Rewarming and Sweating During Cardiopulmonary Bypass

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The hypothesis was tested that facial sweating at the end of cardiopulmonary bypass (CPB) is a thermoregulatory phenomenon. Twenty-two patients undergoing cardiac surgery with fentanyl anesthesia were studied. Nasopharyngeal temperature, nasal skin temperature, rectal temperature, and mean skin temperature were monitored for 90 minutes after the start of rewarming on CPB. Calf-toe and forehead-nose skin temperature gradients were followed as a measure of peripheral and facial thermoregulatory vasoactive responses. Facial sweating was defined as grade 1 (noticeable) or grade 2 (obvious droplets). Fourteen patients (64%) sweated during rewarming at the end of CPB. In 11 cases the onset of sweating was preceded by a dramatic increase in nasal skin temperature (mean ± SEM, 4.6 ± 0.3°C in 5 min), suggesting facial vasodilatation. The maximum rate of increase (°C/5 min) in nasal skin temperature was significantly greater in patients who sweated than in those who did not, 4.1 ± 0.4°C versus 2.6 ± 0.3°C (P < 0.015). There was no difference in the age, weight, or RSA between patients who sweated during CPB and those who did not. The nasopharyngeal temperature threshold for the onset of sweating was not elevated (grade 1, 36.4 ± 0.5°C; grade 2, 37.6 ± 0.4°C), but there was a 5 to 6°C interpatient variation. It was concluded that facial sweating during rewarming on CPB is typical of a thermoregulatory response. Absence of sweating in one third of patients may be due to pharmacokinetic or pharmacodynamic differences in the response to anesthesia. Sweating threshold was not elevated from normal during fentanyl anesthesia, but rapid core rewarming on CPB represents a nonphysiologic thermal event that is quite distinct from external cutaneous warming.

KEY WORDS: temperature, thermoregulation, sweating, surgery

DURING HYPOTHERMIC cardiopulmonary bypass (CPB), rapid changes in body core temperature are provided by convectional heat exchange with the total blood volume, which perfuses the extracorporeal circuit. Rewarming of the body core toward the end of CPB commonly causes facial sweating that may be considered a sign of inadequate anesthesia. The relationship of sweating at the end of CPB to core temperature and peripheral vasodilatation has not previously been characterized.

Anesthetic agents disturb normal homeothermic physiologic responses. Volatile or opioid-based anesthetics delay the onset of vasoconstriction in response to hypothermia and depress the core temperature threshold triggering vasoconstriction approximately 2.5°C.1-2 Inadvertent hyperthermia was a well-known problem in the operating room before the advent of air conditioning,3 and remains a problem in some tropical countries. Isoflurane anesthesia elevates the core temperature threshold that triggers intraoperative sweating.5,6 Sweating is very closely associated with active cutaneous vasodilatation, which can be identified by a sudden increase in skin temperature. This study was designed to test the hypothesis that facial sweating during rewarming on CPB is consistent with thermoregulatory sweating in that it is closely associated with cutaneous vasodilatation and an acute increase in skin temperature.

METHODS

The study protocol was approved by the institutional review board at the Durham Veterans' Affairs Medical Center. Adult patients scheduled to undergo cardiac surgery with hypothermic CPB were visited preoperatively and written informed consent was obtained. Patients undergoing reoperation, those with symptoms of severe congestive heart failure, chronic obstructive pulmonary disease, or other severe systemic disease, and those with symptomatic peripheral vascular disease or absent pedal pulses on preoperative physical examination were excluded.

The patients were premedicated orally with lorazepam (4 to 6 mg), and anesthesia was induced with intravenous fentanyl (20 to 30 µg/kg), midazolam (2 to 10 mg), and either vecuronium (0.1 mg/kg) or pancuronium (0.1 mg/kg). Anesthesia was maintained by a continuous infusion of fentanyl (0.05 to 0.15 µg/kg/min) supplemented by midazolam (1 to 2 mg) and vecuronium (4 to 10 mg) as needed. Atropine or other anticholinergic medications were not administered. Core temperature was monitored at the nasopharynx. The intermediate thermal zone was monitored using a rectal thermocouple. The rectal site was chosen in preference to the bladder because the latter fluctuates as a function of urine flow.7 The peripheral thermal zone was monitored by skin-surface temperature sensors (Mon-a-Therm, St Louis, MO) placed on the right shoulder and arm, and left thigh and calf. Mean skin temperature was calculated by the method of Ramanathan: mean skin temperature = [0.3 (shoulder + arm) + 0.2 (thigh + calf)].8 Thermocouples were also placed on the left toe, the forehead, and tip of the nose (nasal skin). Temperature gradients exceeding 4°C between the calf and the toe, or the forehead and the nasal tip, indicate significant peripheral vasoconstriction.9,10

All temperatures were recorded at 5-minute intervals for a total of 90 minutes, starting at the onset of rewarming on CPB and continuing through separation from CPB. During and after rewarming, the forehead was inspected at 5-minute intervals for the presence of sweating. Sweating was qualitatively graded by the same observer as 0 (no moisture), 1 (some moisture) or 2 (distinct beads of sweat). The forehead was dried with a gauze sponge after each evaluation. The relationship of sweating to rewarming of the core, intermediate, and peripheral thermal zones during CPB was studied. Association was sought between the onset of facial sweating and a sudden increase in nasal skin temperature to indicate local cutaneous vasodilatation. Cutaneous vasodilator responses in the face and leg were examined by measuring the forehead-nasal tip and calf-toe temperature gradients during and

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after warming on CPB. To determine the core triggering threshold for sweating, the temporal relationship between nasopharyngeal temperature and the onset and degree of sweating was noted.

Statistical methods used included ANOVA with Fisher PLSD and $\chi^2$ analysis with the Yate's correction. Results are reported as means ± SEM; a probability value less than 5% was considered significant.

RESULTS

Twenty-five patients were studied. Data from three patients were dropped from analysis; 1 because sweating occurred throughout CPB, and 2 because a temperature probe failed. Surgical procedures consisted of coronary revascularization (17 patients), aortic valve replacement (1 patient), mitral valve replacement (2 patients) and combined aortic valve replacement and coronary revascularization (2 patients).

Mean values for nasopharyngeal, nasal skin, rectal, and mean skin temperature during rewarming on CPB are illustrated in Fig 1. During rewarming, nasopharyngeal temperature climbed rapidly to a peak of 37.9 ± 0.2°C at 50 minutes, followed by an afterdrop of 1.8°C by 90 minutes (Table 1). Nasal skin temperature followed the same pattern, but peaked 5 minutes earlier and about 1.3°C lower, subsequently also decreasing by 1.8°C by 90 minutes. Rectal temperature started at a higher level, increased more slowly, and did not reach a peak until 65 minutes. By 90 minutes it had decreased only 0.3°C, and exceeded nasal skin temperature. Mean skin temperature was close to rectal temperature at the start of rewarming, declined slightly after 15 minutes of rewarming, and then very slowly increased. At 90 minutes, it was still increasing toward nasal skin temperature.

Fourteen patients (64%) sweated during rewarming; in 12 of them (86%), sweating reached grade 2 intensity. Eight patients did not sweat. When patients who did or did not sweat were compared, there were no differences in the age, weight, or body surface area (Table 2) or in nasopharyngeal, nasal skin, rectal, or mean skin temperature (Fig 2). In 11 of the 14 patients who sweated, there was a sudden, rapid increase in nasal skin temperature of between 3.4 and 6.4°C (4.6 ± 0.3°C) during the 5-minute period before the onset of sweating. Representative data from one patient are presented in Fig 3. In the remaining 3 patients, nasal skin temperature increased more slowly. The rapid increase in nasal skin temperature was followed by grade 1 sweating 7.1 ± 2.3 minutes later, and grade 2 sweating in 16.3 ± 3.3 minutes.

The rate of increase in nasal skin temperature during rewarming on CPB was compared between patients who sweated and those who did not (Fig 4). Data are provided on a time axis of 25 minutes, centered on the 5-minute epoch with the greatest net increase in temperature. In patients who sweated, the maximum rate of increase in nasal skin temperature was significantly greater in patients who sweated than in those who did not, 4.1 ± 0.4°C versus 2.6 ± 0.3°C ($P = 0.0125$).

The thresholds for the onset and offset of sweating are listed in Table 3. The threshold for grade 1 sweating as defined by the nasopharyngeal temperature was 36.4 ± 0.5°C, with a very wide interpatient range (31.9 to 38.3°C). The threshold for the onset of grade 2 sweating was 37.6 ± 0.4°C with a range of 34.0 to 39.0°C. Sweating ceased at an nasopharyngeal temperature of 37.5 ± 0.2°C, ie, there was no significant hysteresis. The onset of sweating was noted 31.4 ± 3.1 minutes after the start of rewarming on CPB.

### Table 1. Pattern of Rewarming on CPB

<table>
<thead>
<tr>
<th>Time to</th>
<th>Start</th>
<th>Peak</th>
<th>End 90 Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPT</td>
<td>27.8 ± 0.4°C</td>
<td>37.9 ± 0.2°C</td>
<td>50 min</td>
</tr>
<tr>
<td>NST</td>
<td>26.9 ± 0.4°C</td>
<td>36.4 ± 0.3°C</td>
<td>45 min</td>
</tr>
<tr>
<td>RT</td>
<td>30.0 ± 0.5°C</td>
<td>37.0 ± 0.2°C</td>
<td>60 min</td>
</tr>
<tr>
<td>MST</td>
<td>30.4 ± 0.3°C</td>
<td>33.3 ± 0.2°C</td>
<td>90 min</td>
</tr>
</tbody>
</table>

Abbreviations: NPT, nasopharyngeal temperature; NST, nasal skin temperature; RT, rectal temperature; MST, mean skin temperature; Start, start of rewarming on CPB; Peak, peak temperature reached; End 90 min, temperature at end of study.

### Table 2. Demographic Data

<table>
<thead>
<tr>
<th></th>
<th>Sweating</th>
<th>No Sweating</th>
<th>NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.3 ± 1.7</td>
<td>61.8 ± 3.4</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>83.4 ± 3.6</td>
<td>82.9 ± 6.2</td>
<td>NS</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>2.00 ± 0.05</td>
<td>1.97 ± 0.06</td>
<td>NS</td>
</tr>
</tbody>
</table>

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**Fig 1.** Mean temperatures in °C for all 22 patients during rewarming. Zero time represents the onset of rewarming on cardiopulmonary bypass (CPB). (1) There is a rapid, 9°C increase in nasopharyngeal core temperature over 5 minutes. Nasal skin temperature changes similarly, but about 1.3°C lower. Rectal temperature, (intermediate compartment) starts at a higher level, increases more slowly, and is still increasing after nasopharyngeal temperature has peaked on separation from CPB (2). Nasopharyngeal temperature demonstrates afterdrop as heat moves from the core to intermediate compartments (3), and ultimately equilibrates with rectal temperature (4). Mean skin temperature (peripheral compartment) starts to increase only after core and intermediate compartments are almost completely rewarmed, and is still slowly increasing at 90 minutes. Abbreviations: NPT, nasopharyngeal; NST, nasal skin; RT, rectal; MST, mean skin temperature.
Rewarming and Sweating During CPB

**Fig 2.** Temperature changes: Sweating versus nonsweating patients. Temperature changes in patients with sweating (n) versus patients with no sweating (q). All values are expressed as mean ± SEM. No differences were statistically significant. Abbreviations: NPT, nasopharyngeal temperature; NST, nasal skin temperature; RT, rectal temperature; MST, mean skin temperature.

(To be continued)

Subsequent vasodilation during rewarming was very variable. In 10 patients the calf-toe gradient remained greater than 4°C. In 6 of the 12 patients who did develop cutaneous vasodilation in the leg, the gradient decreased well after core rewarming was completed (nasopharyngeal temperature > 36°C). In only 6 out of 22 patients did leg cutaneous vasodilation occur at an early stage of rewarming (nasopharyngeal temperature < 34°C). There was no correlation between cutaneous vasodilation in the leg and the presence or absence of forehead sweating ($\chi^2$ 1.02, $P = 0.3$).

**Fig 3.** This figure illustrates the relationship of temperature changes to sweating in an individual patient (#4). The pulmonary artery temperature reflects the temperature of the blood entering the heart from the extracorporeal circuit, and precedes all other changes. There is a dramatic increase in nasal skin temperature (5°C in 5 min), presumably reflecting cutaneous vasodilation shortly before the onset of sweating. Sweating commences at a nasopharyngeal temperature of 36.8°C and ceases shortly after it starts to decline from its peak of 38.7°C to 38.3°C, right at the time the patient is separated from CPB (arrow). Nasal skin temperature declines rapidly with afterdrop and actually equilibrates with mean skin temperature after 80 minutes. Abbreviations: NPT, nasopharyngeal; NST, nasal skin; RT, rectal; MST, mean skin temperature; PAT, pulmonary artery temperature.
DISCUSSION

Normally, core temperature is maintained within very narrow limits. The interthreshold range or null zone, in which changes in core temperature do not trigger thermoregulatory responses, is typically less than 0.6°C.1,12 Anesthetic agents depress the thresholds for vasoconstriction and shivering, and simultaneously elevate the threshold for sweating, increasing the interthreshold range to about 4°C.1,2,5

Sweat production by the eccrine glands is mediated by postganglionic cholinergic sympathetic fibers, and is blocked by atropine or sympathectomy.13 It provides extraordinarily efficient cooling by evaporation, and can increase heat loss 10-fold.14 The stimulus for sweating is provided by elevated core and skin temperature, and once the threshold is exceeded there is a very steep gain in the rate of sweat production. The sweating threshold is modified by input from the skin: cool skin delays the onset of sweating.15 Active sympathetic vasodilation is closely linked to sweating.16 The onset times of vasodilation and sweating are nearly simultaneous, and it has been postulated that a mediator released from the eccrine sweat glands stimulates vasodilation. Cutaneous thermoregulation is provided by arteriovenous (AV) shunts, which have 10 times the diameter and one ten thousandth the resistance of capillaries. Shunt flow appears to be centrally regulated through sympathetic α-2 adrenergic vasoconstriction, which is inhibited by high temperatures.17 AV shunts provide a tremendous capacity for thermal regulation. In hyperthermia skin blood flow can increase from 5% to 60% of total cardiac output and reach flow rates of 7 to 8 L/min.18

Skin blood flow is the major determinant of skin temperature. AV shunts are plentiful in acral regions, and cold-induced vasoconstriction decreases finger blood flow more than 10-fold,10 and decreases fingertip temperature by more than 10°C.9 The establishment of temperature gradients of more than 4°C between forearm and fingertip, calf and toe, and forehead and nasal tip have correlated with significant peripheral vasoconstriction.1,3,19 Consequently, skin temperatures and gradients were used to correlate sweating and vasodilation during CPB.

Clinical observation during rapid rewarming during CPB often reveals facial sweating, as it did in 65% of the study patients. Sweating may be interpreted as a sign of sympathetic response to inadequate anesthesia, in keeping with the assumption that anesthetic agents are eliminated more quickly as patients rewarm and that anesthetic requirements increase. However, it was found that when sweating occurred at the end of CPB it appeared to be part of an orderly progression of thermoregulatory responses. Shortly after rewarming was started, nasal skin temperature increased dramatically and was followed shortly by the onset of facial sweating in the majority of patients. The skin of the face and head participates very actively in the thermoregulatory response to rewarming on CPB, presumably because it is close to the high temperature of the core, and the directed jet of warm blood up the aortic arch and cerebral vessels from the aortic cannula. Because of the insulation of surgical drapes, it was possible to directly observe whether sweating occurred elsewhere in the body. However, the dramatic increase in nasal skin temperature that preceded facial sweating was not noted at any of the other skin sites monitored (shoulder, trunk, thigh, calf, toe). Mean skin temperature did increase with rewarming, but more slowly and to a lesser degree than the skin of the face, and did not appear to participate directly in the immediate response to blood rewarming.
Nasopharyngeal and nasal tip skin temperature reached a peak and started to decline even before separation from CPB, probably reflecting vasodilation-induced redistribution of heat from the warm core to the cool periphery. At the end of the 90-minute study period, equilibration had occurred between the nasopharyngeal and rectal temperature, and nasal skin and mean skin temperature. It appears that rewarming at the end of CPB most immediately affects the head, so that the face demonstrates the most overt thermoregulatory response (vasodilation and sweating). This may explain why total body warming is incomplete on CPB, resulting in afterdrop and residual mild hyperthermia, which persists into the postoperative period. Subsequently, full rewarming in the intensive care unit may be associated with severe shivering, resulting in hypercarbia and venous desaturation, and ultimately leads to vasodilation and hemodynamic instability.

The esophageal temperature threshold for grade 2 sweating was elevated to 38.3 ± 0.3°C in patients undergoing general anesthesia with isoflurane, when hyperthermia was induced by warming the skin with forced-air convection blankets. In this study the nasopharyngeal temperature threshold for the onset of sweating appeared nearly normal. Detectable sweating (grade 1) started at 36.4 ± 0.5°C and more profuse sweating (grade 2) at 37.6 ± 0.4°C. This disparity is probably accounted for in these patients because heat was applied internally to the central blood compartiment by convection exchange in the extracorporeal circuit, and the skin remained cool. The temperature of the blood bathing the hypothalamus must have risen extremely rapidly—in two patients, the nasopharyngeal temperature increased by more than 2.0°C in the 5 minutes prior to the onset of sweating. This could account for a sweating response at a lower core temperature. The threshold for the onset of sweating in this study demonstrated a very wide interpatient range (6.4°C for grade 1, 5.0°C for grade 2), presumably reflecting the dramatic fluctuations in blood temperature. It is unlikely that small delays in detecting sweating produced large errors, because this would have artifactually elevated the threshold. It could be concluded that rapid core warming during CPB is a nonphysiologic thermoregulatory stress, and represents a situation very different from moderate external warming.

It is not clear why 35% of the patients did not sweat. It could be due to differences in the afferent pathway (skin temperature), hypothalamus (sweating threshold) or efferent pathway (sympathetic response). During CPB afferent input from the skin is probably overwhelmed by central input from the blood, and no difference could be found in mean skin temperature between patients who sweated and those who did not. Washington et al found that the sweating threshold is elevated more in women than men, and attributed this to their significantly smaller lean body mass. All the patients were male, and neither age nor body morphology appeared to be a factor. It is possible that there are individual variations in the intrinsic physiologic response to rewarming, suggested by the more rapid rate of increase in nasal skin temperature in patients who sweated. Thermoregulatory responses during CPB were not correlated with those occurring after surgery, and it was not identified whether patients who sweated were more likely to shiver in the intensive care unit.

It is conceivable that differences in sweating resulted from pharmacokinetic and/or pharmacodynamic variations in response to anesthesia, in that patients who did not sweat were more deeply anesthetized. During external warming, the elevation of the sweating threshold is a linear function of end-tidal isoflurane concentration (37.6 ± 0.2°C at 0.8%, 38.1 ± 0.1°C at 1.2%), although the gain and maximal sweating rate remain nearly normal. Plasma drug levels were not measured, nor was electroencephalography used to estimate depth of anesthesia during CPB. However, none of the patients reported any recall of the procedure. It is possible that isoflurane and fentanyl have different effects on the sweating threshold. However, the depression in vasoconstriction threshold is similar between volatile agents and opioids, as is the pattern of temperature during cardiac surgery.

This study illustrates the differences in developed temperature gradients when heat is exchanged primarily via the blood rather than through the skin. During external cooling, the nasal skin is colder than that of the forehead because of the preponderance of thermoregulatory AV shunts in acral parts. In the patients on CPB no gradient was present between the forehead and nose, presumably because the face is so close to the core during central cooling and rewarming. Although a large temperature gradient reflecting cutaneous vasoconstriction was present between the calf and toe in all patients at the start of rewarming on CPB, subsequent vasoconstriction occurred in only 55% of the patients, and in half of these it took place only after completion of core rewarming. Gradients between the forearm and finger tip were not measured because the arms were tightly tucked during surgery. Nonetheless, the findings suggest that the thermoregulatory response to rapid core warming on CPB is preponderant in the face and head relative to the body periphery, most likely reflecting the rapid infusion of heated blood into the aortic arch and cerebral circulation.

It was concluded that sweating during rewarming on CPB is consistent with a thermoregulatory response in that it closely follows a dramatic increase in nasopharyngeal and nasal skin temperature. About two thirds of patients sweated, and they had a more rapid rate of increase in nasal skin temperature than those who did not. The mean threshold for the onset of sweating was not elevated compared with unanesthetised individuals, but there was an extremely wide variation probably due to the nonphysiologic nature of the thermal stress of core rewarming. The thermoregulatory response to rewarming on CPB appears to be predominant in the face and head. This may help explain the observation that total body warming is incomplete when the patient separates from CPB, resulting in afterdrop and persistent mild hypothermia at the end of surgery.
REFERENCES