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Temperature Regulation in Preterm Infants: Role of the Skin-Environment Interface

Shaul Dollberg, MD,* and Steven B. Hoath, MD †

Objectives After completing this article, readers should be able to:

1. Define the thermal neutral zone and differences in it among preterm infants, older children, and adults.
2. List the four modes of heat loss and the most important mode in the very low-birthweight preterm infant.
3. Explain the reason for the extraordinarily high transepidermal water loss seen in very low-birthweight preterm infants.
4. Characterize the differences in heater power output from a radiant warmer related to location of a skin surface thermistor.
5. Describe the primary modes of providing an appropriate thermal environment for the very low-birthweight infant and the associated differences in incubator servocontrols.

Introduction
An understanding of the mechanisms of homeothermic adaptation in the newborn and application of this knowledge to thermal support of sick and preterm infants is one of the foundation stones of modern neonatal medicine. Body temperature regulation following birth involves a complex interplay of sensorimotor feedback from the skin, neural, and endocrine mechanisms for controlling metabolic heat regulation and the active intervention of caregivers to maintain a neutral thermal environment. (1)(2) This review focuses narrowly on physical and biologic effects at the interface between the body surface and the environment related to the control of temperature in the newborn. Mechanisms of central (hypothalamic) temperature control and specialized means of metabolic heat production such as brown adipose tissue are beyond the scope of this article.

History and Basic Physiologic Principles
The recognition of the need to protect the very young against heat loss can be dated to at least ancient Egypt, where sophisticated methods of incubation were developed for hatching chicken eggs. These early methods were the forerunners of the convective incubators and radiant warmers that are currently used in neonatal medicine for controlled heat delivery to newborns.

The modern history of neonatal temperature control began in the late 19th century with the observation by Pierre Budin at the Paris Maternity Hospital that mortality rates decreased from 66% to 38% in infants whose birthweights were less than 2,000 g following introduction of temperature control measures (Fig. 1). In 1957, Silverman reported that the survival of preterm infants in the first days of life was higher when the relative humidity was maintained at 80% to 90%. During this study, it was noted that the mean body temperature of infants maintained in humidified environments was significantly higher than the mean body temperature of infants in incubators with lower relative humidity (30% to 60%). This observation led to the formulation of the normothermic hypothesis, which states that the survival of preterm infants is favorably influenced by environments that maintain normal body temperature. (3)

In particular, very low-birthweight (VLBW) preterm infants are ill-equipped to make...
the transition to a cold external environment at birth and are prone to cold stress, metabolic acidosis, and the development of hypothermia. Low body temperature is inversely related to survival, and every effort must be made to maintain infants within their thermoneutral zone (TNZ) (Fig. 2). The TNZ represents the environmental temperature range within which an infant has a normal body temperature and a minimal basal metabolic rate. The TNZ varies with chronologic age and spans a lower temperature range in adults (25°C to 30°C) than in term infants (32°C to 34°C).

Preterm infants exhibit an elevated, narrow, and changing TNZ during the first few days following birth. Infants cared for outside their TNZ exhibit slower growth rates than infants who have the same caloric intake maintained within their appropriate zone. Recognition of the importance of this concept led to the establishment of Scopes charts for preterm infants. Ideally, maintenance of the TNZ in thermoregulated infants reduces the need to direct calories away from growth and differentiation to heat-producing metabolic activity and obviates the need to rewarm infants who become hypothermic. (4)

Physics of Heat Transfer
Like any physical object, the newborn infant, whether term or preterm, loses heat to the environment by four different modes.

Conduction
Conduction is defined as the transfer of energy from the molecules of a body to the molecules of a solid object in contact with that body. In newborn intensive care units, infants usually recline on a flat mattress with approximately 10% of their body surface area in contact with the mattress (Fig. 3). The heat flow through the mattress by thermal conduction is given by the following relation:

$$H = kA \frac{dT}{dx}$$
where

\[ H = \text{heat flow}, \]

\[ k = \text{a thermal conductivity constant for the particular mattress and its coverings}, \]

\[ A = \text{the conductive area through which the heat flows}, \]

\[ \frac{dT}{dx} = \text{the change in temperature per unit distance through the solid mattress}. \]

A commonly used 2.5 cm-thick mattress (closed-pore foam rubber type) has a thermal conductivity of approximately 0.9 watt/m² per degree centigrade. An approximation of conductive heat loss calculated on total resting heat production of 1.7 watts/kg shows that only about 0.5% is conducted through the mattress or 0.012 watt/°C for a 1,500 g infant. Thus, conductive heat losses are generally regarded as minimal in usual infant care situations.

**Convection**

Convection is the transfer of thermal energy from the molecules of the body to the molecules of an adjacent gas. This heated gas expands (Boyle’s law) and is displaced upwards by the force of gravity of the cooler and more dense surrounding gas. Such gas movement is called free convection. Away from the infant’s skin, air currents in the nursery or those produced by the incubator’s fan will result in turbulence and mixing of the hot gas with the surrounding air (forced convection) (Fig. 4). Convective heat losses in infants have been calculated to be between 3.1 watt/m² per degree Kelvin to 8.5 watt/m² per degree Kelvin or, in one study, approximately 40% to 50% of nonevaporative heat losses. The contribution of convective heat losses is related, among other variables, to the infant’s position (flexed or extended), body surface area, body weight, air temperature and currents in the nursery or in the incubator, and the maturity of the epidermal barrier. These factors act in combination and may result in marked differences in convective heat losses between infants.

**Evaporation**

Evaporation is defined as the total heat transfer by energy-carrying water molecules from the skin and respiratory tract to a drier environment (Fig. 5). Evaporation is affected by gestational age as well as postnatal age and by differences in the partial pressures of water vapor next to the skin and in the surrounding air. In the term infant and the older child, the outermost layer of the skin, the stratum corneum, serves as a barrier to evaporative heat loss unless covered with amniotic fluid following birth or after a bath. The skin of the newly born preterm infant who is less than 28 weeks’ gestation converts a surface of high evaporative heat loss due to immature formation of the stratum corneum. In addition to a poor epidermal barrier to water transport, the velocity of the air surrounding the skin has a large effect on evaporative heat losses in the preterm infant. In VLBW infants, during the...
first days of life, evaporative heat losses exceed all other sources of heat loss and often exceed total heat production.

**Radiation**

Radiant heat loss is defined as the net rate of heat loss in the form of electromagnetic waves between the body and environmental surfaces not in contact with the body (e.g., the walls of the incubator) (Fig. 6). Radiant heat loss depends on a number of factors, including the temperature of the skin, the relative surface area and geometry of the exposed body part, the distance and angles to irradiated objects (such as the incubator walls or nearby windows), the emissivity of the infant’s skin, and the emissivity of the irradiated objects. Based on studies in adults, emissivity is defined as the ratio of the total radiant energy emitted by a body to the energy emitted by a full radiator (maximal radiant output) at the same temperature. Typically, adult human skin is given the value of 1. There are no data regarding the emissivity of the skin of a preterm infant. In general, radiant heat loss is not dependent on the air temperature. Therefore, it is possible for an infant to be cold stressed despite an air temperature higher than skin temperature if the walls or windows are sufficiently cold. In contrast, an infant in an incubator that has a relatively cool air temperature may become hyperthermic if the walls are too hot.
Ro = resistance of thermistor, and 
\[ \frac{dRo}{dT} = \] the rate of change in resistance.

For temperature measurement, the resistance is measured over a resistance bridge where two resistances are known. Because the current will be inversely proportional to the resistance, it is easy to calculate the actual resistance of the thermistor. Another option is to measure the voltage against a known voltage source.

Other types of temperature sensors include thermocouples, liquid crystals, and infrared detectors. Thermocouples are durable, stable, inexpensive, and have fast response times, making them especially popular for research purposes. Liquid crystal and chemical strip indicators have been used for chromatic display of surface temperatures in newborns. Another technique based on infrared thermometry that has become widely available for home use is an ear canal temperature transducer. However, the accuracy, coefficient of variation, and general usefulness of this method in preterm and term infants has been questioned. Vernix in the ear canal may interfere with this mode of temperature measurement. Techniques using diodes and transistors, crystal resonators, and microwave radiometers have a variety of properties and accuracy levels but have not become commonplace for thermal management in clinical neonatology.

Recently, zero-heat flow thermometers have been investigated for noninvasive transcutaneous measurement of body temperature in preterm infants. These surface-based thermistor systems are based on the principle that, at steady state, any body that has an internal heat-producing component will have a continuous flow of heat to its surface as long as the surface is cooler than its internal component. Insulation of the surface thermistor will lead to zero heat flow between the core and the periphery, thereby allowing core temperature to be obtained from the skin. This principle forms the basis for axillary measurements of core body temperature using mercury-in-glass thermometers. Newer methods have been validated in newborn animal models and infants that allow continuous transcutaneous monitoring of core body temperature using well-insulated surface thermistors (Fig. 8). (5)

**Electrical Characteristics of the Thermistor**

Thermistors typically exhibit very steep resistance-temperature profiles compared with other sensors. This rapid change in resistance in response to small variations in temperature allows the use of a simple driving circuit that corrects for any nonlinearity of the relationship curve between temperature and resistance over the measured temperature range.

Clinically, it is often necessary to replace thermistors rapidly to correct a malfunction or to clean and sterilize them. Thermistors must be interchangeable with an error within the range of accuracy required for the measurement. An interchangeability tolerance of 0.2°C or less within the physiologic temperature range is acceptable for clinical practice.

Aging of thermistors results in a change in resistance-temperature characteristics over time that can be expressed as \( \frac{dR}{dt} \). Resistance usually increases with time and is dependent on individual manufacturing processes. Typical acceptable stability values are about 0.01°C over 100 days. Other factors to consider when designing or selecting a thermistor include the avoidance of self-heating of the thermistor element. Because a small current must be passed through the element to achieve resistance measurement, some ohmic heating will occur. The applied current, therefore, must be low enough not to increase thermistor temperature artifactually.

**Probe Location**

The surface of the body is in dynamic equilibrium with the environment. Visualization of the skin surface of newborns using noncontact methods (infrared telemetering) demonstrates that skin temperature distributions are not uniform. Surface temperatures are frequently higher over the abdominal cavity (eg, liver) and
interscapular area (brown fat) and lower over the vasoactive distal extremities. Consequently, placement of individual thermistors at distal sites (eg, arms or legs) will result in lower temperature readings, which may lead to increased heater output in servocontrolled incubators. Placement over bony structures may also lead to lower skin temperature readings, thereby causing inadvertent overheating. Conversely, location of thermistors over the brown fat area may result in higher measured skin temperatures with a secondary decrease in heater power output.

Various disease states may also change surface temperature distributions. In febrile patients, for example, cold feet are common, despite a high temperature at other body sites. This phenomenon reflects an increase in central temperature associated with peripheral vasoconstriction. In infants, the simultaneous measurement of skin temperatures over the abdomen and toe has been proposed as a diagnostic index of the temperature instability associated with sepsis. A “tummy-toe gradient” greater than expected (approximately 2°C) may indicate the presence of sepsis. In contrast, external overheating due to incubator malfunction, for example, would result in peripheral vasodilatation and the equilibration of central and peripheral temperatures.

Finally, physiologic temperatures may vary both laterally (along the skin surface) and vertically (from surface to core). In 1965, Adamsons and colleagues (6) studied the relationship between systemic oxygen consumption and rectal, skin, and environmental temperatures in term newborns subject to environmental cooling. Their results indicated a direct relationship between metabolism and the gradient between the skin and the environment (Fig. 9). Rectal (core) temperature was not predictive of metabolic rate (Fig. 10). This study supports the concept that the skin-environment temperature gradient in the immediate newborn period is directly regulatory of body metabolism; central mechanisms based on core temperature are less important.

**Sensor Microenvironment—Physical Factors**

The microenvironment of the thermistor may be very different from that of the surrounding skin. Commonly, an artificially high skin temperature will be recorded when the baby’s position is changed and the thermistor is sandwiched between the mattress and the skin. This can result in an inadvertent decrease in heater power output under conditions of skin servocontrol. Similar observations, but to a lesser degree, are noticed when the thermistor is covered with a diaper or with the baby’s hand.

Other factors affecting the thermistor microenvironment include how the thermistor is attached to the skin. Use of an insulated foam rubber disk (commonly used to shield thermistors from energy emitted by a radiant warmer) results in higher temperature readings compared with thermistors secured with noninsulated clear tape. (7)

The water content of the air may also affect skin temperature. A low relative humidity inside a convective incubator, for example, has been shown to decrease body temperature by 1°C. Contact pressure applied directly to the skin is linearly related to the temperature measured...
by the thermistor and varies according to body site. The size of the thermistor probe is a major determinant of its time constant. This factor may be important if rapid temperature readings are required. If an instantaneous change in temperature occurs, the time constant is defined as the time to reach the target temperature. The smaller the probe head, the shorter the time constant and, hence, the earlier that changes in body temperature will be detected.

Sensor Microenvironment—Biologic and Physiologic Factors
The thermal conductivity of the skin is directly related to cutaneous blood flow. Vasoconstriction of the periphery, e.g., the hands and feet, decreases the temperature of the limbs and is an important mechanism of heat conservation. This phenomenon underlies the common observation of acrocyanosis or blueness of the hands and feet in the newborn. Vasodilatation of the periphery has the opposite effect. A warm environment may trigger autonomic activation of eccrine sweat glands, with resultant cooling of the skin surface by evaporation.

For the newborn, evaporative heat loss may be disadvantageous during the immediate period following birth, and mechanisms appear to have evolved to protect the infant during this vulnerable period. During the latter part of gestation, for example, the fetus is covered with a product of sebaceous secretion called the vernix caseosa, which is both an electrical and possibly a thermal insulator. Recently, it has been proposed that the hydrophobic properties of vernix play a potentially important role in diminishing heat loss due to evaporation following birth. (8)

Protecting the Preterm Skin After Delivery
The skin of preterm infants is immature and ineffective as an epidermal barrier. In normal development, the stratum corneum, which is responsible for epidermal barrier function, does not become functionally mature until 32 to 34 weeks’ gestation. Acceleration of the maturation process occurs after birth in response to the dry environment. Transepidermal water loss is inversely related to gestational age. Transepidermal water loss may be 10 to 15 times greater in preterm infants of 25 weeks’ gestation compared with term infants. (9)(10)(11)(12) Poor epidermal barrier function leads to significant disturbances in temperature regulation and water balance. Even at 4 weeks of age, VLBW preterm infants have increased transepidermal water loss compared with term infants. (13)

Recently, Vohra et al (14) reported that placement of polyethylene wrap over the exposed skin surface effectively protects VLBW infants who are younger than 28 weeks’ gestation from a precipitous fall in rectal temperature. Significantly, there was also a reduction in overall mortality in the infants receiving the thermal wrap. This approach reduces evaporative heat loss while permitting radiative heat transfer. The study emphasizes the importance of coupling between the infant and the environment immediately after birth and highlights early intervention in the delivery room as the optimal time to initiate thermal support, particularly in VLBW preterm infants.

Maturation of Thermal Capabilities in Preterm Neonates
With convective incubation, most VLBW preterm infants initially need an environmental temperature that is higher than the exposed skin temperature to maintain normal core body temperatures. The relative immaturity of both the epidermal barrier and central mechanisms of heat production lead to a situation wherein heat losses exceed heat production. Over the days following birth, VLBW infants may be gradually weaned from higher environmental temperatures to a point where the air temperature is lower than their skin temperature. The postnatal age at which VLBW infants switch from an environmental temperature higher than their skin temperature to environmental temperatures lower than their skin temperature has been studied. (15) Not surprisingly, there is a close relationship to both gestational age (Fig. 11) and birthweight (Fig. 12).

The abrupt increase in thermal maturational capability of the preterm infant around 28 weeks’ gestation correlates with the diminution of transepidermal heat loss observed at this gestation point. Evaporative heat exchange is the most important mode of heat loss early after birth in very preterm infants. Of note, there was no difference between the time required to reach a skin temperature equal to or lower than the ambient air temperature in VLBW infants who were treated with antenatal betamethasone versus those who did not receive any antenatal steroid therapy. (15)

Infant Warming Techniques
Most infants, especially those who are born preterm, arrive in the nursery with some degree of hypothermia. Drying the skin surface, swaddling, or placement in a thermally controlled environment is required to maintain body temperature or initiate rewarming. Initiation of selected infant warming techniques requires an understanding of the mechanisms of heat loss described previ-
An effort to minimize each of the components of heat loss will improve survival and reduce morbidity with better caloric utilization.

At present, there are two primary, device-based methods for managing the thermal environment of low-birthweight infants in neonatal intensive care units. The historically older of these methods involves the servocontrol of forced air by means of convective incubators using either skin temperature or air temperature as the controlled variable. The second widely used method consists of infrared radiant warming, a method that is generally servocontrolled to the skin temperature.

In convective incubators, increasing the relative humidity or swaddling the infant results in a decrease in evaporative heat losses. Using double- rather than single-walled incubators or adding plastic heat shields decrease radiative heat losses. Handling the baby through specially designed portholes reduces convective heat losses, and using an incubator rubber foam mattress decreases conductive heat transfer.

Radiant warmers are typically used because of the ease of handling and visualizing the infant compared with closed convective incubators. Unlike convective incubation (or the intrauterine state), this mode of heat delivery results in large differences in surface temperature between exposed and unexposed skin areas. Insensible water loss and, thus, evaporative heat losses are 40% to 50% higher under radiant warmers than in convective incubators. This increase is due to a combination of factors, including higher skin-air temperature gradients and a lower relative humidity in the nursery (macroclimate) than in the incubator (microclimate). To compensate for this increased water loss, the infant’s total fluid intake should be adjusted.

**Servocontrol**

Several modes of temperature control in infant incubators are used to regulate the heater power output. Most modern incubators allow the caregiver to choose between skin temperature servocontrol, air temperature servocontrol, and manual (nonservo) control. With skin servocontrol, heater power output automatically adjusts to changes in the temperature of the infant’s skin thermometer. Air temperature servocontrol acts the same as skin temperature servocontrol, but the controlling variable is the temperature of the air. Manual control requires human intervention to maintain the desired temperature. A knob is changed in response to intermittent measurement of skin or air temperature. Manual control is seldom used in modern neonatology.

At present, no servocontrol mode is clearly the best. Skin servocontrol keeps the baby’s skin temperature constant at all times. Changes in humidity, air currents,
wall temperature will have a smaller effect on the baby’s skin temperature when compared with constant heater output (manual control). Dislodgment of the probe or accidental placement of the thermistor between the body and the mattress may result in over- or underheating, respectively. In addition, potential large fluctuations in air temperature may have untoward side effects (eg, apnea). Use of skin temperature servocontrol loses a major sign of disease (ie, fever). Air temperature servocontrol, on the other hand, produces a more stable environment, but the patient is omitted from the thermal feedback loop.

In an effort to combine the benefits of skin and air servocontrol, mixed servocontrol systems have been developed. Mixed modes of servocontrol use skin temperature as well as air and incubator wall temperatures as input variables to a computerized algorithm that controls the heater output. Such systems can maintain relatively stable environmental temperatures similar to an air servocontrolled incubator, but also incorporate infant skin temperature as input in the thermal feedback loop. Multiple input servocontrol systems are inherently more stable because major changes in one variable (eg, detachment of the skin thermistor or accidental removal of the air probe) results in relatively small changes in heater power output.

Summary

In terrestrial mammals, birth marks a transition from a warm and wet environment to one that is cold and dry. Homeothermic mechanisms that have evolved to facilitate this transition include metabolic heat production by brown adipose tissue and the development of a hydrophobic skin surface to minimize evaporative heat loss. Newborns are assisted in this transition by caregivers who dry, swaddle, and temporarily place them within a controlled thermal environment. The prevention of cold stress, particularly in the vulnerable preterm or growth-retarded infant, is important to reduce morbidity and mortality. An understanding of the basic mechanisms of heat loss by conduction, convection, evaporation, and radiation facilitates the use of newborn thermal life support systems, such as convective incubators and radiant warmers. Servomechanisms control the thermal environment maintained by these devices to a desired skin temperature, air temperature, or a combination of both. These temperatures are measured with thermistors in which a change in electrical resistance is related to a change in measured temperature. Close attention to the details of thermal management will facilitate the process of homeothermic adaptation in VLBW preterm and ill newborns and optimize the conditions for survival, growth, and early discharge in this high-risk patient population.

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NeoReviews Quiz

7. The thermoneutral zone represents a range of environmental temperatures that varies based on the gestational and postnatal ages of a neonate. Of the following, the thermoneutral zone is most associated with a:
   A. High base deficit.
   B. High energy need.
   C. Low basal metabolic rate.
   D. Low body temperature.
   E. Slow growth rate.

8. A newborn is delivered at 28 weeks of estimated gestational age following a pregnancy complicated by placental abruption. Thermoregulation is one of the important measures to stabilize the infant in the delivery room. Of the following, the highest source of heat loss in this infant would be by:
   A. Conduction.
   B. Convection.
   C. Diffusion.
   D. Evaporation.
   E. Radiation.

9. An ideal device for measuring body temperature is accurate, stable, inexpensive, and rapid in response. Of the following, the temperature sensor most consistent with these ideals is a(n):
   A. Chemical strip indicator.
   B. Infrared detector.
   C. Liquid crystal.
   D. Microwave radiometer.
   E. Thermocouple.

10. The site for measuring body temperature is critical in evaluating the metabolic status of a neonate. Of the following, the site that is most predictive of the metabolic rate is the:
    A. Abdominal skin surface.
    B. Distal extremity.
    C. Interscapular area.
    D. Rectum.
    E. Tympanic membrane.
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