Sensing Cold and Producing Heat

The defense of thermoneutrality is an important physiologic function in homeothermic mammals. The guarding mechanisms are vasoconstriction to reduce heat loss and shivering and nonshivering thermogenesis to increase heat production. If, during a survival course in an arctic climate, the deep body temperature drops by 2°C, it indicates a failure not only of facultative (compensatory) but also obligatory (basal) thermogenesis. The person participating in the course will immediately be told to interrupt and move into a warm environment. During anesthesia administration, the guards have changed position. Temperature control functions have been reset—or, are they abolished? A decline in core body temperature of 2 or 3°C does not, as in the survival course, result in a termination of ongoing anesthetic or surgical procedures. Does this mean that we are carelessly operating in dangerous temperature territory? Can we allow a 2 or 3°C drop in deep body temperature without narrowing the margins of safety for our patients?

In this issue of Anesthesiology, some effects of mild hypothermia were studied by Plattner et al. They found that endogenous catecholamine response and nonshivering thermogenesis were abolished by fentanyl and propofol anesthesia and that vasoconstriction, to prevent heat loss, was initiated at a higher temperature in infants than in older children. The effects on nonshivering thermogenesis confirm earlier findings in infants anesthetized with halothane, but it also takes us further. Plattner et al. have focused their study on anesthetized infants because neonates and infants are equipped with an active, specialized, thermoregulatory tissue, the brown adipose tissue (BAT). It is not their findings of an early initiation of vasoconstriction in response to a mild hypothermia that surprises most. It is not even that two of the studied infants (numbers 4 and 5) had low O_2 consumption (<4 ml·min⁻¹·kg⁻¹) that is of concern. It is the absent catecholamine response and the nonexistent compensation via nonshivering thermogenesis that shocks the horn. After all, infants have their specialized BAT capable of an effective heat production that should have been active, even during anesthesia, to protect them from hypothermia.

The main scientific problem is to determine why this important compensatory temperature function is eliminated in infants, even at light levels of anesthesia. Is this loss of a valuable physiologic defense mechanism caused by anesthetic effects on central thermoregulatory functions, peripheral tissues, or both? Because catecholamine release in cold stress is a reflection of activity in the sympathetic nervous system, which also is involved in the control of the peripheral vascular tone, a lack of catecholamine response ought to have been paralleled by a slow vasoconstrictor response. This was not what Plattner et al. found. The discrepancy between vasoconstriction and the endocrine stress response indicates that the vasoconstrictor response most probably is mediated locally or via spinal reflexes.

There now are interesting new data on regulation of the peripheral vascular system. Specifically, there are two different flow systems, nutritive and nonnutritive, and different vasoconstrictors can direct flow into one or the other. It was recently found, in experimental studies, that one group of vasoconstrictors (low-dose norepinephrine < 1 μM, vasoressin, and angiotensin II) increase skeletal muscle heat production, whereas another group (serotonin, high-dose norepinephrine) had the opposite effect. How the two peripheral vascular systems are controlled and interact is not known, and it will be of great interest to follow the development of this research frontier. It will be even more interesting to learn about the mechanisms behind the increased heat production in skeletal muscle produced by certain vasoconstrictors because heat production did not increase via shivering but from nonshivering thermogenesis. Also, it has recently been found that general anesthesia increases heat production in skeletal muscle by a factor of five compared with in patients in the awake state, provided that amino acids are infused either before or during anesthesia and surgery; a thermogenesis also claimed to be the result of nonshivering thermogenesis in the skeletal

Accepted for publication January 16, 1997.
EDITORIAL VIEWS

muscle. At least one explanation for this could be a reduction of descending inhibitory impulses from central thermoregulatory areas caused by anesthesia. A support for this hypothesis is the observation that the thermogenetic effect of orally ingested proteins increases in tetraplegic patients.

The basic mechanisms behind this non-BAT nonshivering thermogenesis in skeletal muscle are not fully understood. There may be, at the mitochondrial level, an uncoupling mechanism similar to the one in BAT wherein an uncoupling protein, thermogenin, short-circuits ADP phosphorylation via interference with the proton transport over the mitochondrial membrane. Theoretically, however, any increased mitochondrial proton permeability will increase the mitochondrial membrane potential and consequently enhance heat production.

There is obviously a lot more to be learned about thermoregulatory control mechanisms in anesthetized humans. From the previous, it can be stated that anesthetic effects on temperature balance result from influences on central and peripheral mechanisms. The paper by Plattner et al. certainly contributes to a better understanding of these complex functions. Further, the opening of two new areas of thermoregulatory research—nonshivering thermogenesis in skeletal muscle and improved generation of heat from amino acids during anesthesia—will most certainly shed more light on this field.

Until then, we know that the neuroendocrine response to mild hypothermia, as reflected by catecholamines in plasma, is absent during anesthesia and that nonshivering thermogenesis in BAT does not protect from mild hypothermia in anesthetized infants.

Sten G.E. Lindahl, M.D., Ph.D. F.R.C.A.
Professor & Chair
Department of Anesthesiology & Intensive Care
Karolinsky Hospital & Institute
S-171 76 Stockholm
Sweden
E-mail: sten.lindahl@kirurgi.ki.se

References