



Thermal Protection of the Premature Infant

Summary: Where are we now and
where should we go

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Clinicians and researchers have strived to eliminate neonatal hypothermia due to exposure to cold environmental temperatures and improve thermal stability in premature infants for over 100 years. Early researchers found hypothermia in infants to be linked to increased mortality and morbidity¹⁻³ and the need for controlled heat and added humidity was determined to be beneficial to the outcomes of these vulnerable infants.^{4,5} Over the years, researchers have contributed valuable knowledge to improve thermal stability in infants; however, there is still much work to be done in this area. This paper will review thermal physiology in the premature infant, mechanisms of heat loss, and provide a review of the way we control the thermal environment of the premature infant.

Thermal Physiology

Because environmental temperature is constantly changing and influencing body temperature, regulation of body temperature is maintained by balancing heat production against heat loss.⁶ Variations in metabolic rates also influence balance in body temperature. Control of the generation and transfer of heat, or thermoregulation, is activated and performed through thermal sensors, afferent pathways, an integration system in the central nervous system, efferent pathways, and target organs.⁷

Central and peripheral thermoreceptors sense the alteration in temperature on the skin and internally. Peripheral thermoreceptors are free nerve endings that are distributed over the entire skin surface and are thermosensitive.⁷ Cold and warm areas on the skin will trigger the peripheral thermoreceptors to send information to the temperature control pathway.⁶ Afferent nerve fibers that carry sensory information to the hypothalamic regulatory center provides an early warning when there is a change in the ambient temperature of the skin. In adult humans, behavioral reactions are triggered through these sensory impulses which travel by thalamic pathways to the cerebral cortex. Central thermoreceptors are located in deep body structures found mainly in the spinal cord, abdominal viscera and in or around the great veins.⁶ Deep thermoreceptors are mainly concerned with detecting cold and cause a shift in blood flow to reduce heat loss in a cold environment.

Peripheral and central thermoreceptors send information to the hypothalamus in the brain, which enables signals to be sent through neuronal pathways. Variations in body temperature due to external sources will cause the hypothalamus to send efferent commands to alter the rate of heat generation and modify the rate of heat transfer within and from the body.

Neuronal effector mechanisms attempt to change body temperature through sending signals by way of sympathetic nerves going to the sweat glands, adjusting smooth muscle tone of cutaneous arterioles to control blood flow to the skin surface, activating motor neurons to the skeletal muscles or activating chemical thermogenesis.⁶ The autonomic system controls cutaneous blood flow over most of the skin, the body's largest organ. The flow of blood to the skin is the most effective way to transfer heat from the body core to the skin.⁶ A minor reduction in skin blood flow is caused by cutaneous vasoconstriction which causes heat to be conserved when the body temperature decreases. Changes in skin temperature is one of the most important variables in control of body temperature.⁷

Because infants less than one year old cannot shiver or sweat, chemical thermogenesis, also called brown fat metabolism or non-shivering thermogenesis (NST), is the primary method of heat production.⁸ NST provides heat without muscle activity by increased sympathetic stimulation causing increased norepinephrine and epinephrine circulation in the blood leading to an immediate increase in the rate of cellular metabolism.⁶

NST yields heat through oxidation of free fatty acids in the brown fat adipose tissue (BAT)⁶ and depends on adequate components of heat production, mainly brown fat, 5'/3'-monodeiodinase, and thermogenin. Cold body temperatures in a premature infant will cause signals to be sent from the brain to trigger norepinephrine release in the brown fat, causing T4 conversion to T3 via the action of 5'/3'-monodeiodinase and activation of thermogenin. The protein thermogenin or uncoupling protein allows transport of protons across the inner membrane of the mitochondria, causing oxidation of free fatty acids, which produces heat instead of ATP storage. Due to decreased amounts of uncoupling protein and 5'/3'-monodeiodinase, extremely premature infants cannot produce adequate heat to replace heat lost; therefore, their body temperature falls when exposed to cold environmental temperatures.⁹

Once an infant is born and the umbilical cord is clamped, exposure to the cold environment of the delivery room will trigger NST.¹⁰ Researchers have found that NST begins immediately in term infants after the umbilical cord is clamped and continues until at least 6 hours of age.¹⁰ However; premature and small for gestational age infants have minimal capability of initiating NST. Brown adipose tissue begins to develop as early as the 75 mm fetal stage.¹¹ A study performed by Hull calculates that 20-30 grams of brown fat are necessary to handle all the observed NST of a term infant.⁸ Researchers have found the structure of BAT to be well developed in infants as early as 25 weeks gestational¹², with BAT comprising about 1-2% of body weight.¹³ Therefore, there appears to be enough BAT available to fuel NST. However, uncoupling protein and 5'-monodeiodinase are also essential for NST to occur. Uncoupling protein increases with advancing gestational age; 29.4 ± 3.3 pmol/mg of uncoupling protein can be found in infants at 25 weeks gestational age and as much as 62.5 ± 10.2 pmol/mg in infants of 40 weeks gestational age.⁹ There is a major increase in uncoupling protein at approximately 32-weeks gestational age, increasing an infant's ability to achieve effective heat production. Content of the enzyme 5'-monodeiodinase also increases at 32 weeks gestational age, with a fourfold increase by term gestation.^{9,14} The low levels of uncoupling protein content and 5'-monodeiodinase content prior to 32 weeks gestational age are the likely source of inefficient heat production through NST in extremely premature infants. The most important time of development related to thermoregulation is 32 weeks gestational age. Infants less than this milestone gestational age, need thermal protection by their clinicians through auxiliary heat sources.

Mechanisms of Heat Loss in the Premature Infant

Infants suffer thermal instability through the loss of body heat, mainly through their skin and respiratory tract to the environment by way of radiation, conduction, convection and evaporation (see Figure 1). Body fat can act as an insulator to prevent heat loss; however, most premature infants have decreased body fat. It is important to understand the mechanisms of heat loss so that interventions can be aimed to block the transfer of heat from the infant to the environment.

Mechanisms of Heat Loss

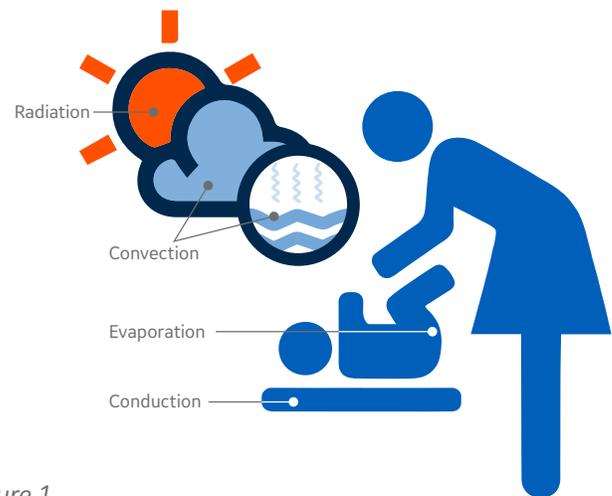


Figure 1

Radiation. All body surfaces emit heat in the form of electromagnetic waves⁶ which is called radiation. Energy transferred through radiation will cause the body temperature to change, depending on the rate of heat loss and the proportional temperature difference between the skin and the radiating surface.¹⁵ An infant may be warmed through the radiant heat from an overhead warming table or lose heat to a cold wall located near the infant.

Conduction. If the skin surface is placed against a cold surface, an infant can lose heat. Conductive heat loss is responsible for heat transfer from the infant to the colder object such as placing a cold blanket on the infant. Conductive heat loss can occur through exposure to colder air, fluids, or solid surfaces. In the process of conduction, heat is transferred from the warm molecules of the infant's skin to the colder molecules of the alternate surface as the molecules collide. Pre-warming surfaces and fluids will minimize conductive heat losses while caring for a premature infant.

Convection. Moving cold air or fluid across an infant's warm body can cause convective heat transfer. Heat will be transferred from an infant's skin to the air, when the skin is warmer than the air. The molecules rise into the air from the skin due to being less dense than colder molecules, then the heat molecules are swept away by convection through air or water. A common example of convective heat transfer is after an infant's birth, when the infant is delivered into a cold room, then carried from the mother to a nearby warming table. As the infant is carried through the cold air, heat easily rises off the skin and is swept away.

Evaporation. One of the most common sources of heat loss in a premature infant is through evaporation through the skin or respiratory tract. The evaporative rate is proportional to the water vapor-pressure gradient between the skin and environment; there is a linear relationship between the ambient humidity and the evaporation rate, with higher evaporation rates at lower levels of humidity.¹⁶ Evaporation causes 0.6kcal of heat to be lost for every 1 gram of water lost from the body.⁶ A study performed by Hammerlaud et al. found evaporative heat loss is greatest right after birth;¹⁷ therefore, interventions in the delivery room to reduce heat loss should be targeted towards reducing evaporative heat loss.

Euthermia in Premature Infants

Body temperature limits and the range of euthermic temperatures has been debated over the decades. A discussion around hypothermia begins with an attempt to define hypothermia. The American Academy of Pediatrics (AAP) defined the lower limits of normal temperature for an infant as 36.4°C in their 1988 perinatal guidelines.¹⁸ In an updated guideline, the AAP suggests an axillary temperature of 36.5°C in the delivery room and a range of 36.5° to 37.4°C prior to discharge.¹⁹ The World Health Organization (WHO) defines normal body temperature as 36.5°-37.5°C with the extent of hypothermia stratified into three levels: mild hypothermia, which should trigger cause for concern (36° to 36.4°C), moderate hypothermia which should cause immediate rewarming of the infant (32° to 35.9°C), and severe hypothermia where the outlook for the infant is grim (temperature less than 32°C).²⁰ From these guidelines, it is evident that clinicians should strive to keep infant body temperature above 36.5°C as a minimum safe level to prevent hypothermia. In one of our studies of 10 infants using continuous skin temperatures and heart rates for their first 12 hours of life, we found that extremely low birth weight (ELBW) infants born weighing less than 1000 grams have more stable heart rates if they are kept at a body temperature of 36.8° to 36.9°C.²¹ Therefore, our team recommends a minimal skin temperature of 36.5°C for premature infants and a minimal skin temperature of 36.8°C for ELBW premature infants.

Thermal Stability after Birth

Heat loss after birth is one of the most important problems plaguing neonatal researchers today because initial hypothermia has been historically and presently linked to increased mortality and morbidity. Hypothermia during the admission period, which reflects thermal stability in the delivery room and through transport to the NICU is associated with increased mortality^{22,23} and much of the

research conducted today is aimed at decreasing heat loss in the delivery room. There are two main ways to decrease heat loss: barriers such as plastic wrap, hats, blankets and external heat sources such as increasing ambient room heat, heat from blankets, use of radiant heat on warming tables, as well as heat and humidity within incubators. Many research teams are combining elements of heat loss prevention; however, it is important to study these combined interventions to make sure we are not inducing hyperthermia through these combinations.

Delivery Room Ambient Environment

One of the most difficult environments to control is the temperature of the delivery room in the United States.^{24,25} Delivery rooms are usually controlled to the comfort of the delivery team and the laboring mother, without consideration to the vulnerable premature infant. Convective heat loss can be reduced if the infant is not whisked through the cold air of the delivery room. The latest WHO guidelines recommend that delivery rooms be minimally $\geq 26^{\circ}\text{C}$ for infants less than 28 weeks gestational age and at least $\geq 25^{\circ}\text{C}$ for all infant births.²⁶ Our research team found that heat loss was decreased by placing infants in plastic bags at birth but as an additive effect, a warmer delivery room was associated with less admission hypothermia in infants less than 29 weeks gestational age.²⁷ It is now clear that ambient environmental temperature must be kept warmer than 25°C to prevent heat loss in the premature infant, even if the infant is cared for in heated incubators or radiant warmers.

Heated Humidified Respiratory Gases

Another intervention needing further study and standardizing is the heating and humidification of respiratory gases given to a premature infant. Evaporative heat loss is reduced when respiratory gases are warmed and humidified by sending warm air into the nose, mouth or trachea of the infant. The European Consensus Guidelines on management of RDS in premature infants latest update specifies that respiratory gases should be heated and humidified.²⁸ Several small trials have shown adding heated, humidified gases to the respiratory management of premature infants is associated with ongoing reduction of hypothermic body temperatures.^{29,30} Most trials investigating heated, humidified respiratory gases have been small and it is difficult to control this aspect of care, therefore more research is needed in this area.

Thermal Blankets and Exothermic Mattresses

Conductive heat loss can be reduced by making sure the mattress against the skin of the newly born infant is not cold; thermal mattresses or blankets may emit warmth which can increase the temperature of the infant. Although chemical warming blankets have been used over the years in neonatal transport, the use of exothermic or thermal mattresses in the delivery room is relatively recent in an effort to reduce heat loss after birth. One research study compared using thermal mattresses against wrapping with vinyl bags and even though both were effective in improving admission temperatures, both groups had hypothermic admission temperatures ($36.1^{\circ}\text{C} \pm 0.7^{\circ}\text{C}$ in the vinyl group vs $35.8^{\circ}\text{C} \pm 1.3^{\circ}\text{C}$ in the mattress group).³¹ Another study conducted a trial doing the same comparison and favored the mattress group and even though admission temperatures were higher in this study, neither significantly improved admission temperatures.³² Studies are also combining this conductive heat loss intervention with barrier interventions such as plastic wrap or bags. These combination studies are proving to be more effective than mattress heat alone.

Barriers to Heat Loss: Polyurethane and Polyethylene Wrap or Bags

Studies using plastic to envelop a premature infant's body after birth have confirmed that this barrier to evaporative heat loss significantly improves body temperature and reduces the incidence of hypothermia on admission to the NICU.^{27,33,34} The ILCOR and the American Heart Association now recommend plastic wrapping and the use of exothermic mattresses to reduce heat loss after birth in infants less than 28 weeks gestational age.³⁵ Some researchers are also studying adding plastic caps instead of the traditional stockinette hats that have been used for over 50 years.³⁶ Several trials combine different interventions;^{34,37,38} however, there is no combination of interventions using plastic wrap, bags, hats, and/or mattresses that has become standard of care. Researchers have found that successful programs to decrease admission hypothermia are structured and involve paying special attention to thermal management through education and strict procedures.^{39,40} More research is needed in this area.

Thermal Care in the NICU

It has long been established that premature infants should be cared for in heated, humid incubators or under the radiant heat of a warmer. Research has been aimed at minimizing heat loss while being cared for in these environments due to the many procedures and nursing care events that may disrupt the stability of the controlled environment.

Incubators

Incubators have been in use since the 19th century.^{41,42} Over the years, incubators have been improved with newer materials, the capability of distributing humidity, insulated double walls, and better airflow with the addition of airflow that keeps heat within even with doors open. Researchers have shown that incubators provide thermal stability, less energy expenditure, better growth and outcomes.^{1,43,44} A Cochrane Review completed in 2007 and last updated in 2009 conducted a meta-analysis of the advantages of double walled versus single walled incubators.⁴⁵ The 2009 update revealed no additional studies have been done in this area. The review determined that double walled incubators are superior over single walled incubators for decreasing heat loss, decreasing radiant heat loss and reducing oxygen consumption; however, there were no long term benefits for infants due to care in a double walled incubator.

One debated issue with incubator use is whether to use servo control or air temperature control to maintain euthermic body temperature for premature infants. Researchers have determined long ago that both modes can be effective in reducing heat loss in the infant;⁴⁶ however, while infant temperatures may be more stable using servo control, environmental air temperature may have more variability⁴⁷ which could lead to more body temperature variation and extremes. A more stable environmental temperature using air control may result in less energy expenditures.⁴⁸

Humidity

Adding water to an incubator to produce a humid environment has been standard of care for at least 50 years because of large evaporative heat losses due to thin skin of the premature infant.^{49,50} Caring for infants in a heated, humid environment improves thermal stability, fluid and electrolyte balance, and skin integrity.^{51,52} There is great variation in practice as to what relative humidity level should be set in the incubator according to particular days of life, gestational age and birth weight,⁵³ although researchers continue to confirm the benefits of added humidity.⁵⁴ Studies are showing that frequent incubator openings due to nursing procedures cause a reduction in humidity levels so that levels are maintained below the set level.⁵⁵ One research team in France has developed an algorithm for determining incubator air temperature based on relative humidity, infant age and weight by examining the impact of humidity on the air temperature.⁵⁶ More research is needed on the impact of humidity and mode of incubator temperature control (air vs servo).

Warming Tables versus Hybrid Incubators

Many neonatal units utilize radiant warmers for stabilization of premature infants after birth; however, the trend is towards use of hybrid incubators⁵⁷ which can be used in either warmer or incubator mode. Radiant warmers have been found to cause an increased insensible water loss⁵⁸ and therefore, even when using hybrid incubators in canopy mode, these time periods should be minimal and mainly for invasive procedures that cannot be accomplished through the portholes of incubator mode.⁵⁹ Hybrid incubators such as the Giraffe Omnibed™ have been used widely and reported to lower insensible water losses and minimize weight loss in ELBW infants when compared to infants cared for in non-humidified conventional incubators.⁶⁰ The team that conducted this research also found a reduction in the incidence of severe cases of bronchopulmonary dysplasia in infants cared for in the Warming Tables versus Hybrid Incubators.

Temperature Measurement in the Neonate. Where Should We Measure Temperature?

Ideal placement of skin temperature probes has generally been determined to be in the flank area of the infant where there is more fat than bone prominence and not positioned so that the probe is against the mattress. In a very low birthweight infant, abdominal skin temperature closely correlates with core temperature if covered with a cover for zero heat flux.⁶¹ Some studies have found that axillae skin temperature monitoring is as good as abdominal skin temperature; however, other researchers have found great variability between the two sites.^{61,62} Several research teams advocate for dual point skin temperature monitoring.⁶³⁻⁶⁵ Our research team has studied temperature surveillance using the abdominal and foot temperature as an indicator of core or central temperature and peripheral temperature for the last 10 years with success.⁶⁶⁻⁶⁹ Our team and others hypothesize that dual point skin temperature surveillance will give clinicians an indicator of temperature differentials that may be indicative of stress.^{63,64,69} In our latest study of 22 infants, we found evidence of a negative temperature differential over infants' first two weeks of life, or a case where the foot temperature is higher than the abdominal temperature, is associated with infection.⁶⁹ This finding needs to be examined in a larger clinical trial to determine if dual point temperature monitoring can be used as a biomarker for morbid conditions.

Body temperature in premature infants- What do we need to consider?

Surveillance of body temperature for indicators of hypothermia and hyperthermia is extremely important to the care and well-being of very low birth weight infants less than 32 weeks gestational age due to their inability to conserve heat and limited ability to produce heat. Clinicians must use the latest technology to maximize thermal stability for these vulnerable infants, starting in the delivery room and through hospital discharge. The clinicians and engineers at GE Healthcare have created a figure to show the many indicators and factors that play into optimizing thermal care of the neonate (see Figure 2).

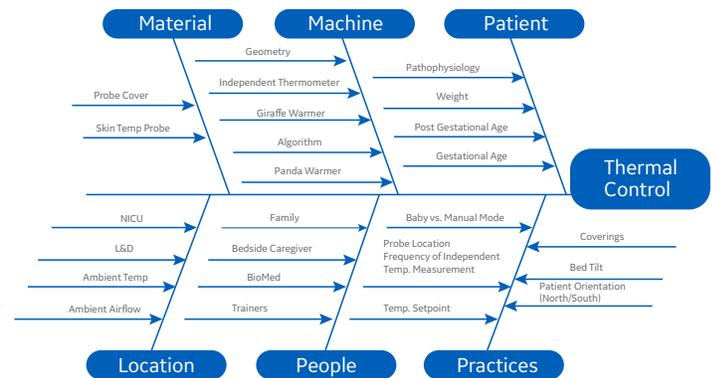


Figure 2

Optimal thermal care should start with good education, evidence based procedures, the environment, taking into consider the patient and the resources available to prevent heat loss. Our research team is dedicated to studying the best modes of thermal care and determining how body temperature surveillance can optimize infant outcomes and decrease mortality and morbidity. We welcome others to participate in this important endeavor and we advocate for growth and advances in thermal care.

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