P value in Fisher's exact test would have climbed to insignificance. The sweeping changes in surgical practice that would result from accepting the conclusions of this article should be based on more than two possibly clinically insignificant wound infections.

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To the Editor: Kurz and colleagues admit that the overall incidence of infection (12 percent) was "35 percent higher than in previous reports." In fact, the 6 percent infection rate in the normothermia group is similar to the average of 5.4 percent among patients who undergo colon operations and receive a single dose of antibiotics as prophylaxis.[1] The 19 percent infection rate in the hypothermia group is obviously excessive, if we assume that patients in the real world are not warmed to the extent that patients in the normothermia group were. It is hard to accept the authors' statement that they considered "all wounds draining pus that [yielded] a positive culture to be infected, although some may have been of minor clinical importance." In fact, their criteria for diagnosing wound infection were very strict, since a finding of pus containing bacteria always indicates infection. Should the authors adopt less stringent criteria, such as those used by others[2] their infection rate could be even higher.

The authors state that antibiotics were started during the induction of anesthesia and that "this treatment was maintained for about four days postoperatively." In Table 1 of their article, such administration is termed "prophylactic." It is obvious that the authors have confused the concepts of prophylaxis against and treatment of surgical infection. According to the state of the art, the prophylactic administration of antibiotics in patients undergoing elective surgery is limited to the perioperative period and may amount to "single-shot" therapy [3] Instead, by definition, prolonged postoperative administration, as practiced in this study, cannot be considered prophylactic and is

indicated only as a treatment for patients with established infection. Moreover, the notion that excessive antibiotic therapy could interfere with normal wound healing has been indirectly supported by studies showing a higher rate of postoperative infection among patients receiving inappropriate (i.e., excessive) antibiotic prophylaxis.[1]

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To the Editor: Kurz et al. report in a prospective, doubleblind, randomized study of 200 patients who were undergoing colorectal surgery that mild perioperative hypothermia delayed wound healing, predisposed patients to operative-site infections, and prolonged hospitalization. We caution that the findings may not apply to all surgical procedures. This may be particularly true of procedures in which the base-line incidence of infection is much lower than that seen with clean-contaminated procedures, for which the hospital stay is markedly shorter and for which hypothermia has been safely used.)

In a case-control study comparing the degree of perioperative hypothermia in 25 patients with craniotomy wound infections with that in 47 age-matched, noninfected controls[1] we found no difference in the degree of hypothermia between the two groups. Furthermore, no differences in the length of stay or time of suture removal were noted (unpublished data). Although this was a retrospective case-control study, power analysis predicted that more than 1000 patients would be required to complete a prospective trial. Such a trial would definitely answer whether hypothermia increases the incidence of wound infections and the length of stay in this population, but it would be problematic, since the normothermia cohort would be denied the well-documented cerebroprotective effects of perioperative hypothermia[2,3]

Currently, there are no data demonstrating that hypothermia has any deleterious effects in patients undergoing craniotomy. Without such data, mild perioperative hypothermia should continue to be used in patients at risk for cerebral injury during craniotomy.

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The authors reply:

To the Editor: Benzer, Sparr, and Kempen question the ethical basis for our study, apparently believing that patients were actively cooled. To maintain blinding, the blower inflating the forced-air cover over the unwarmed patients was set to ambient temperature. After passing over the fan motor housing, however, the ambient air temperature increased from approximately 22°C to approximately 26°C. Measured systemic heat loss with forced air at this temperature only slightly exceeds the loss from insulation with surgical draping (71±4 vs. 68±1 W). This trivial difference decreases mean body temperature by only 0.05°C per hour.

Benzer and Sparr confuse hypothesis with proof: suggestive results in small-animal trials do not obviate the need for clinical studies. Our study and another conducted concurrently" are the only randomized trials demonstrating adverse outcomes associated with mild hypothermia. Despite the assertion of Benzer and Sparr, maintaining normothermia has not been the standard of care [2,3]—largely because outcome data were lacking. Our protocol, comparing routine care with extra warming, was thus ethical and appropriate.

Benzer and Sparr apparently miss the point that hypothermia is comparable in all large operations, hence our citation of Frank et al[4] Nearly all unwarmed patients who undergo major surgery lose sufficient heat to decrease their core temperature to approximately 34.5°C; thermoregulatory vasoconstriction, which causes a core-temperature plateau[5] prevents additional hypothermia. Carli et al.[3] identified 34.5°C as the average postoperative temperature in patients undergoing colon surgery—a value virtually identical to that in our unwarmed patients.

Kempen's assertion that we failed to report ambient temperatures is curious: the values (approximately 22°C) were listed in Table 1 of our paper. He also asks whether the surgeons were blinded. We stated repeatedly that the surgeons in our study were formally blinded to (not simply unaware of) the patients' thermal care. But in any case, wound infections were not evaluated by the operative surgeons. Instead, wounds were evaluated by physicians who first saw patients the morning after surgery. Kempen's cited references [6,7] do not support the statement to which they are linked; we wrote these papers, and our conclusions were very nearly the opposite of what Kempen asserts. In the first study, blankets alone decreased heat loss only 30 percent, which is insufficient to maintain normothermia in most patients. The second study showed that effective prewarming required increasing the body-heat content by 50 to 200 kcal—an amount that can be achieved only by active warming.

Osler et al. ask whether the infected patients had lower temperatures than those without infection. They did: 35±1°C vs. 35.8±1.1°C (P<0.001). Furthermore, the infections were clinically important, and they significantly delayed discharge; nonparametric analysis indicated that prolonged hospitalization was not simply a statistical artifact (Table 1).

We disagree that the study size was inadequate. The results were statistically significant after 200 patients were enrolled (P<0.01), and the study was stopped at that point according to prospective criteria.

The infection rate in our patients was high, but only 35 percent higher than expected on the basis of a study of more than 84,000 patients[8] The expected rate was greater than

Schein et al. might anticipate because our university based population had a substantial degree of underlying disease and required long operations. Both of these factors markedly increase the risk of infection.[3] We agree that the duration of prophylactic antibiotic administration should be restricted. Although we requested a two-day treatment, the surgeons routinely administered antibiotics for longer periods, even in uninfected patients. However, neither the relatively high infection rate nor the suboptimal use of prophylactic antibiotics diminishes our finding that the infection rate was tripled in the hypothermia group.

TABLE 1. DURATION OF HOSPITALIZATION AMONG INFECTED AND UNINFECTED PATIENTS. ~

DURATION OF HOSPITALIZATION	INFECTED PATIENTS	UNINFECTED PATIENTS
	<i>days</i>	
Median	15.5	12
Maximum	50	44
Highest quartile	28	14
Lowest quartile	12.3	10
Minimum	7	6

*The duration of hospitalization differed significantly between infected and uninfected patients (P<0.001 by the Wilcoxon signed-rank test).

We agree with Winfree et al. The risk of infection after neurosurgery is so low that even a threefold increase would be hard to detect statistically. The induction of mild therapeutic hypothermia for protection against cerebral ischemia thus remains appropriate in patients who undergo neurosurgery.

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