Physiological effects of thermoregulation in transitional ELBW infants

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ABSTRACT
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Physiological Effects of Thermoregulation in Transitional ELBW Infants
(Under the direction of Dr. Diane Holditch-Davis)

Problem: Extremely low birth weight (ELBW) infants are vulnerable to cold stress during the first 12 hours of life (extra-uterine transition) due to stabilization in the delivery room and NICU. Little research has examined thermoregulation in ELBW infants or the body temperature range that would lead to optimal physiological status.

Purpose: The purpose of this study was to explore the physiological aspects of thermoregulation as a first step toward determining the optimal body temperature for ELBW infants during transition. The study used a multiple case design to explore the relationships between body temperature and oxygenation, heart rate, peripheral vasoconstriction, acid-base balance, and blood glucose in 10 ELBW infants over their first 12 hours in the NICU.

Methodology: Infants were continuously monitored from admission to the NICU for 12 hours. Ten variables were collected using physiologic monitoring, observation and chart review.

Results: Infants had a mean abdominal temperature range of 35.17˚ C to 36.68˚ C. One infant exhibited peripheral vasoconstriction 8.8% of the time, and the remaining nine had poor vasomotor control, appearing to lack the ability to vasoconstrict. The peripheral temperature was greater than the abdominal temperature for the most of the study period for 7 of 10 infants. Abdominal-peripheral temperature differences significantly increased for 9 of the 10 infants when abdominal temperature ≤ 36.4˚ C. Caregiver handling of the infant

was associated with an increase in the abdominal-peripheral temperature difference on graphic trends. Abdominal temperature and heart rate were significantly correlated in 7 of 10 infants. In addition, more observations in the normal heart rate range for 6 of 10 infants when abdominal temperatures were greater than 36.4˚C. The abdominal temperature range in which normal heart rates for the ELBW infants in this study were maximized was 36.8˚C to 37.0˚C.

Relevance to Nursing: These results will add to the data to guide nurses in setting control points for body temperature, inform nurses when it is necessary to augment incubator heat with additional heat sources, and help nurses guard against cold stress during stabilization procedures.

To my husband, Manni, who has given me untiring support and encouragement over the last five years. If not for you, I would have quit a thousand times. Your love and cheers have made me smile through the toughest of times.
Mein schatz, ich leibe dich sehr.

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LIST OF ABBREVIATIONS AND SYMBOLS

ATP	Adenosine triphosphate
ELBW	Extremely low birth weight
mRNA	Messenger ribonucleic acid
NICU	Neonatal intensive care unit
O_2	Oxygen
pH	Potential of Hydrogen
T_3	Triiodothyronine
T_4	Thyroxine
TSH	Thyroid stimulating hormone
UCP	Uncoupling protein

CHAPTER ONE

Significance and Specific Aims

Extremely-low-birth-weight (ELBW) infants are infants weighing less than 1000 grams, which corresponds to less than about 27-28 weeks gestation at birth. The earliest that an ELBW infant can be delivered and stand a chance of survival is 23 weeks gestation, with a birth weight as low as 400 grams (Kattwinkle, 2000). Altogether, about 29,000 ELBW infants are born each year in the United States (Center for Disease Control, 2002). Technology has advanced to the point that most ELBW infants survive (O'Shea, Klinepeter, Goldstein, Jackson, & Dillard, 1997; Subramanian, Yoon, & Toral, 2002). Survivability is dependent on birth weight corresponding with the gestational age; therefore, survival rates are approximately 11% for infants weighing less than 500 grams survive, 51% for infants weighing 500-749 grams, and 84% for infants weighing 750-1000 grams (Subramanian et al., 2002).

Initial physiological stabilization of ELBW infants occurs during the first 12 hours of life, termed the transition period. Fetal lung, heart, metabolism and temperature regulation are completely dependent on maternal systems. Transitional ELBW infants must adapt from fetal life to extra-uterine life, relying on their lungs for respiration and hearts for circulation. Nurses and physicians must provide support for immature physiological systems to help the infant achieve extra-uterine stabilization and a normal state in the transitioning organ systems. ELBW infants become stabilized under heated radiant warmers to optimize thermal

stability (Baumgart, Engle, Langman, Fox, & Polin, 1980), however many stabilization procedures result in interruptions in the heat output of warmers leading to cold stress.

The term cold stress defines the situation in which an infant is exposed to a cool environmental temperature that causes the infant to lose more heat than he/she can produce. Consequently, the infant will attempt to generate heat, resulting in physiological reactions (norepinephrine increase, peripheral vasoconstriction, increased oxygenation) to the cold environment. This situation is stressful on the infant's normal physiological balance, because energy will need to be expended (oxygen will be metabolized) to produce heat. Increased energy expenditure in an already sick and unstable infant can cause changes in vital signs, pH balance, glucose balance and oxygenation.

Before 30 weeks gestation, preterm infants have very little body fat and thin skin. They typically rest with arms and legs extended outward, instead of being flexed like term infants, exposing more of their body surface to the environment (Jones & DeCherney, 2003). ELBW infants also have poor vasomotor control at birth (Lyon, Pikaar, Badger, & McIntosh, 1997). Because of these factors, ELBW infants are at greater risk of cold stress than larger infants. Temperature regulation is particularly important during the transition period because cold stress can lead to increased oxygen consumption (Adams et al., 1964; Bruck, 1961; Malin & Baumgart, 1987) in a time of respiratory and cardiovascular instability. The body attempts to regulate temperature through heat production in the face of heat loss.

Heat production is accomplished through non-shivering thermogenesis. Full-term infants rely on brown fat metabolism or non-shivering thermogenesis for heat production (Houstek, Vizek, Pavelka, Kopecky, Krejocova, & Hermanska, 1993). The metabolism of brown fat is inefficient in the ELBW infant due to extreme immaturity (Bruck, 1998; Houstek, et al.,

1993) and may not produce enough heat to prevent body temperature from falling. This process consumes oxygen and glucose (Voet, Voet, & Pratt, 2002), depleting the ELBW infant's minimal energy stores and causing hypoxemia in an infant already at risk for respiratory distress because of immature lungs (Delivoria-Papadopoulos & McGowan, 1998; Voet et al., 2002). As a result, lactic acid accumulates (Deshpande & Platt, 1997) and the cardiovascular system must work harder to increase cardiac output (Anderson, Kleinman, Lister, & Talner, 1998; Lister, Moreau, Moss, & Talner, 1984). Decreased oxygenation (Adams et al., 1964; Bruck, 1961; Malin & Baumgart, 1987), increased acidosis (Deshpande & Platt, 1997; Seri, 1998), peripheral vasoconstriction (Horns, 2002), decreased blood glucose (Cowett, 1985; Hardikar & Suchy, 2003), and increased heart rate (Anderson et al. 1998; Lister et al., 1984) due to cold stress lead to increased morbidity and mortality (Richardson, Corcoran, Escobar, & Lee, 2001).

Because ELBW infants are vulnerable to cold stress, knowing the optimal range for their temperature is important in order to protect the infant from cold stress and organ system insult. However, very little research has examined this range in ELBW infants. Most of the research on optimal body and environmental temperatures for premature infants occurred 20-40 years ago, before significant numbers of ELBW infants or ventilated infants survived (Adams et al., 1964; Bruck, 1961; Buetow & Klein, 1964; Day, Caliguiri, Kamenski, & Ehrlich, 1964; Silverman, Fertig, & Berger, 1958; Yashiro, Adams, Emmanouilides, & Mickey, 1973).

Many studies have linked cold stress to increased mortality and morbidity (Buetow & Klein, 1964; Day et al., 1964; Hazan, Maag, & Chessex, 1991; Vohra, Grent, Campbell, Abbott, & Whyte, 1999) and shown the importance of a warm environment in caring for

preterm infants (Baumgart, Engle, Langman, Fox, & Polin, 1980; LeBlanc, 1982; Meyer, Payton, Salmont, Hutchinson, & de Klerk, 2001; Miller & Oliver, 1966; Yashiro et al., 1973) to prevent cold stress. In one of the few recent studies, Horns (2002), by monitoring foot and abdominal temperature, found that ELBW infants in the first 2 days of life spent about 20% of the time compensating for cold stress by peripheral vasoconstriction. Yet many ELBW infants generally exhibit low body temperatures even with current technology. Therefore, research should examine the physiological responses of ventilated ELBW infants during the first few hours of life to provide nurses with the evidence necessary to develop protocols for regulating the environmental temperature of ELBW infants. Researchers have not closely examined physiologic parameters such as oxygenation, acid-base balance, peripheral vasoconstriction, glucose stability, and heart rate trends related to cold stress have not been closely examined in transitional ELBW infants nor have they determined the optimal body temperature range.

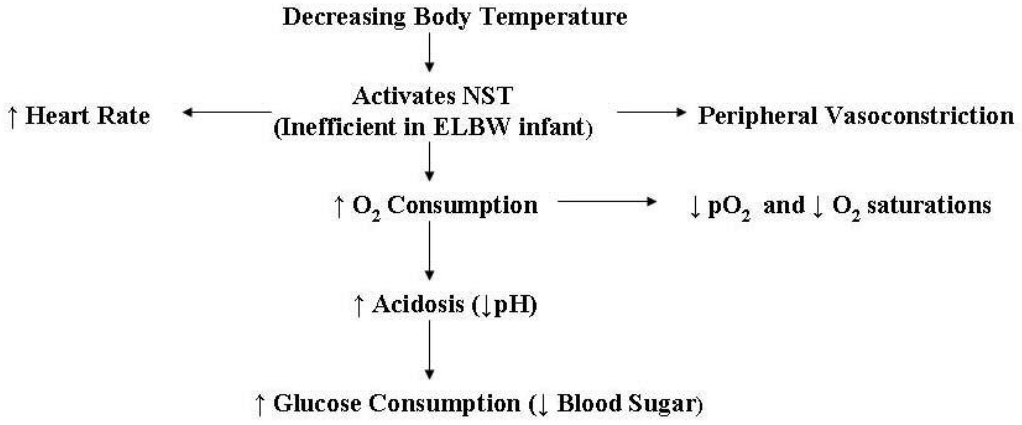
Research Questions/Hypotheses

The purpose of this study was to explore the physiological aspects of thermoregulation as a first step toward determining the optimal body temperature for ELBW infants during the first 12 hours of life. Specifically, the study used a multiple case study design to explore, over the first 12 hours in the NICU, the relationships between body temperature and oxygenation, acid-base balance, peripheral vasoconstriction, blood glucose, and heart rate in 10 ELBW infants weighing 500-1000 grams at birth.

These physiological variables were used because of their link with cold stress and non-shivering thermogenesis in the ELBW infant. Because no previous research has explored the

variation in oxygenation, acid-base balance, peripheral vasoconstriction, blood glucose and heart rate in relationship to variations in body temperature in the ELBW infant, this study was exploratory in design. Its conceptual framework proposes the pathway of non-shivering thermogenesis in the ELBW infant and linked the study variables as they occurred through the pathway (see Figure 1.1). According to the previously described physiology, decreasing body temperature in the preterm infant will trigger non-shivering thermogenesis. Non-shivering thermogenesis requires oxygen for fuel, therefore oxygen needs will increase and it is likely that the ELBW infant will have a decreased oxygen saturation and lower arterial pO_2.

Figure 1.1 Proposed Relationship Between Body Temperature, Oxygenation, Acid-base Balance, Glucose Balance, and Heart Rate in the ELBW Infant



As oxygen is consumed in the already compromised ELBW (because of the respiratory

distress syndrome), the infant is likely to have an increased acidotic state, manifested by a lower arterial blood pH. In addition, the infant is likely to have an increased heart rate because of the norepinephrine increase. If the condition persists, the blood sugar will likely decrease as glucose is consumed. The situation of hypothermia leading to abnormal physiological variables may lead to increased morbidity in the ELBW and if the condition persists, can increase mortality.

To explore the proposed relationship between these physiological variables in the transitional ELBW infant, this study answered the following research questions.

Research questions:

1) During the transition period (first 12 hours of life), what are the relationships between temperature, oxygenation (oxygen saturations), heart rate, peripheral vasoconstriction (> 2º C difference between peripheral and abdominal temperature), and trends in the intermittent variables of pO_2, pH, and chemstrip (indicator of blood glucose) within individual infants born weighing 500-1000 grams?

2) Are these relationships between temperature and oxygenation, heart rate, peripheral vasoconstriction, and trends in the intermittent variables of pO2, pH, and chemstrip (indicator of blood glucose) similar over infants?

3) During the transition period, what is the optimal body temperature range for each individual infant in which oxygenation and heart rate are most stable while accompanied by decreased peripheral vasoconstriction?

   a) When core temperature is below 36.4º C (traditional definition of

hypothermia in term infants), do individual infants show more abnormal values in oxygenation and heart rate than when the temperature is above 36.4º C? Does the infant spend more time exhibiting peripheral vasoconstriction below 36.4º C than above 36.4º C?

b) Is the degree of abnormality in oxygenation and heart rate related to the extent to which body temperature falls below 36.4º C in infants? Is the amount of time spent in peripheral vasoconstriction related to the extent to which body temperature falls below 36.4º C?

c) Is there an optimal cut-point in body temperature at which the number of abnormal physiological variable observations are minimized and amount of normal physiological variable observations are maximized?

CHAPTER TWO

Theoretical Framework and Literature Review

Thermoregulation of ELBW infants is inefficient because they have extremely immature organ systems and decreased contents of thermogenin and 5'/3'-monodeiodinase which are needed to produce heat (Houstek et al., 1993). Neonates (infants less than 30 days of age) produce heat secondary to heat loss by non-shivering thermogenesis. Non-shivering thermogenesis yields heat through oxidation of free fatty acids in the brown fat adipose tissue (Guyton & Hall, 2001; Vander et al., 2001). In order to produce heat, a preterm infant must have adequate components of heat production, mainly brown fat, 5'/3'-monodeiodinase, and thermogenin (Jones & DeCherney, 2003). Once a preterm infant becomes cold, signals from the brain trigger norepinephrine release in the brown fat, causing T4 conversion to T3 via the action of 5'/3'-monodeiodinase and activation of thermogenin (Voet et al., 2002). The protein thermogenin allows transport of protons across the inner membrane of the mitochondria, causing oxidation of free fatty acids, which produces heat instead of ATP storage. However, ELBW infants cannot produce adequate heat to replace heat lost; therefore their body temperature falls when exposed to cold environmental temperatures (Bruck, 1998; Houstek, et al., 1993). Which physiological factor prevents adequate heat production is unclear. One can only speculate that decreased amounts of 5'/3'-monodeiodinase and/or thermogenin may limit heat production because concentrations of these proteins are low before 32 weeks gestational age.

The extent of physiologic costs incurred by the infant due to the inability to produce adequate heat is also unclear. Because oxygen is needed to produce heat, oxygenation of the ELBW infant during cold stress may be decreased (Voet, Voet, & Pratt, 2002). Consequently, the ELBW infant may become acidotic (Deshpande & Platt, 1997; Seri, 1998). Decreased oxygenation and acidosis are two possible consequences of inadequate heat production in ELBW infants.

Thermoregulation in Humans

Humans are homeothermic in that they can regulate their core body temperature within a narrow limit (Nadel, 2003; Vander et al., 2001). Core (internal) body temperature is maintained at approximately 37º C, but ranges from 36º C to 37.5º C (Nadel, 2003; Vander et al., 2001). Humans require precisely regulated body temperature because large elevations in temperature can cause nerve malfunction and protein denaturation, and the brain ceases to control temperature after large increases (Vander et al., 2001). Convulsions may occur at 41º C and 43º C is the absolute limit of survival (Vander et al., 2001). Alternatively, severe hypothermia will cause the heart to slow down. Once the internal body temperature reaches 25º C humans will suffer cardiac standstill or fibrillation (Guyton & Hall, 2001).

Temperature is regulated by balancing heat production against heat loss (Guyton & Hall, 2001), a balance that is continuously being disturbed by changes in metabolic rate or external environment (Vander et al., 2001). The thermoregulatory system in a human consists of thermal sensors, afferent pathways, an integration system in the central nervous system, efferent pathways, and target organs that control heat generation and transfer (Nadel, 2003).

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 (Nadel, 2003). These peripheral thermoreceptors provide information that is sent forward through the temperature control pathway and have the ability to detect warm or cold areas on the skin (Vander et al., 2001). A change in the skin's normal temperature causes the receptors to increase their firing rate from the steady state rate (Nadel, 2003). The skin thermoreceptors provide, by way of afferent nerve fibers that carry sensory information to the hypothalamic regulatory center, an early warning when there is a change in the ambient temperature of the skin. This information also travels by thalamic pathways to the cerebral cortex to cause a conscious perception of the thermal environment and behavioral adjustments (Nadel, 2003). Central thermoreceptors are located in deep body structures including the hypothalamus, spinal cord, and abdominal organs (Vander et al., 2001). These thermoreceptors are an example of a negative feedback system because they modify heat transfer rates to restore core temperature to its regulated level once they detect a core temperature that is colder or warmer than normal (Nadel, 2003).

Peripheral and central thermoreceptors send information to the brain control center, the hypothalamus, which enables signals to be sent through neuronal pathways. The principal area of thermoregulatory regulation is the preoptic and anterior hypothalamic nuclei of the hypothalamus (Guyton & Hall, 2001). The hypothalamus monitors the prevailing thermal status with a normal set of thermal conditions and then sends efferent commands to alter the rate of heat generation and modify the rate of heat transfer within and from the body (Nadel, 2003).

Neuronal effector mechanisms attempt to increase or decrease 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 (Guyton & Hall, 2001; Nadel, 2003; Vander et al., 2001) or activating chemical thermogenesis. Changes in muscle activity constitute the major control for temperature regulation. In the case of cold exposure, the hypothalamus causes motor neurons to the skeletal muscles to produce shivering which is oscillating rhythmical muscle contractions and relaxations occurring at a rapid rate (Vander et al., 2001). The rapid muscle contractions produce heat and can be called shivering thermogenesis. When there is too much heat, basal muscle contractions are reflexively decreased and voluntary movement slows. The autonomic system controls cutaneous blood flow over most of the skin, the body's largest organ. Active vasodilation can increase blood flow up to 10 times the resting level (Nadel, 2003), thereby releasing heat from the skin to the environment. A minor reduction in cutaneous blood flow is caused by cutaneous vasoconstriction, mediated by sympathetic nerves because of changes in core body temperature, which causes heat to be conserved. If the heat load increases, the autonomic nervous system activates the eccrine sweat glands, which cause sweat to be secreted onto the skin's surface. The sweat increases the partial pressure of water vapor on the skin and causes evaporation and loss of heat.

Chemical thermogenesis 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 (Guyton & Hall, 2001; Vander et al., 2001). Chemical thermogenesis, also called brown fat metabolism or non-shivering thermogenesis, is the primary method of heat production for the infant up to 1 year of age (Hull & Smales, 1978). Chemical thermogenesis, if any, is minimal in adults. The degree of chemical thermogenesis that occurs in an animal is directly proportional to the amount of brown fat that exists in that animal (Guyton & Hall, 2001).

Heat Transfer

Heat is a by-product of metabolism. The metabolic rate of the body (rate of heat production) is determined by the basal rate of metabolism of all body cells and extra metabolism caused by muscle activity, thyroxine on the cells, sympathetic stimulation of the cells, and an increase in chemical activity in the cells themselves (Guyton & Hall, 2001).

Human thermoregulation attempts to keep body temperature in a steady state, in which heat production equals heat loss. The rate at which heat is lost depends on how rapidly heat can be conducted from where it originates within the body and how fast heat can be transferred from the skin to the environment. The skin along with subcutaneous tissues and fat, acts as an insulator for the body. Fat conducts heat only one third as readily as other tissues in the body (Guyton & Hall, 2001). The skin transfers heat to the environment by way of radiation, conduction, convection and evaporation.

Heat decreases or increases by way of radiation, which is the process by which all body surfaces emit heat in the form of electromagnetic waves (Guyton & Hall, 2001; Nadel, 2003; Vander et al., 2001). The infrared portion of the electromagnetic energy spectrum carries this energy. The rate of heat loss is proportional to the temperature difference between the skin and the radiating body. For example, heat to be transferred from the infant's body to a colder wall near the infant. Alternatively, heat may be absorbed into the skin from a heat lamp near the infant.

Moreover, heat transfers to or from the skin surface by way of conduction when the skin touches another solid object of different temperature (Guyton & Hall, 2001; Nadel, 2003; Vander et al., 2001). In the NICU, this heat gain or loss is minimal because infants usually rest on prewarmed surfaces. Heat moves from molecule to molecule as the molecules from

the skin surface and another surface collide. This object might be air, water, or a solid surface on which the infant rests.

Heat is transferred by convection when a moving fluid such as air or water carries heat between the body surface and the environment (Guyton & Hall, 2001; Nadel, 2003; Vander et al., 2001). If the body surface is warmer than the surrounding environmental air, heat is first conducted into the air, then swept away by convective air currents. Warm molecules are less dense and therefore rise into the air from the skin.

Heat loss by evaporation is a major route of heat transfer when water is lost from the skin and membrane linings of the respiratory tract. The evaporative rate is independent of the temperature gradient between the skin and the environment and is proportional to the water vapor-pressure gradient between the skin and the environment (Nadel, 2003). Evaporation causes 0.6 kcal of heat to be lost for every 1 gram of water lost from the body (Guyton & Hall, 2001; Nadel, 2003; Vander et al., 2001).

A neutral thermal environment is a set of environmental conditions in which the temperature of the naked body does not change when the subject is at rest and there is no muscle activity (Nadel, 2003). These environmental conditions of air temperature, airflow, humidity, and temperature of surrounding radiating surfaces will minimize heat loss or gain by radiation, conduction, convection and evaporation to keep the infant in a steady metabolic state related to thermal balance.

Heat transfer from the body causes problems for the thermoregulation of infants. Because infants have less subcutaneous fat and relatively larger surface areas exposed to the environment than adults and because they rely solely on non-shivering thermogenesis for

heat production, we must examine thermoregulation in infants, and in particular in preterm infants.

Fetal Temperature Regulation in the Fetal Period through Transition to Extra-Uterine Life

The fetal ambient environmental temperature is the maternal temperature. Heat builds up in the fetus until the temperature gradient between the fetus and the mother causes heat to dissipate from the fetus to the mother (Power, 1998). Under normal conditions, the temperature of the fetus remains about 0.5ºC higher than that of the mother, or about 37.6º C to 37.8º C (Blackburn, 2003; Power, 1998). This tight linkage with the mother prevents the fetus from regulating its own temperature independently. The heat generated by the fetal metabolism offloads to the mother through the amniotic fluid to the uterine wall or via the umbilical cord and placenta to the maternal blood stream (Blackburn, 2003). Cooling of fetal sheep in utero does not elicit non-shivering thermogenesis (Gunn & Gluckman, 1995); therefore, it is likely that the human fetus cannot independently produce heat in response to cooling. Evidence indicates that placental inhibitors, primarily prostaglandin E_2 and adenosine, prevent non-shivering thermogenesis (Gluckman, Sizonenko, & Bassett, 1999; Gunn & Gluckman, 1995; Sawa, Asakura, & Power, 1991). The inhibitors of non-shivering thermogenesis rapidly decrease once the umbilical cord is clamped upon birth. Non-shivering thermogenesis can then be activated by stimulating the infant's cold receptors by virtue of the change into a colder environment, increasing oxygenation consumption of the infant (Gunn & Gluckman, 1995; Power, 1998).

Additional physiological adaptations to extra-uterine life take place once the infant is born. The infant must change from fetal circulation to neonatal circulation and from placental gas

exchange to pulmonary gas exchange (Askin, 2002; Gluckman et al., 1999). The onset of neonatal breathing causes a drop in pulmonary vascular, which is a critical part of adaptation to extra-uterine life (Mathew, 1998). Initial closure of the ductus arteriosus, which completes the switch to neonatal circulation, is a gradual process and takes 10-15 hours of life (Askin, 2002; Mathew, 1998; Verklan, 2002). The following sections will refer to the first 12 hours of life as the transitional period, because this is a time of physiological change and adaptation to extra-uterine life. This adaptation may be more difficult for preterm infants, because these infants may also have lung surfactant deficiency, commonly called respiratory distress syndrome, altering ventilation and oxygenation (Askin, 2002).

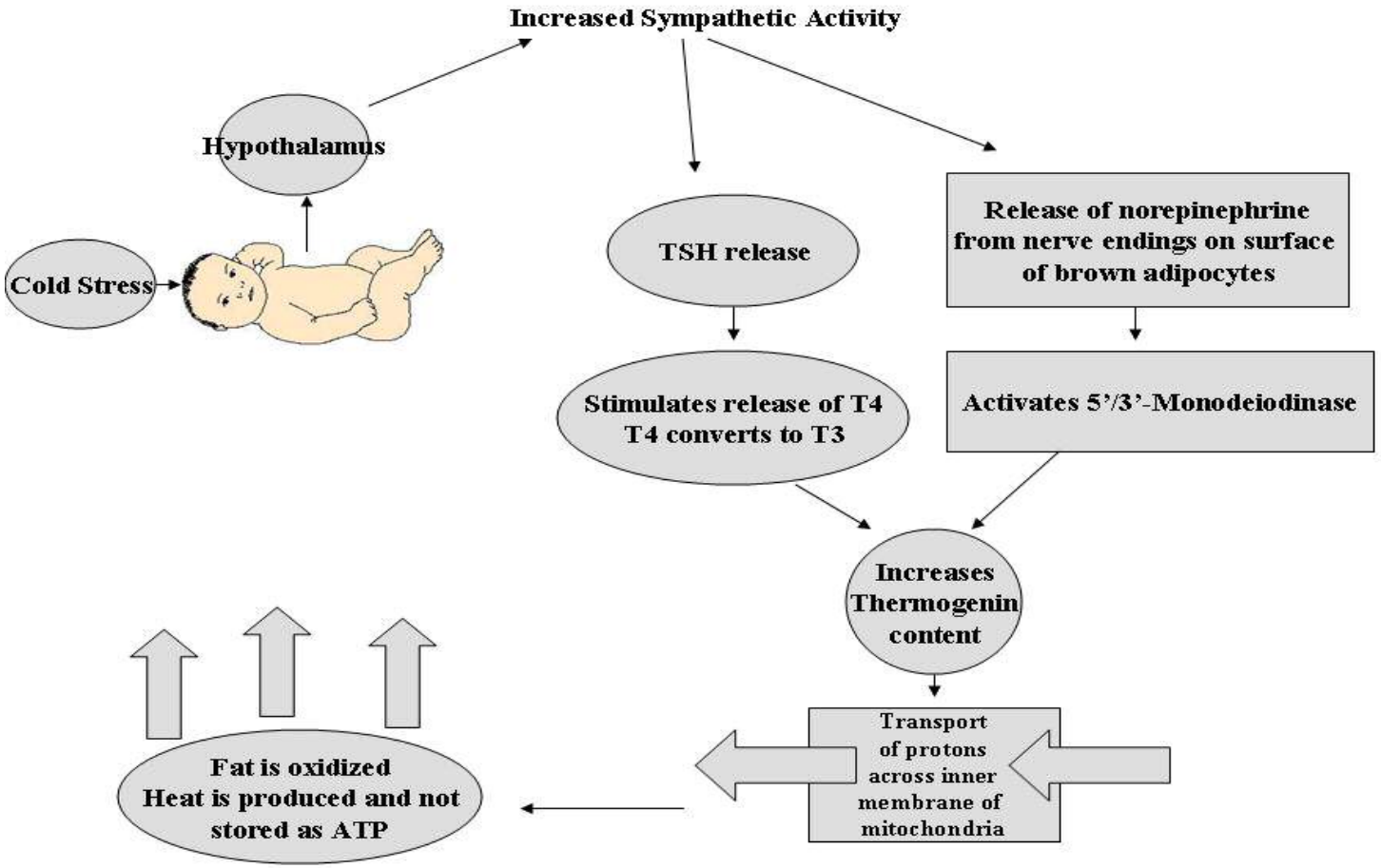
Non-Shivering Thermogenesis

Once the infant is delivered and the umbilical cord is clamped in the relatively cold delivery room, exposure to a cold environment will trigger non-shivering thermogenesis (see Figure 2.1). The infant's body temperature decreases and peripheral and central thermoreceptors detect change (Vander et al., 2001). The immediate response of the peripheral skin receptors in adults is to cause vasoconstriction of the peripheral vessels to diminish heat loss and inhibit sweating and shivering with a resultant increase in body heat production. The neonate lacks the ability to shiver and sweat; therefore, vasoconstriction is the predominant result of activation of peripheral skin receptors (Guyton & Hall, 2001). Central thermoreceptors send messages to areas of the hypothalamus located bilaterally in the posterior hypothalamus near the level of the mamillary bodies (Guyton & Hall, 2001). The anterior hypothalamic-preoptic area also transmits temperature signals into this posterior hypothalamic area. The hypothalamus serves as the primary overall integrator of hormonal and system responses because it is the single most important control area for homeostatic

regulation and has different pathways that form the master command center for neural and endocrine coordination. A peptide, neuropeptide Y, is abundant in the hypothalamus and at normal body temperatures may inhibit thermogenesis to maintain a normal body temperature and regulate energy homeostasis (Wilding, Widdowson, & Williams, 1997).

Because the effector mechanisms of skeletal muscle stimulation are minimal in the infant, the infant will not shiver in response to cold stress. Non-shivering thermogenesis is the predominant effector mechanism. An increase in sympathetic activity, controlled in the hypothalamic ventromedial nucleus, will cause norepinephrine to be released from the nerve endings that terminate on the surface of brown adipocytes, while simultaneously causing an increase in thyroid stimulating hormone (TSH). The catecholamine, norepinephrine, acts via adrenergic receptors, primarily type β3 but also via α1 receptors (Power, 1998). Cold stress also causes inhibition of synthesis of Neuropeptide Y, which allows thermogenesis (Billington, Briggs, Harker, Grace, & Levine, 1994). TSH stimulates the release of thyroid hormones, mostly T_4. Working simultaneously, norepinephrine activates 5'/3'-monodeiodinase, which causes T_4 to convert to T_3 (Barrett, 2003). In brown adipose tissue, T_3 generated locally acts to upregulate an uncoupling protein referred to UCP or Thermogenin. T_3 acts locally to uncouple mitochondrial oxidation from phosphorylation in the brown adipose tissue, causing heat production. Norepinephrine mediates the production of the second messenger, cAMP that activates cAMP-dependent protein kinase (Voet et al., 2002). The kinase activates the hormone-sensitive triacylglycerol lipase by phosphorylating it. The activated lipase hydrolyzes tricylglycerols to yield free fatty acids and glycerol (Power, 1998; Voet et al., 2002). Free fatty acid presence causes an inhibitory effect of purine nucleotides (ADP, ATP, GDP, GTP) on thermogenin.

Figure 2.1 Physiology of Non-shivering Thermogenesis



The major components of non-shivering thermogeneisis in infants are brown adipose tissue, thermogenin, and 5'/3'-monodeiodinase. Hatai (1902) first described brown adipose tissue in humans in 1902. Brown fat is a tissue with thermogenic capabilities, rich in mitochondria and blood supply innervated with sympathetic nerve fibers. Brown adipocytes arise from mesenchymal cells, which are associated with blood vessels and proliferate rapidly simultaneously with the blood vessels developing inside the brown fat (Nechad, 1986). Mitochondria develop and increase in size and number depending on the metabolic activity of oxidation in the tissue. During this time of development, sympathetic nerve fibers grow into the tissue and become densely innervated on the nerve endings of each blood vessel and each adipocyte (Sauer, 1995). Protein content increases considerably, as does mass of mitochondria in the tissue. The inner mitochondria membrane becomes specifically enriched with thermogenin, the rate-limiting enzyme in the process of heat production (Sauer, 1995).

Thermogenin is a 306-residue polypeptide chain protein (Bing, Frankish, Wang, Hopkins, Keith, Trayhurn, et al., 1996) that makes up approximately 15% of the protein in the inner mitochondrial membranes of brown adipose tissue (Voet et al., 2002). Thermogenin mRNA transcription probably only occurs in brown adipose tissue (Ricquier & Bouillaud, 2000). Signals activated after norepinephrine stimulation of brown adipose tissue strictly control thermogenin gene expression at the transcription level (Voet et al., 2002). Thermogenin is an H^+ channel protein located in the inner mitochondrial membrane of brown adipose tissue (Jones & DeCherney, 2003). Free fatty acids relieve the inhibition of H^+ channel and allow conduction of protons. This action allows the protons generated by electron transport to enter the mitochondrion through Thermogenin that dissipates the H^+ gradient needed by the H^+ translocating ATP synthase. Under physiological conditions, heat is produced by the

dissipation of an electrochemical H^+ gradient, which is generated by electron transport and uncoupled from ATP synthesis (Voet et al., 2002). Therefore, the mitochondria in brown adipose tissue can produce heat without storage of energy through ATP (Jones & DeCherney, 2003).

Brown adipose tissue is very vascular allowing stimulation by norepinephrine to cause a tremendous increase in blood flow to the tissue. It ccurs as discrete lobes, found predominantly in the interscapular, thoracic, and cervical regions, as well as beside the great vessels and contiguous with the spinal cord (Huttunen, 2002). It has a brown red color because of the rich vascularization and the presence of mitochondrial cytochromes. Brown adipose tissue quickly exports the heat to critical organs through the massive vascularization. Most brown adipose tissue deposits are deep, located next to internal organs, and supply heat by direct conductance. Some interscapular brown fat causes heat by vascular convection because of its superficial location. A high rate of brown adipose tissue thermogenesis requires high rates of blood flow to provide oxygen for metabolism and to remove heat.

In humans, T_4 is bound more tightly to plasma proteins than T_3, causing a net effect of two times the amount of free T_4 than T_3 in circulation (Barrett, 2003). Exposure to a cold environment triggers an increase in the levels of norepinephrine and TSH. TSH stimulates the release of T_4, which is converted to T_3 because of the enzyme 5'/3'-monodeiodinase in the brown adipose tissue. The conversion of T_4 to T_3 is crucial for the thermogenic response (Sauer, 1995) because T_3 locally acts to upregulate thermogenin leading to heat production (Voet et al., 2002).

All infants retain the capacity for non-shivering thermogenesis up to 6-12 months of age. However, preterm infants may be unable to meet heat loss demands from exposure to a cold

environment quickly enough to prevent a fall in body temperature. Low birth weight (less than 2500 grams) and preterm infants are more susceptible to stress from a cold environment than term infants because of greater heat exchange with the environment and because non-shivering thermogenesis becomes inefficient before about 30-32 weeks gestational age due to less thermogenin and 5'/3'-monodeiodinase content.

Developmental Properties Related to Non-shivering Thermogenesis

Brown adipose tissue begins to develop as early as the 75 mm fetal stage (Hatai, 1902). Hull (1977) calculates that 20-30 grams of brown adipose tissue are necessary to handle all the observed non-shivering thermogenesis of a newborn baby. Studies have shown that the structure of brown adipose tissue is well developed in the preterm infant as early as 25 weeks gestational age (Sauer, 1995), with brown fat comprising about 1-2% of body weight (Nechad, 1986). However, brown adipose tissue is not the only essential element for non-shivering thermogenesis. The specific content of thermogenin in infants increases from 29.4 ± 3.3 pmol/mg at 25 weeks gestational age to 62.5 ± 10.2 pmol/mg at 40 weeks gestational age (Houstek et al., 1993). A major increase in thermogenin occurs at 32-weeks gestational age, which is approximately the time when a neonate can effectively use non-shivering thermogenesis to generate heat adequately. The enzyme 5'/3'-monodeiodinase is active by 25 weeks gestational age and increases fourfold by term. A major increase in this enzyme also occurs at 32 weeks gestational age (Houstek et al., 1993). The low levels of thermogenin content and 5'/3'-monodeiodinase content prior to 32 weeks gestational age are the likely causes of inefficient non-shivering thermogenesis.

Because non-shivering thermogenesis is inefficient, preterm infants less than 30-32 weeks gestational age are more susceptible to cold stress from cold environments. Cold stress is

more likely during transition, when the infant is delivered from the warm intrauterine environment to the cold, drafty environment of the delivery room. The newly born infant is covered in amniotic fluid; therefore much heat is lost quickly by evaporation. Hammarlunc and Sedin (1979) found transepidermal water loss in infants to be inversely correlated with gestational age possibly because more premature infants have thinner skin. Transepidermal water loss is 15 times higher in infants born at 25 weeks gestational age than in term infants; therefore, heat loss would be proportionate to this evaporation of water through the skin. The high evaporative heat losses in preterm infants during the first few hours of life and even first few days will gradually decrease with advancing postnatal age (Sedin, 1995). Lyon et al (1997) found that infants with birthweight less than 1000 grams (usually less than 28-29 weeks gestational age) did not exhibit peripheral vasoconstriction in response to cold stress before 29 hours of age; however, Horns (2002) found ELBW infants spent about 20% of their time trying to vasoconstrict in response to cold stress. Radiative heat losses are initially low immediately after birth in preterm infants 25-27 weeks gestational age but become the most important route of heat transfer after the first postnatal week (Sedin, 1995). In infants older than 28 weeks gestational age, heat loss from radiation is most important route of heat transfer from birth onward. The heat loss through radiation gradually increases with age. For an infant 25-27 weeks gestational age, evaporative heat loss transfers the most heat during the first 10 days of life, if the infant is in a dry environment. If the infant is kept in an environment of 60% humidity, heat loss will be much lower and a greater heat loss will result from radiation from the fifth day of life onward (Sedin, 1995).

Neonatal Hypothermia

Hypothermia, or a low body temperature, can lead to a syndrome in infants characterized by slowness of movement, refusal to eat, lethargy, edema, and often sclerema (Sinclair, 1992) as described by Mann (1955) and Elliot (Mann & Elliot, 1957). The syndrome results from prolonged exposure to a cold environment, especially during the transitional period. Hypothermia has been associated with a fall in systemic arterial pressure, a decrease in plasma volume, decreased cardiac output, increased peripheral resistance, and metabolic acidosis (Sinclair, 1992).

No studies have specified the body temperature that defines hypothermia for infants. Some early researchers exposed preterm infants (1120- 2270 grams) at less than 24 hours of age to environmental temperatures of 21-23º C and found an increase in oxygen consumption (Adams et al., 1964; Bruck, 1961). Bruck (1961) also noted that body temperature fell more rapidly for preterms than for term infants when they were in an environment with a temperature of 28º C. Research in which infants were deliberately exposed to colder temperatures was only done in the 1950-1960's. Studies at that time linked exposure to cold to increased mortality (Buetow & Klein, 1964; Day et al., 1964; Silverman et al., 1958), and it is no longer ethical to deliberately expose preterm infants to cold environmental temperatures. Yet cold body temperature, or hypothermia, continues to be a problem for ELBW infants (Horns, 2002; Knobel et al., 2005; Loughead et al., 1997; Thomas, 2003).

Nurse researchers have shown that ELBW infants continue to have cold stress in today's technologically advanced NICUs (Horns, 2002; Knobel et al., 2005; Loughead et al., 1997; Thomas, 2003). Knobel (2003) and Loughead et al., (1997) found 66-93% of ELBW infants were admitted to the NICU with hypothermic temperatures. Horns (2002) found 90% of her ELBW sample had extremely cold peripheral temperatures when cared for in the controlled

environment of an incubator. Thomas (2003) found temperatures of preterm infants as low as 33.1º C associated with caregiver interventions occurring while the infant remained in an incubator.

Neonatal Hyperthermia

An infant with a body temperature greater than 37.5º C is said to be hyperthermic (LeBlanc, 2002). Because ELBW infants have immature thermoregulation, thin skin and a large body surface area to weight ratio, they can also take on too much heat from a heat-enriched environment and become hyperthermic (too high a body temperature). Preterm infants can be prone to overheating due to large surface area, limited insulation, and limited sweating ability (Jones & DeCherney, 2003; Guyton & Hall, 2001; Thomas, 1994). Full term infants and larger preterms (35-37 weeks gestation) are able to sweat and raise their evaporative losses; however, the maximal sweating rate is related to gestational age (Sulyok, Jequier, & Prod'hom, 1973). The set-point temperature for sweating tends to be lower with increasing gestational age, and Sulyok et al. (1973) found sweating rates for larger preterm infants were found to be 1.43 W/kg compared to full term infants who had a rate of 1.81 W/kg. They measured sweating rates in watts (W) with 1 W = 14.334 calories/minute = 0.860 Cal/hr = 2.975 ml of oxygen consumed per minute.

Hypothalamic thermoreceptors sense an increase in body core temperature and compare this temperature with a reference signal, then direct neural output to activate heat dissipation (Nadel, 2003). Skin blood flow and sweating will increase as core temperature increases, prompting an increase in the rate of heat transfer to the environment. The capacity to elevate skin blood flow is an essential defense against hyperthermia. ELBW infants have little

ability to vasoconstrict peripherally (Horns, 2002; Lyon et al., 1997); therefore, it is likely that their ability to vasodilate is also inefficient.

Hyperthermia may be associated with fever in term infants related to infection; however, early onset infection is likely to coincide with normal temperatures after birth for term infants and with hypothermia in preterms (Weisman, Stoll, & Cruess, 1992). Preterm infants with hyperthermia are most likely overheated due to iatrogenic heat transfer. Horns (2002) found temperatures as high as 38.7º C associated with caregiver interventions with infants in incubators, with some incubator temperatures recorded as being high as 40.49ºC.

Neonatal Mortality Due to Cold Stress

In early research, Silverman et al. (1958) exposed infants to "hypothermic" environments of 28.3-29.4º C. Sinclair (1995) conducted a secondary analysis on Silverman et al.'s data and found that the warmer incubator environment prevented one death for each six infants treated. In the Silverman study, 28 of 91 infants weighed less than 1,000 grams. Buetow and Klein (1964) and Day et al. (1964) found that maintaining abdominal body temperature servo control at 36º C produced an overall reduction of one death for each five infants treated, as calculated by Sinclair (1995). These studies examined infants 800-1,599 grams in weight.

Several confounding factors were associated with these early studies. Infants during this era of treatment were not ventilated on a respirator, rather treated for respiratory insufficiency with blow by oxygen or chambers with free flow oxygen. Oxygen consumption was measured with infants in a climitized oxygen chamber, while they were exposed to the colder environments. Today most preterm infants with immature lungs would receive treatment by ventilator; therefore oxygen consumption measurements may be differ

from these early studies. Undoubtedly, many infants in the early hypothermia and mortality studies also experienced respiratory distress syndrome because of their preterm gestation, thereby increasing their chance of mortality because of inadequate treatment of respiratory distress. In addition, infants during that time were "starved and thirsted" for 24-48 hours after birth as standard practice (Sinclair, 1995), unlike the current practice of hydration immediately following birth.

Current ethical standards prevent research in which an infant is deliberately exposed to a cold environment. However, if those studies were conducted today, the absolute reduction in mortality would likely be less because today infants are adequately hydrated and treated for respiratory distress. One modern retrospective study examined mortality rates of hypothermic (axillary temperature < 35º C) term and preterm infants and found that hypothermia in preterms was not associated with increased mortality (Hazan et al., 1991).

Technology does not exist today to adequately measure oxygen consumption, using indirect calorimetry in transitional, intubated preterms (personal communication, Thureen, April 2003), because ELBW preterms have very low tidal volumes (5-7cc/kg; Gomella, 1994). Also, no metabolic cart currently on the market can measure tidal volumes as low as 5-7cc/kg. Therefore, using oxygen consumption as the primary outcome to be correlated with low body temperatures, as was done in early research, is impossible. Most ELBW infants are intubated and ventilated, so oxygen consumption cannot be evaluated in the presence of hypothermia until a metabolic cart is developed to measure very low tidal volumes.

Neonatal Hypothermia and Morbidity

Neonatal hypothermia, or low body temperature, can lead to increased morbidity. System homeostasis is interrupted when cold exposure leads to non-shivering thermogenesis, or brown fat metabolism, in the preterm infant (Adams et al., 1964; Bruck, 1961; Malin & Baumgart, 1987; Voet et al., 2002). If the infant is mature enough (gestational age of 30-32 weeks or greater) a good possibility exists that heat production will exceed heat loss and system homeostasis will be maintained; therefore the infant will not experience hypothermia (Bruck, 1961; Vohra et al., 1999). However, because ELBW infants (usually less than 28-29 weeks gestational age) have inefficient non-shivering thermogenesis (Houstek et al., 1993), heat loss is likely to exceed heat production and the infant's body temperature will continue to decrease unless nursing intervention succeeds in raising body temperature (Bjorklund & Hellstrom-Westas, 2000; Knobel et al., 2005; Vohra et al., 1999; Vohra et al., 2004).

Hypothermia is most likely to occur during the unstable transitional period. Oxygen consumption has been shown to increase because of energy used in generating non-shivering thermogenesis (Adams et al., 1961; Malin & Baumgart, 1987). In an ELBW infant, or preterm infant who has a compromised respiratory status, this increased oxygen consumption can lead to acidosis and increased glucose utilization. If left unchecked, these conditions can lead to permanent tissue damage, brain damage or death (Cowett, 1985; Deshpande & Platt, 1997). These conditions are even more likely during the transition period when the preterm infant is attempting to adapt from intrauterine to extra-uterine life. The extreme immaturity of the ELBW infant during transition also potentiates these conditions. Therefore, when ELBW infants are exposed to cold environmental temperatures, most likely they will develop

increased oxygen consumption, increased acidosis, increased glucose utilization, and increased heart rate.

Oxygenation and Non-shivering Thermogenesis

Exposure to cold triggers heat production through aerobic metabolism which fuels non-shivering thermogenesis (Jones & DeCherney, 2003). Aerobic metabolism depends on a constant supply of oxygen (O_2) (Delivoria-Papadopoulos & McGowan, 1998). Molecular O_2 is the final electron acceptor in the mitochondrial chain, in which energy is ultimately released as heat (Voet et al., 2002). Birth and the transition period stress the oxygen transport system more than any other periods in life do (Delivoria-Papadopoulos & McGowan, 1998) because the lungs and heart must adapt to extra-uterine life. The O_2 transport system depends on inspired oxygen content, lung ventilation, cardiac output, blood volume, hemoglobin concentration, and the affinity of hemoglobin for oxygen (Delivoria-Papadopoulos & McGowan, 1998).

ELBW infants are born with surfactant-deficient lungs, resulting in poor ventilation (Jones & DeCherney, 2003). These infants require supplementary and pressurized oxygen from a ventilator. During the transition period, term infants have 77-84% fetal hemoglobin (Kirschbaum, 1962); ELBW infants have an even higher percentage. Fetal hemoglobin allows oxygen to bind tightly to the hemoglobin molecule (Delivoria-Papadopoulos & McGowan, 1998). Because fetal hemoglobin has an increased affinity (tighter bond) for oxygen, blood does not easily release oxygen to the tissues. Preterm infants have a smaller oxygen unloading capacity for the first three months than term infants, resulting in increased potential for impaired tissue oxygenation (Guyton, 1971). Cold exposure results in an increased oxygen need to fuel non-shivering thermogenesis.

Acid-base Balance and Non-shivering Thermogenesis

When ELBW infants become hypoxic due to immature lungs and inadequate oxygenation and ventilation, they reach a point at which oxygen delivery to the tissues is too low to sustain aerobic metabolism (Seri, 1998). When tissue oxygenation is impaired and oxygen needs are too great, the body switches to anaerobic metabolism. Anaerobic metabolism uses pyruvate instead of oxygen to generate lactate. ELBW infants are unable to handle increased levels of lactate and become acidotic (Seri, 1998). With preterm lungs and a need for increased oxgyenation due to cold stress, ELBW infants may develop hypoxemia (low blood oxygen content); and continued hypoxemia leads to acidosis.

Non-shivering thermogenesis increases the need for oxygen causing a cellular oxygen deficit. Tissues switch to anaerobic glycolysis to meet energy needs (Voet et al., 2002). Anaerobic glycolysis causes an increase in lactic acid production (Deshpande & Platt, 1997). Preterm infants have a severely limited threshold for bicarbonate reabsorption and are unable to compensate for metabolic acidosis. Infants with preterm lungs have limited ability to eliminate acid through increased respirations. Renal compensatory mechanisms take 2 to 3 days post birth to develop and urinary excretion of acids increases as a function of gestational age and postnatal age (Seri, 1998). Therefore, the metabolic acidosis due to cold stress can lead to an increased chance of death (Deshpande & Platt, 1997; Richardson, Corcoran, Escobar, & Lee, 2001).

Blood Sugar and Non-shivering Thermogenesis

Cold stress may also cause the ELBW infant to deplete glycogen stores, resulting in hypoglycemia. Fetal glucose supply depends on maternal stores of glucose, and at birth this source abruptly ceases (Cowett, 1985). The liver is a source of plasma glucose by

synthesizing glucose and generating glucose from the breakdown of glycogen (Hardikar & Suchy, 2003). In gluconeogenesis, the liver's most important function, glucose is synthesized from precursors such as lactate, pyruvate, glycerol, and amino acids (Burrrin & Price, 1985). Glycogenolysis is the process that delivers glycogen stored in the liver from maternal glucose to the blood plasma as glucose (Hardikar & Suchy, 2003). ELBW infants also receive glucose by dextrose infusion upon admission to the neonatal intensive care unit (NICU).

During the instability of the transitional period, ELBW infants are likely to use anaerobic glycolysis to provide additional oxygen because brown fat metabolism will consume oxygen that might otherwise be available for aerobic glycolysis. This process requires glucose to be broken down to pyruvic acid, decreasing the blood plasma supply of glucose. As a result, an ELBW infant with cold stress is likely to exhibit hypoglycemia. The brain requires a constant supply of glucose, and severe hypoglycemia can lead to seizures and even death (Cowett, 1985).

Heart Rate and Non-shivering Thermogenesis

The relationship of cold stress to heart rate has not been well studied. The normal neonatal heart rate in preterm infants can range from 100-180 bpm (Sansoucie & Cavaliere, 2003). Increased sympathetic input to the heart increases heart rate (Anderson, Kleinman, Lister & Talner, 1998). Cold exposure causes the hypothalamus to increase norepinephrine release, leading to brown fat metabolism and heat production (Nedergaard, Golozoubova, Matthias, Asadi, Jacobsson & Cannon, 2001). Cooling of the sheep fetus in utero and outside the uterus has been shown to increase heart rate, blood pressure and norepinephrine concentration, consistent with sympathoexcitation (van Bel, Roman, Iwamoto, & Rudolph,

1993). Therefore, cold stress should lead, at least initially, to increased norepinephrine release and increased heart rate in infants.

Current Recommendations: Thermal Care of the Preterm Infant.

Current recommendations for thermal care for the preterm infant have improved as research has found new ways to guard against cold stress. Research has determined that caring for preterm infants under radiant warmers and in incubators can reduce cold stress and evaporative losses (Baumgart, 1987; Bell & Rios, 1983; LeBlanc, 1982; Yashiro et al., 1973), with some studies using servo control and setting the desired skin temperature (Buetow & Klein, 1964; Day et al., 1964; Malin & Baumgart, 1987; Meyer, Payton, Salmont, Hutchinson & de Klerk, 2001).

Yashiro et al. (1973) conducted an early study evaluating convective and radiant heat in improving the body temperature of infants, finding that both types of heat would increase the body temperatures of infants to above 36º C. Baumgart (1987) found that infants nursed in an incubator with convective heat had lower convective heat losses compared to infants nursed under radiant warmers. LeBLanc (1982) also found that infants' oxygen consumption was less when nursed in incubators rather than radiant warmers. Bell and Rios (1983) found that manual air temperature control could be just as effective in maintaining a warm environment and body temperature for infants as using the servo temperature control in which an infant's body temperature is controlled by a computer.

Buetow and Klein (1964) found that infants controlled at a body temperature of 36º C or more for the first 96 hours had a significantly greater chance of surviving. Day, Caliguiri, Kamenski and Erhlich (1964) found lower mortality in infants heated to maintain an abdominal temperature at 36º C compared to infants given constant heat at 31.8º C regardless

of their temperature. Malin and Baumgart (1987) found that an abdominal temperature of at least 36.5º C, rather than lower temperatures, kept oxygen consumption to a minimum for preterm infants. Meyer et al. (2001) found maintaining abdominal temperatures at a target temperature of at least 36.8º C under a radiant warmer was easier than in an incubator during the first 24 hours of life.

These researchers contributed very valuable changes to the thermal care of preterms, greatly reducing radiative, evaporative, conductive, and convective heat loss. Caring for preterms less than 32-34 weeks gestational age or less than approximately 1500 grams, in an incubator or on a radiant warmer is the current standard of care. However, researchers have given no clear indication about how they selected their control points for environmental temperature or body temperature, and most of these early studies were done on infants weighing more than 1,000 grams. None of the studies evaluated the physiological effects of differing body temperatures specifically on ELBW infants, the very group that needs the most thermal support.

Thus, neonatal nurses have little information to apply to the thermal care of ELBW infants. A current neonatal nursing text recommends trying to achieve thermoneutrality for normal growth and to meet the infants' energy needs (Kenner, 2003). The thermal neutral environment is generally 32-33.5º C for term infants, 34-35 º C for preterm infants greater than 30 weeks gestational age, and unspecified higher temperatures for infants less than 30 weeks gestational age (Blackburn, 2003). One nursing text states that what constitutes a normal range for preterm infants is not precisely known and needs further research (Kenner, 2003). Because an optimal body temperature range has not been specified for preterm

infants of different gestational ages determining the appropriate temperature during transition for ELBW infants is difficult (Kenner, 2003).

Nursing and medical texts recommend using radiant warmers and incubators to decrease evaporative losses and promote conductive gain (Bell & Glatzl-Hawlik, 1998; Blackburn, 2003; Kenner, 2003), however, no text gives precise control points. Various researchers have recommended plastic wrap as a way to reduce evaporative and convective heat losses in the NICU (Baumgart, 1984; Baumgart et al.,1982; Knauth et al., 1989) and in the delivery room (Besch et al., 1971; Bjorklund & Hellstrom-Westas, 2000; Knobel et al., 2005; Vohra et al., 1999; Vohra et al., 2004). Placing ELBW infants in plastic bags just after delivery has been especially helpful in reducing initial hypothermia in this gestational age group (Bjorklund & Hellstrom-Westas, 2000; Cramer, Wiebe, Hartling, Crumley, & Vohra, 2005; Knobel et al., 2005; Vohra et al., 1999; Vohra et al., 2004); however this procedure has not been adopted as the current standard of care because of the limited publication of these studies.

Consequently, nurses are without specific thermal guidelines for ELBW infants. This lack of information can be especially detrimental during the transitional period when cold stress is likely following delivery and stabilization of the infant. Unless heat loss can be prevented, attempting to produce heat could potentially stress system homeostasis (balance of normal oxygenation, acid-base, glucose, and heart rate) for the ELBW infant in transition. Guidelines are needed for a specific body temperature range for the ELBW infant during transition so that cold stress does not cause harm to physiological homeostasis. This range probably varies with gestation similar to the ability to generate non-shivering thermogenesis (Houstek et al., 1993).

CHAPTER THREE

Methods

This study used an exploratory, multiple case study design to explore the relationships between body temperature and oxygenation, heart rate, peripheral vasoconstriction, blood glucose and acid-base balance in ELBW infants. To determine the appropriateness of the planned methods, a pilot study of one infant was first conducted to assess for need for modifications, however, no modifications were needed.

Setting

The study was conducted at Pitt County Memorial Hospital, University Health Systems of Eastern Carolina in Greenville, NC. Enrollment and data collection took place in the 50-bed tertiary neonatal intensive care unit (NICU) of this hospital. Mothers gave consent (Appendix I) within the labor and delivery unit at Pitt County Memorial Hospital after they were admitted in preterm labor. The NICU admits 800 preterm infants annually, of which 13% are ELBW. These infants are about 65% African American, 34% White, and 1% Hispanic and Asian infants (Knobel, 2003). An interdisciplinary team consisting of a nurse, an attending neonatologist, a neonatal nurse practitioner, a respiratory therapist, a social worker, residents, a pharmacist and a nutritional expert provided medical and nursing care. The study used observation and standard monitoring to avoid interrupting the care of the infant.

Subjects

The subjects for the study were 11 ELBW infants (see Table 3.1). One infant was excluded from analyses because of equipment failure: the heart rate and saturation did not record into the laptop computer. Therefore, an additional infant was enrolled for analyses. Sample size was set at 10 in order to have a sample large enough to have representation of various weights, genders, and races of ELBW infants while maintaining a sample size small enough to permit detailed within-subject analyses. Inclusion criteria were a birth weight between 500-1,000 grams, gestational age by obstetrical by ultrasound if available or dates if not on admission to the labor and delivery unit between 23-28 6/7 weeks, and delivery at Pitt County Memorial Hospital. Infants with visible anatomical anomalies were to be excluded because they may have required emergent surgical care; however, none had such anomalies.

Given the low number of admissions of ELBW infants, all mothers in labor with infants expected to be born less than 28 weeks gestational age were to be approached. Because the infants admitted at the NICU at Pitt County Memorial Hospital are about 65% African American and 34% White, I attempted to enroll a subject mix of five to seven African American infants and three to five White infants, equally divided by sex. The sample analyzed included six African American infants and four White infants. The sample should have been about 50% male but because infants were enrolled prior to delivery, there was no way to be certain of the gender distribution. However, gender should not have affected the physiological variables in this study. The sample consisted of six females and four males.

Instrumentation

The study examined 10 variables: five primary variables (oxygen saturation, heart rate, abdominal and peripheral temperatures and peripheral vasoconstriction) that were measured

by physiological monitors, two secondary variables measured by observation (O_2 requirement and stimulation), and three secondary variables (pO_2, pH, glucose) measured by chart review (see Table 3.2). The standard monitors in the NICU at Pitt County Memorial Hospital used in the study were the Spacelabs Clinical Workstation cardiopulmonary monitor, Nellcor Pulse Oximeter, and Lifescan Glucometer. A Mini-Logger (Mini Mitter, Oregon) monitor was used to obtain foot and abdominal temperatures by thermistor probe. Thermistor probes were already used in this NICU, but they were attached to the Giraffe incubator/warmer to control the environmental heat by monitoring the infant's skin temperature. The research thermistor probe was easily positioned next to this probe.

Table 3.1 Study Sample Demographic Characteristics

Number	Gender	Ethnicity	Gest. age	Weight in gms	Delivery Mode	Apgar Scores
170	Female	African American	25	630	Csect	1,5,7
240	Male	African American	24	680	Vag	1, 7
311	Female	White	25	550	Csect	1,2,6
320 (excluded)	Male	African American	25	710	Csect	5,7
360	Male	African American	26	880	Vag	8,8
410	Female	White	25	720	Csect	4,7
450	Female	African American	25	670	Vag	2,4,6
510	Female	White	26	510	Csect	4,8
590	Male	African American	25	710	Vag	1,5,7
680	Male	White	24	590	Csect	2,6
730	Female	African American	26	960	Vag	4,5

Much of the routine instrumentation for ELBW infants at Pitt County Memorial Hospital NICU was used for data collection in this study. Each infant was placed on a Giraffe radiant warmer, which converted to an incubator after stabilization. The warmer was equipped with

a computerized heat control system. In the Pitt County Memorial Hospital NICU, nurses place the warmer control on manual at maximum heat output to prepare for an ELBW infant admission. Once the infant was placed on the warmer and monitors were attached, the nurse set the control temperature at about 36.5º C. However, no protocol directed the selection of a control point for body temperature. Each infant was attached to a ventilator which

Table 3.2 Instrumentation Used in Evaluating Physiological Effects of Body Temperature Variation

Variable	**Instrument**	**Measurement**
Oxygen saturation	Nellcor pulse oximeter	Continuous: Nearest one percentage
Heart Rate Trend	Spacelabs Clinical workstation	Continuous: Heart rate to nearest beat, average for 1 minute.
Abdominal temperature	Mini-Logger Thermistor	Continuous: to nearest 10th degree Centigrade
Peripheral foot temperature	Mini-Logger Thermistor	Continuous: to nearest 10th degree Centigrade
Peripheral Vasoconstriction	Abdominal-peripheral difference	Δ T = % time when $T_c - T_p > 2º$ C
Glucose: blood glucose	Lifescan Glucometer	Periodic measurement as ordered by medical providers
Arterial blood pO_2	Blood gas analyzer output	Periodic measurement as ordered by medical providers to nearest mmHg
Acid-base balance: blood pH	Blood gas analyzer output	Periodic measurement as ordered by medical providers to nearest hundredth degree of pH units
Covariate	**Instrument**	**Measurement**
Blood Pressure	Spacelabs Clinical workstation	If available, continuous: Arterial BP to nearest 1 degree of mHg
Stress Stimulation	Observation	Continuous: start and stop times of infant stimulation
Oxygen Requirement	Observation	Periodic recording: FIO_2 ventilator delivery every 5 min.
Medical Record Review	Medical Chart	Review of medical chart: demographic and disease data

provided oxygen and pressurized breaths. Nurses added water to the incubators to raise the humidity to between 60-80%. Infants were routinely placed on a cardiopulmonary monitor and attached to a pulse oximeter, which displays oxygen saturation. Nurses obtained blood from an umbilical catheter for arterial blood gas readings. They also checked blood glucose with a glucometer using a chemstrip at the bedside.

Temperature

Nurses routinely measured body temperature using an electronic thermometer under the axillae every 4-6 hours. Abdominal and peripheral temperatures were measured by a Mini-Logger Monitor (Mini Mitter, Oregon) using a thermistor, the preferred method for temperature measurement in research (Thomas, 1993). Accuracy of the thermistor was calibrated in the factory before each probe was packaged. A new probe was opened and used for each infant to reduce the possible infection risk from reusing or calibrating probes on site. The Mini-Logger Monitor was used to measure abdominal temperature by a thermistor probe attached to the infant's abdomen because in clinical practice, abdominal temperature is commonly used to represent central temperature (Simbrunner, 1995) and warmer probes are routinely secured to the infant's flank, to avoid invasive trauma caused by inserting probes into the rectum (Bailey & Rose, 2000). The temperature probe was placed in a keyhole cutout in a piece of duoderm secured to the infants' skin. Duoderm allows for a heat reflective tape to be placed over the probe to secure the probe in place on the infants' skin without actually touching the fragile skin with adhesive tape. The foot temperature probe was also secured under a piece of duoderm to avoid using adhesive tape to secure the probe to the skin. All temperatures were sampled at one measurement per minute and recorded using Mini-Logger software on a laptop computer.

The Mini-Logger Monitor was also be used to measure the peripheral temperature using a thermistor probe attached to the sole of one foot (Simbrunner, 1995). Peripheral vasoconstriction was assessed by taking the difference between the abdominal and peripheral temperatures (Simbrunner, 1995). A change in peripheral temperature that occurs before an alteration in the abdominal temperature is an early sign of thermal stress. Larger differences (> 2º C) indicate vasoconstriction (Lyon et al., 1997). This method permitted the determination of whether ELBW infants react to cold stress by peripheral vasoconstriction.

Oxygenation

Because production of heat takes place by increasing metabolism through metabolism of brown fat, oxygen consumption is a proxy for non-shivering thermogenesis. Because brown fat metabolism cannot be directly measured, oxygenation was measured continuously using the proxy of O_2 saturation. Periodic measurements of pO_2 were recorded to examine any trends related to temperature; however, these comparisons were only exploratory and used for future direction because of the sporadic nature of collection. Nurses routinely obtained arterial blood gases in ELBW infants every 1-6 hours by drawing arterial blood samples through umbilical arterial catheters. The desired range of pO2 levels for a preterm infant is 40-100 mmHg (Paky & Koeck, 1995; Poets & Southall, 1995).

Oxygen saturation was measured continuously by Nellcor Pulse Oximeter and inputted into the Spacelabs Clinical Workstation. The pulse oximeter measures oxygen saturation of hemoglobin by emitting two specific wavelengths of light through the tissue of the infant's extremity, which correlates with the proportion of oxygenated to deoxygenated hemoglobin in the tissue (Poets & Southall, 1994). The monitor then gives the percentage of oxygenated hemoglobin. Oxygen saturation readings were recorded into the Spacelabs monitor and

outputted into the computer through the use of a datalogger option. The datalogger program connects to the laptop using the Hyperterminal program to record oxygen saturation every minute. Analyses used oxygen saturation measurement means for each 1-minute interval. The normal oxygen saturation range measured by pulse oximetry for preterm infants should be 92-96%; however, it can go as high as 100% (Ng, Subhedar, Primhak, & Shaw, 1998; Paky & Koeck, 1995; Poets, 1998 Rey, 2004). For data analyses of these study questions, normal oxygen saturations were defined as 92-100%.

Acid-Base Balance

Acid-base balance was measured through periodic measurement of arterial blood for blood gas analysis. Nurses routinely assessed arterial blood pH every 1-6 hours by drawing a sample of blood from the umbilical catheter. Periodic measurements of pH were recorded to examine any trends related to temperature; however, these comparisons were only exploratory and used for future direction because of the sporadic nature of collection. Generally, normal plasma pH should be 7.35 to 7.45 (Askin, 2002; Seri, 1998); however, the critical level of acidosis in a preterm infant is 7.20 (Deshpande & Ward, 1997).

Blood Glucose

As clinically indicated, the nurse measured blood glucose using a Lifescan (Johnson & Johnson company) glucometer. These measurements were obtained when clinically indicated and ordered by the care provider. Readings were obtained by the research observer from the medical record. Periodic measurements of glucose were recorded to examine any trends related to temperature; however, these comparisons were only exploratory and used for future direction because of the sporadic nature of collection. Normal glucose for a preterm infant should be above 45 mg/dL (Cornblath et al. 2000).

Heart Rate Trends

Heart rate was measured using a routine cardiopulmonary monitor, Spacelabs 90385 Clinical Workstation. Heart rate was recorded continuously and sampled at a rate of 12 samples per minute, then the outputted directly from the Spacelabs Monitor to the laptop computer through the datalogger option and using Hyperterminal communications program. Analyses used mean heart rate over each 1-minute interval. When I attempted to record the heart rate from the umbilical arterial signal, the heart rate would not transfer into the communications program through datalogger; therefore, using limb-leads for the 12-hour study period to collect heart rate data was always necessary. The normal heart rate range for each infant was defined as the heart rate data 25^{th} and 75^{th} percentile limits specific for each infant found in the analyses of heart rate data for the 12-hour study period.

Blood Pressure Reading (Covariate)

Arterial blood pressure was recorded with the Spacelabs monitor through a pressure transducer attached to the umbilical arterial catheter (standard measure for ELBW infants at Pitt County Memorial Hospital NICU) when an umbilical line was in place. This reading was recorded continuously into the Spacelabs Monitor and sampled at a rate of 12 measures per minute, then outputted to the laptop computer through the datalogger option using the Hyperterminal communications program. Blood pressure means for each 1-minute interval were recorded in case they were needed as a possible covariate. If the infant suddenly became hypotensive, oxygenation, pH, and heart rate may have been affected.

Observation of Stimulation and Oxygen Requirement (Covariates)

A research assistant or I sat at the infant's bedside and observed for stimulation and oxygen requirement. Because all touching stimulation to the infant may affect thermoregulation, any

physical touching of the infant whether to conduct medical or nursing procedures or for parental visitation was recorded. The observer recorded start time and stop time of the stimulation onto the data collection sheet (Appendix III). A research assistant or I also observed and recorded oxygen delivered to the infant by the ventilator, CPAP or nasal cannula. An oxygen analyzer was attached inline (standard in Pitt County Memorial Hospital NICU) to the ventilator, giving a percentage of oxygen reading on a monitor. The observer recorded the reading every 5 minutes because the reading was unlikely to change significantly in less than 5 minutes. The amount of oxygen delivered by the ventilator (oxygen requirement) was recorded in case it was needed as a covariate because oxygenation might have needed to be interpreted in light of how much oxygen the infant was receiving.

Observational measures were recorded in 6-hour shifts by two research assistants and/or me. Inter-rater reliability was checked by dual scoring of a 30-minute period between the two 6-hour shifts. Inter-rater reliability was assessed by Cohen's kappa (Cohen, 1960). Kappa scores were calculated for each variable across infants and were as follows: infant servo control temperature (ISC) 0.96, air temperature of incubator 0.96, ventilator temperature 0.88, oxygen delivered to infant (FiO_2) 0.98, humidity in the incubator 0.90, and presence of stimulation to the infant 1.0. The recorder was able to take 5-minute breaks away from the bedside as needed when the infant was not being touched. Observational measures were collected to provide clinical information to reference with physiological data.

Medical Record Review (Descriptive Information)

I reviewed each infant's medical record for demographic data (name, sex, birth weight, gestational age, birth history (vaginal or cesarean delivery, Apgar score [Apgar, 1953], time of delivery, treatments in the delivery room, time of NICU admission) and disease history

(medical diagnoses, treatments during the first 12 hours of life, laboratory values collected during the first 12 hours) for case description on the demographic data sheet (Appendix II). The review occurred after physiological data collection was complete. Medical chart review occurred in the NICU at PCMH with data being recorded on data collection sheets (Appendix III), which were identified only by a patient study number.

Procedures

A pilot study was done with one subject to test procedures, monitoring devices, and data collection. After Institutional Review Board approval from University of North Carolina, Chapel Hill and East Carolina University/Pitt County Memorial Hospital, one mother was approached to consent for her infant. After one subject was enrolled and data collection was completed for the 12-hour study period, I met with my dissertation chair and with the doctors on staff at Pitt County Memorial Hospital NICU to discuss procedures and monitoring devices. No modifications were needed. Therefore, this subject's data were included in the sample for this study.

Potential subjects were identified through my daily visits to the labor and delivery unit at Pitt County Memorial Hospital. Either the charge nurse of the NICU or labor and deliver unit notified me of mothers in labor with an infant less than 28-weeks gestation. I would talk with the mother and family, if present, specifically about the study after I had given her or them a typical NICU consult educational talk, which is part of the job of the neonatal nurse practitioners at this hospital. If I was working as a neonatal nurse practitioner on that day, the consult and discussion were a part of my work routine. If I was not working on that day, I would be notified by telephone and then go to the hospital to visit with the mother and discuss the study. Sometimes I did not know about mothers being admitted in the labor and

delivery unit at a gestational age of less than 28 weeks, yet between March and December 2005 I approached 33 mothers in labor with a preterm infant less than 28-weeks gestation to ask them for consent. Mothers expected to deliver within the hour were not approached because of the stress they were probably experiencing. The mother was told that I was a nursing doctoral student and a neonatal nurse practitioner who works in the NICU at Pitt County Memorial Hospital. I described the study as an observational study that would take place over the baby's first 12 hours to look at his/her temperature, oxygenation, acid-base balance, blood sugar, and heart rate using the normal NICU monitors. I told the mothers that my research assistant or I would sit at the bedside for the 12 hours and watch the monitors and record the nurse's and doctor's activities. I also told the mothers that I was studying temperature in babies weighing less than 2 pounds to understand how to best keep a baby that small warm so that nurses and doctors can better prevent complications. The entire study was explained in writing, with the risks, benefits, and my contact information. All mothers approached gave consent. Once the mother signed consent, they were given a copy of the consent to retain for their records.

Once consent was obtained, it remained in my locked file cabinet in the neonatal nurse practitioner office. With mother's consent, I kept a list of mothers signing consent in a notebook in the neonatal nurse practitioner's office, with the mother's due date. Keeping the consent list in plain view was necessary because when neonatal nurse practitioners went to a delivery, they needed to first check to see whether the infant was a possible study subject. Once the infant was born, the name was marked through on the list so that it was not recognizable.

If a consented infant was about to be delivered and had not gone beyond 28-weeks

gestational age, the neonatal nurse practitioner called me using a pager. I was on call 24 hours a day, 7 days a week because consented infants were delivered at random times. The infant was enrolled if inclusion/exclusion criteria were met upon admission to the NICU. The enrolled infant was assigned a study number, and all data collected was used with that study number. Data collection began once the infant was placed on the radiant warmer and attached to monitors. All study data were available to the physician or nurses taking care of each infant because we were sharing many of the monitoring devices. Every 5 minutes, a research assistant or I recorded oxygen delivery from the oxygen analyzer attached to the ventilator as well as stimulation of the infant on a data collection sheet (Appendix III). Data collection by observation for 6-hour periods required two research assistants per infant. Each of us sat at the infant's bedside for no more than 6 hours 30 minutes to prevent fatigue. After 6 hours had passed, the second person began recording for 30 minutes with the first person to check inter-rater reliability for that 30 minutes on each infant. If needed, the research assistant or I was able to take a break for 5 minutes from the bedside, as needed, as long as the infant was not being stimulated.

Abdominal and peripheral (foot) temperatures were collected continuously by the Mini-Logger Monitor (Mini Mitter, Oregon) and recorded by into the Mini-Logger monitor for 12 hours following admission to the NICU. The data were transferred to a laptop computer using Mini-Logger software once temperature data collection was complete. Oxygenation was indicated by oxygen saturations and periodic blood O_2 content (pO_2) through blood gas analysis. Oxygen saturation was measured by Nellcor pulse oximetry from the time the probe was attached to the infant upon admission to the NICU. The pulse oximeter probe was attached to the infant under a small duoderm strip as part of the normal NICU routine

minimizing any threat to skin integrity of the infant. Oxygen saturation readings were collected in a datalogger program and then outputted into the bedside laptop computer using the Hyperterminal communications program. Oxygen requirement was measured by the ventilator analyzer and recorded by the observer on a data collection sheet every 5 minutes from the time the infant was enrolled in the study through 12 hours of age. Heart rate was recorded continuously by the Spacelabs Clinical Workstation cardiopulmonary monitor, stored using the datalogger program and then outputted into the bedside laptop computer using the Hyperterminal communications program. Periodic acid-base balance (blood pH) was recorded by the observer from blood gas analysis recorded on the nursing notes. Blood glucose was recorded from the nursing notes by the observer through the periodic chemstrip readings. Blood pressure was also recorded continuously when available, by the Spacelabs monitor, in the event that alterations in blood pressure affected heart rate or oxygenation. I recorded demographic information on to the demographic data sheet (Appendix II) once the infant met inclusion criteria and was attached to the study monitors. Remaining disease status information was obtained and recorded at the end of data collection.

Potential Risks

The subjects of this study were members of a critical and unstable population. Infection and/or death could have occurred during the hours of this study because these are normal risks to this population. No deaths occurred during the study period and no infections were identified during the study period. This observational study was extremely unlikely to cause any additional risks to the infant above the normal risks for an ELBW infant admitted to a NICU.

Using the additional study monitor, the Mini-Logger Temperature Monitor presented no

additional risk to the infants. The Mini-Logger Monitor thermistor probe is identical to the current warmer thermistor probes, used as the standard of care in neonates. The standard PCMH NICU use of duoderm dressing in attaching temperature probes was followed; therefore, disruption of skin integrity to the infant was minimized.

Breach of confidentiality was another potential risk because any person in the NICU was able to identify subjects under study due to the extra monitors at the bedside as well as the presence of the researcher. Medical personnel were able to view study data as they were being collected because monitoring these data was necessary for routine NICU care of the subject. Data collection sheets were labeled with a study number only, instead of names or other identifying factors.

Protection Against Risk

To reduce the risk of breech of confidentiality, each enrolled infant was assigned a study number and all data were associated with the study number instead of the infant's name. Data collection sheets were identified with the study number. Downloaded computerized information from the monitors was also identified with the study number. The consent forms were kept in a notebook, locked in my file in the neonatal nurse practitioner office. A list of consenting mothers was kept in the neonatal nurse practitioner office to identify consented infants and when an infant was born whether or not they were enrolled, their name was marked through on the consent list.

The infant had a doctor, neonatal nurse practitioner, and nurse available at all times as was standard care in the Pitt County Memorial Hospital NICU. I or my research assistant (an experienced NICU nurse or respiratory therapist) sat at the bedside in a position to observe the ventilator oxygen analyzer but far enough away not to block access to the infant by

medical personnel. Even though I am a neonatal nurse practitioner, I was not in that role while conducting this research and did not intervene medically in any way with the infants because of the potential for conflict of interest. At least two neonatal nurse practitioners were working in the NICU at Pitt County Memorial Hospital at all times; therefore, I never for an instance had to step out of my role as researcher into the role of an neonatal nurse practitioner.

No additional blood sampling was conducted solely for this study. When labs were drawn as a normal course of care, I or my research assistant recorded the results.

As during routine practice, readouts of the data continuously shown on the monitors were available to the medical personnel who used them in the medical and nursing care of the subject.

Potential Benefits of the Research to the Subjects and Others

Although the monitoring devices routinely used in the NICU imposed no increased risk to the study infants nor offered any additional benefit, the one additional monitor may have offered additional benefits. The temperature monitor provided the medical care staff two additional continuous temperature readouts (in addition to intermittent axillary temperatures taken by the staff nurse) to guide medical care.

Knowledge gained from this study adds to the science of thermoregulation of ELBW infants and gives valuable information about the relationship between body temperature and oxygenation, heart rate, peripheral vasoconstriction, acid-base balance, and glucose. Analyses from this study may lead to future hypotheses to better define the relationship between temperature and these physiological variables in ELBW infants. These data should also help to determine the optimal body temperature for ELBW infants and help nurses and

doctors set temperature controls for these infants.

Data Safety Monitoring Plan

I constantly monitored for any adverse event occurring during the study period. I had two data safety monitoring committees because of the critical and unstable nature of the ELBW infant population. My dissertation committee acted as my offsite data safety monitoring committee, at the University of North Carolina at Chapel Hill. The six neonatologists on staff at East Carolina University/Pitt County Memorial Hospital NICU acted as my data safety monitoring committee on site at Pitt County Memorial Hospital. I was able to discuss any adverse events occurring with the infant during my study with both committees; however, no adverse events occurred over the course of this study. The critical and unstable nature of this ELBW infant population created an increased possibility of infection, complications, or death during NICU hospitalization is increased. It was extremely unlikely that this study would be directly related to any of those complications; however, in the event of any adverse events occurring to a study infant during the 12-hour study period, protocol dictated that I consult with both data safety monitoring committees. The Institutional Review Boards at University of North Carolina and East Carolina University/Pitt County Memorial Hospital were to be notified in writing of any adverse event occurring during the study. No additional subjects were to be enrolled until both data safety monitoring committees and the Institutional Review Boards had reviewed all study procedures and agreed that adequate safeguards were in place. This was not a clinical trial; therefore, the data data safety monitoring committees did no routine monitoring. The committees were available as resources for consultation related to adverse events had any occurred during the study.

Importance of Knowledge Gained

This study addressed many unanswered questions about the optimal body temperature range for ELBW infants based on routine physiological measurement. No existing research has examined temperature in comparison to oxygenation, acid-base balance, peripheral vasoconstriction, blood glucose and heart rate for ELBW infants in the first 12 hours of life. Consequently, nurses have no evidence-based guidelines about the optimal body temperature range for ELBW infants so that they may experience normal parameters of oxygenation, acid-base balance, peripheral vasoconstriction, blood glucose and heart rate. This research provides useful evidence that will be helpful in determining this body temperature range.

Data Analysis Plans

Each study question was answered using separate analyses. The SAS System, Version 8, statistical analysis software was used to analyze data using descriptive statistics, Pearson correlations, Chi square analyses, Student *t*-test and linear regressions. The 720 individual time periods (1 per minute x 12 hours) for each subject were the units of analysis. For a within-subject sample size of n=720, a logistic regression analysis at the two-sided 0.05 significance level exceeds 90% power to detect a difference of at least 0.12 in rates of outcome for low and normal temperature ranges. Further, for this same sample size, a two-sided 0.05 test of the correlation coefficient would reject a value of 0.80 (representing high correlation) with power exceeding 90% in favor of a true correlation greater than 0.84.

Question One: During the transition period (first 12 hours of life), what are the relationships between temperature, oxygenation (oxygen saturation), heart rate,

peripheral vasoconstriction (greater than 2º C difference between peripheral and abdominal temperature), and trends in the intermittent variables of pO_2, pH, and chemstrip (indicator of blood glucose) within individual infants born weighing 500-1000 grams?

Each variable that was recorded continuously over time (abdominal and peripheral temperature, heart rate, and oxygen saturation) was analyzed using the mean reading for each 1-minute interval. First, each variable measured for the 1-minute intervals was plotted for trend over time, with the measured variable on the y-axis and time on the x-axis. Descriptive statistics were calculated for each primary variable, including measures of central tendency (mean) and variability (standard deviations or ranges) for: abdominal and peripheral temperature, heart rate, oxygen saturation, and peripheral vasoconstriction (abdominal-peripheral temperature difference) within each infant. Trends over time were printed out in the form of plotted curves for abdominal and peripheral temperature, heart rate, and oxygen saturation and those plots were then visualized in comparison to the stimulation and clinical course of each infant. Peripheral vasoconstriction was determined by subtracting the peripheral temperature value from the abdominal temperature value for each minute of data collection. Percentage of observations defined as peripheral vasoconstriction was calculated for each infant. Abdominal temperature at 1-5 minute lags was examined in relationship to each infant's heart rate and oxygen saturation to determine if there was a stronger relationship between abdominal temperature and heart rate or oxygen saturations prior to the observation compared to simultaneously with the observation. A Pearson correlation coefficient was computed to determine the strength of the correlation between each primary variable pair. Secondary variables measured intermittently by the NICU staff (pO_2, pH, base

deficit, and glucose values) were tabulated for each infant as available from the medical chart. Only 1-6 measures of these variables occurred during the 12-hour study period; therefore, summary measures of these variables were compared to trends in temperature. Due to infrequent measurement, results involving the secondary variables were cautiously evaluated and were used to provide evidence of whether future study of pO_2, pH, base deficit, and glucose in relation to body temperature is warranted.

It was hypothesized that infants may have colder temperatures in the beginning of the study period due to the delivery and NICU stabilization procedures. I expected the trends of heart rate and oxygen saturations, as well as secondary variables (pO_2, pH, base deficit, and glucose values) to become more stable or in the normal range as the infants warmed over the study period.

Question two: Are the relationships between temperature and oxygenation, heart rate, peripheral vasoconstriction, and trends in the intermittent variables of pO_2, pH, and chemstrips (blood glucose) similar over infants?

To answer question two and to look for trends over infants, the correlation of each variable pair was computed. The value of the correlation coefficient for each subject for each variable pair was tabled, to visualize any pattern over infants. I compared the correlation coefficients to determine how many of the ten infants had a similar relationship between variable pairs. I also compared the percentage of observations defined as peripheral vasoconstriction as well as an abdominal-peripheral temperature difference at 1.5, 1, -1, -1.5 and -2 ˚ C. This comparison over infants was strictly descriptive and used to generate hypotheses for future

study.

Question three: **During the transitional period, what is the optimal abdominal temperature range for each individual infant at which oxygenation and heart rate are most stable, while there is decreased peripheral vasoconstriction?** Question 3 was answered with analyses for each subpart.

Question 3-a: When core temperature is ≤ 36.4º C (traditional definition of hypothermia in term infants; American Academy of Pediatrics & College of Obstetrics and Gynecologists, 1988), do individual infants show more abnormal values in oxygenation and heart rate than when temperature is above 36.4 º C ? Does the infant spend more time exhibiting peripheral vasoconstriction when the temperature ≤ 36.4 º C than when above 36.4 º C?

Question 3a was answered using 36.4º C as the cut point to compare frequencies of abdominal temperature observations above and below the cut point to the frequencies of observations dichotomized as presence or not of O_2 saturation and heart rate in their normal range using chi square analyses. Because most infants did not exhibit peripheral vasoconstriction, the abdominal-peripheral temperature difference was examined in relationship to the hypothermic cut point and the presence of normal values for heart rate and oxygen saturation. This approach was used within each infant. I also determined how many of 10 study infants had similar patterns of variables.

Question 3b: **Is the degree of abnormality in oxygenation and heart rate related to the**

extent to which abdominal temperature falls below 36.4 º C? Is the amount of time spent in peripheral vasoconstriction related to the extent to which body temperature falls below 36.4 º C?

Question 3b was answered using simple linear regression and Pearson correlations, modeling the independent variable as the deviation from 36.4º C for each 1-minute interval and the dependent variables as the deviation from normal for each variable (O_2 saturation, heart rate and abdominal-peripheral temperature difference). Each variable pair within infants was analyzed in this manner, summarizing relationships for each infant. I determined how many of the 10 study infants had similar patterns of variables. Each infant was examined as to the abdominal-peripheral temperature difference in relationship to the extent in which the infant's temperature falls below 36.4ºC.

Question 3c: Is there an optimal cut-point in body temperature at which amount of abnormal physiological variable observations are minimized and amount of normal physiological variable observations are maximized?

Oxygen saturation data were not used to answer this question because the values were confounded because of oxygen delivery to the infant, with most values being in the normal range for each infant due to oxygen delivery to the infants. Therefore, this question was addressed using heart rate data for each subject. Normal heart rate was defined as heart rate observations between the 25th and 75th percentile for each infant because all infants had a wide range in heart rate values. A frequency table was calculated for each infant for abdominal temperatures at 35.5˚- 37.5˚ C and percentage of heart rate observations at the below normal, normal, and above normal ranges. Below normal heart rate range was defined

as observations less than the 25th percentile heart rate limit and above normal heart rate range was defined as observations above the 75th percentile limit for each infant. Percentage of heart rate observations within each heart rate level was plotted on the y-axis and abdominal temperature observations were rounded to the nearest 10th degree and plotted on the x-axis for each infant. Frequency tables and plots were examined across infants to look for a similar abdominal temperature range that minimized heart rate observations at the below and above normal levels while maximizing normal heart rate observations. In this way, evidence was gathered to generate hypotheses for the optimal body temperature range for ELBW infants.

CHAPTER FOUR

Results

Description of Participants

Unless otherwise specified, all subjects were delivered in one of four delivery rooms, placed on a warmer table, then placed in polyurethane bags up to their necks as the routine standard of care. Infants were then resuscitated according to Neonatal Resuscitation Program protocol, assigned Apgar scores, and transferred to the NICU on a warmer table with warm blankets over the infant. Once the infants were placed on a incubator/warmer table in the NICU, the bags were removed and the infants were weighed. If the infant's weight and gestational age met inclusion criteria, they were enrolled in the study and the study monitors were attached. Umbilical line placement and placement on the ventilator took precedence over insuring adequate data output from the study monitor. Thus, many times I was unable to touch the infant until these procedures were accomplished. The nurses attached the heart rate electrodes, therefore the start of heart rate and oxygen saturation data output was dependent on their actions. I attached the temperature probes (temperature measuring apparatus) or assisted the nurses in their application of the temperature probes. Therefore, stabilization usually took place first.

Subject 170

This infant was a 630-gram African American female delivered by cesarean section at 25-weeks gestation. The heart rate and oxygen saturation data began recording when the infant

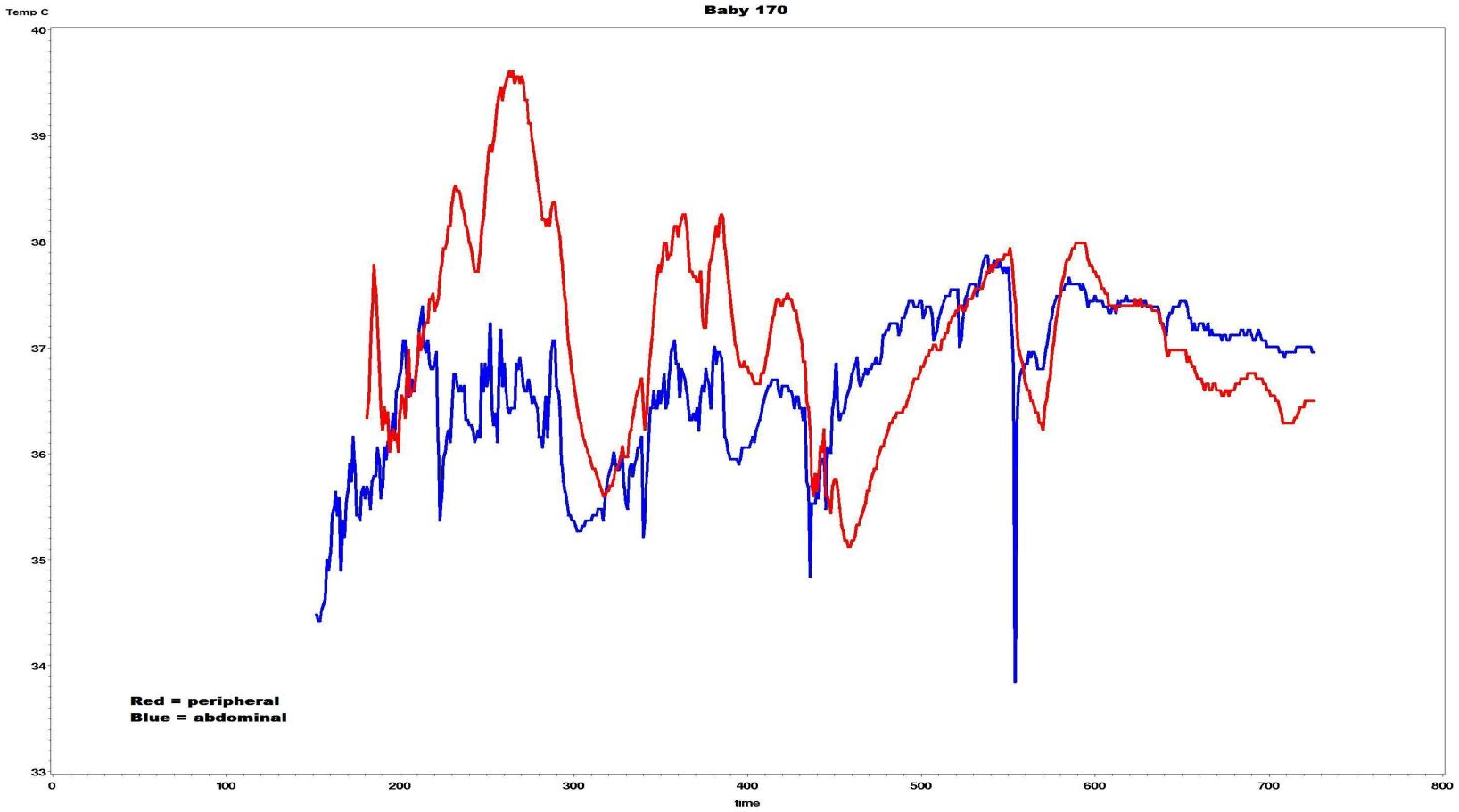
was 30 minutes of age and the abdominal and peripheral temperatures began recording when the infant was approximately 3 hours of age. Table 4.1 gives the values for the primary variables over the 12-hour study period for this infant. Figure 4.1 shows the infant's abdominal and peripheral temperatures over the 12 hours of the study. The infant's peripheral temperature was higher than the abdominal temperature for the first 8 hours of life, then the abdominal temperature became higher as the temperature became more stable. Because this infant did not exhibit peripheral vasoconstriction as defined for this study, percentage of observations at different temperature levels were calculated (see Table 4.2).

Table 4.1 Descriptive Statistics of Primary Variables for Infant 170

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	36.68 ˚ C	0.71	33.85˚ C	37.87˚ C
Peripheral Temperature (foot)	37.10˚ C	0.91	35.12˚ C	39.61˚ C
Adominal – peripheral temperature	-0.35˚ C	0.99	-3.61˚ C	1.63˚ C
Oxygen saturation	93.57 %	4.36	63.0 %	100.0 %
Heart rate	139.38	7.53	124.0	188.0

Figure 4.1 Abdominal and Peripheral Temperature for Infant 170

Red = peripheral temperature Blue = abdominal temperature



This infant had many heart rate fluctuations (see Figure 4.2) over the study period, many associated with clinical events.

The infant was placed on the ventilator at 60% FiO_2 and was gradually decreased to 30% FiO_2 by 2 hours of age and to 25% FiO_2 by 3 hours of age. The infant remained at 21% to 26% FiO_2 until 7 hours of age, then received 35% to 40% FiO_2 for the remainder of the study period. Figure 4.3 presents the infant's O_2 saturation over the 12 hours of the study.

Table 4.2 Abdominal – Peripheral Temperature Difference for Infant 170

Abdominal – Peripheral Temperature	**% of observations**
2˚ C	0.0%
1.5˚ C	0.9%
1˚ C	4.0%
-1˚ C	24.5%
-1.5˚ C	15.9%
-2˚ C	6.8%

The infant had 4 arterial blood gases drawn during the study period. The infant had a metabolic acidosis which improved over time (see Table 4.3).

Figure 4.2 Heart Rate for Infant 170 for the Study Period

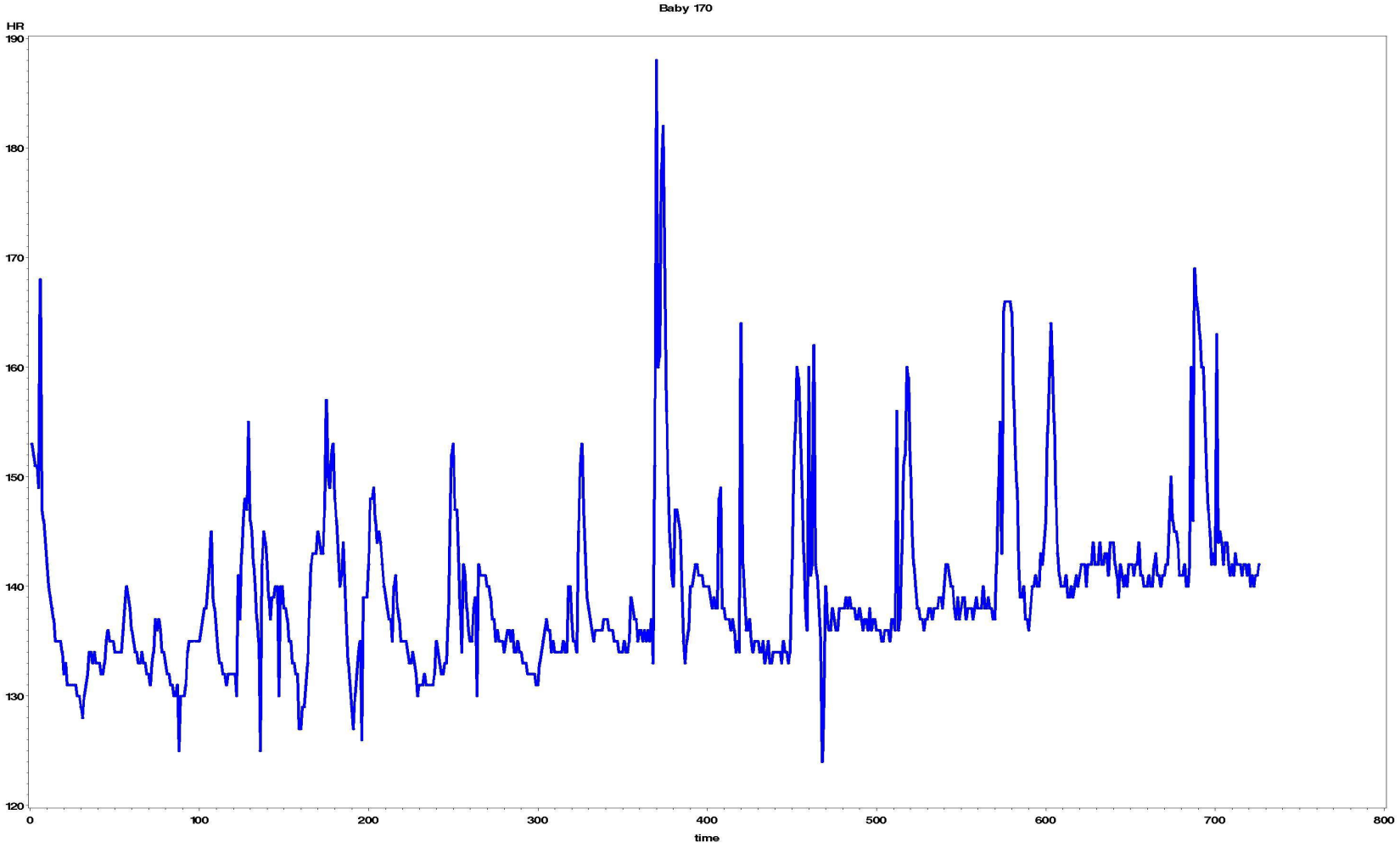


Figure 4.3 Oxygen Saturation for Infant 170 for Study Period

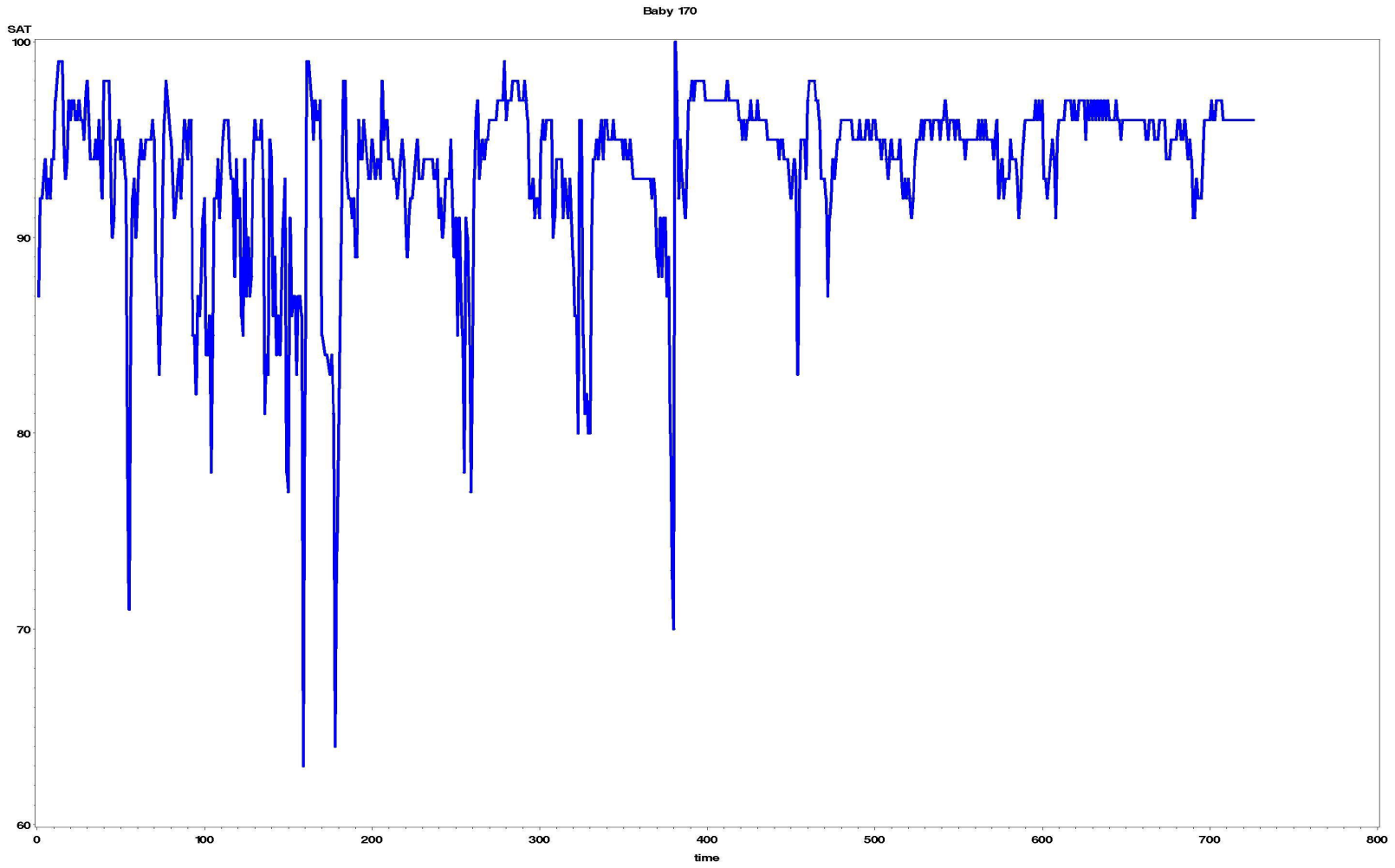


Table 4.3 Secondary Variables from the Medical Chart Review for Infant 170

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
30 min	35.7				
1 hr	35.6				
2 ½ hr	35.3				
4 hr	34.9	151	7.33	-8.8	125
4 ½ hr	35.7				
5 ½ hr		68	7.34	-4.7	125
6 ½ hr	37.1	68	7.36	-1.7	127
7 hr	37.4				
7 ½ hr	36.9				
9 ½ hr	36.8				
12		140	7.43	-1.2	100

Subject 240

This infant was a 680-gram African American male delivered precipitously by vaginal delivery at 24-weeks gestation. This infant was delivered in the bed, received chest compressions for low heart rate for approximately 1 minute and was intubated at delivery. This infant was unstable for the entire 12-hour study period, requiring two blood transfusions, three fluid infusions for low blood pressure, intravenous medications for low

blood pressure (Dopamine, Dobutamine then Epinephrine) and eventually ended up on high frequency ventilation. Because so many medical procedures needed were needed, the nurses and doctors had to enter the incubator frequently; consequently the infant remained with a low body temperature most of the 12-hour study period. Separating instability due to hypothermia versus instability due to hypovolemia and acidosis was very difficult. Discerning which event preceded the other was difficult. Table 4.4 presents descriptive statistics of the primary study variables for the 12-hour study period.

Table 4. 4 Descriptive Statistics of Primary Variables for Infant 240

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	36.05 ˚ C	1.25	31.09˚ C	37.01˚ C
Peripheral Temperature (foot)	36.49˚ C	0.69	33.55˚ C	37.19˚ C
Adominal – peripheral temperature	-0.29˚ C	0.61	-5.2˚ C	0.41˚ C
Oxygen saturation	92.04 %	3.72	76.0 %	100.0 %
Heart rate	165.47	13.46	123.0	194.0

The peripheral temperature remained higher than the abdominal temperature for the first 5 hours of data collection and then was the same or slightly lower than the abdominal temperature for the next 3 hours (see Figure 4.4). After this 8-hour period, the peripheral temperature returned to being higher than the abdominal temperature. This infant spent very

little time with the difference between abdominal and peripheral temperature greater than 1˚C (see Table 4.5). The peripheral temperature was higher than the abdominal temperature in all the periods with a greater than a 1˚ C difference.

The infant was on intravenous infusions for low blood pressure for much of the study and tachycardia is a side effect of these drugs. Therefore, the infant's maximum heart rate was higher than most of the other study infants. Interestingly, the two most unstable periods for this infant during the study occurred the first few hours of stabilization procedures and the last 2 hours when the infant had to be placed on an epinephrine infusion and high frequency ventilation. The graph shows higher heart rates during these two periods (see Figure 4.5).

Table 4.5 Abdominal – Peripheral Temperature Difference for Infant 240

Abdominal – Peripheral Temperature	**% of observations**
2˚ C	0%
1.5˚ C	0%
1˚ C	0%
-1˚ C	6.8%
-1.5˚ C	4%
-2˚ C	3%

Figure 4.4 Abdominal and Peripheral Temperature for Infant 240

Red = peripheral temperature Blue = abdominal temperature

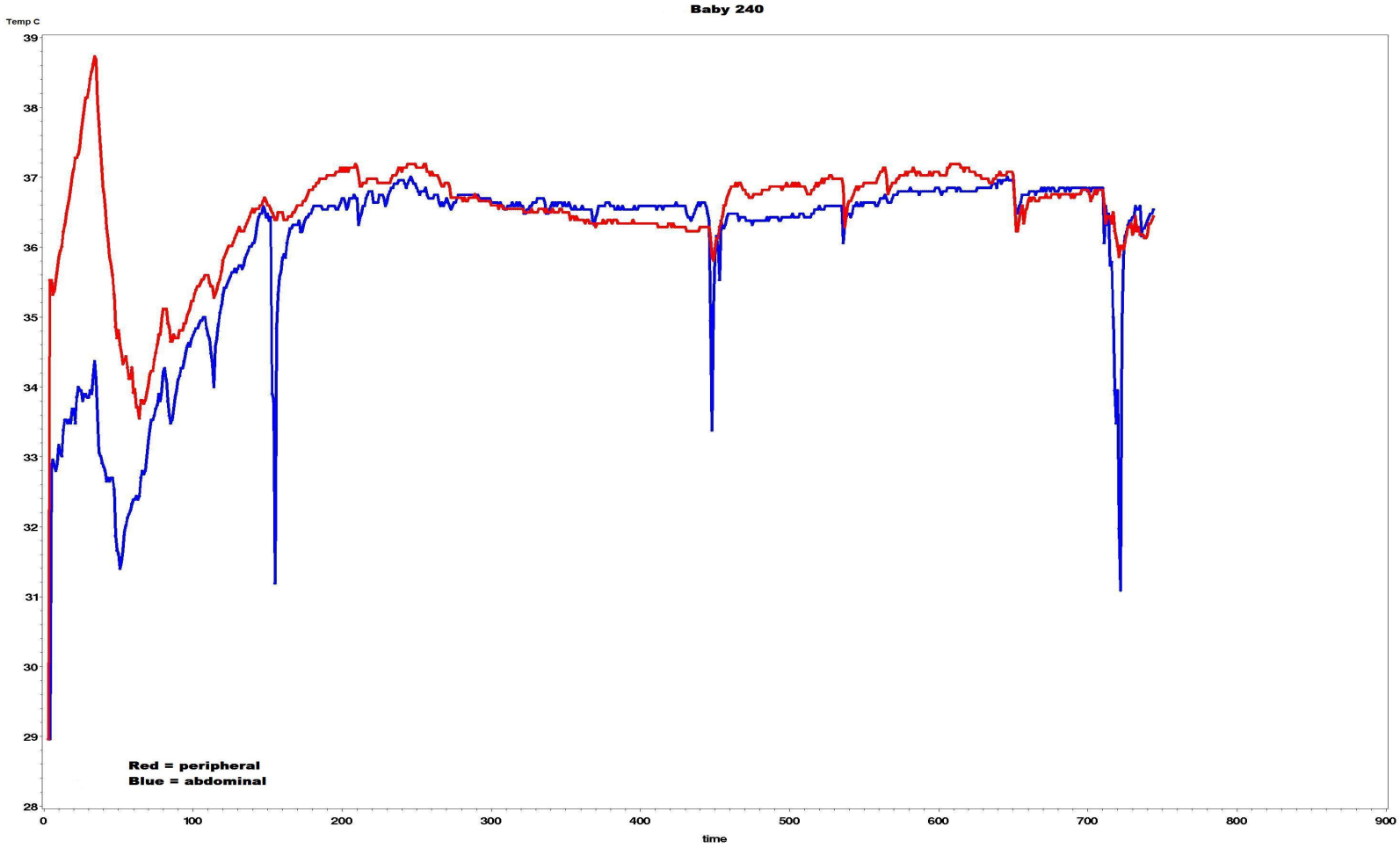


Figure 4.5 Heart Rate for Infant 240 for Study Period

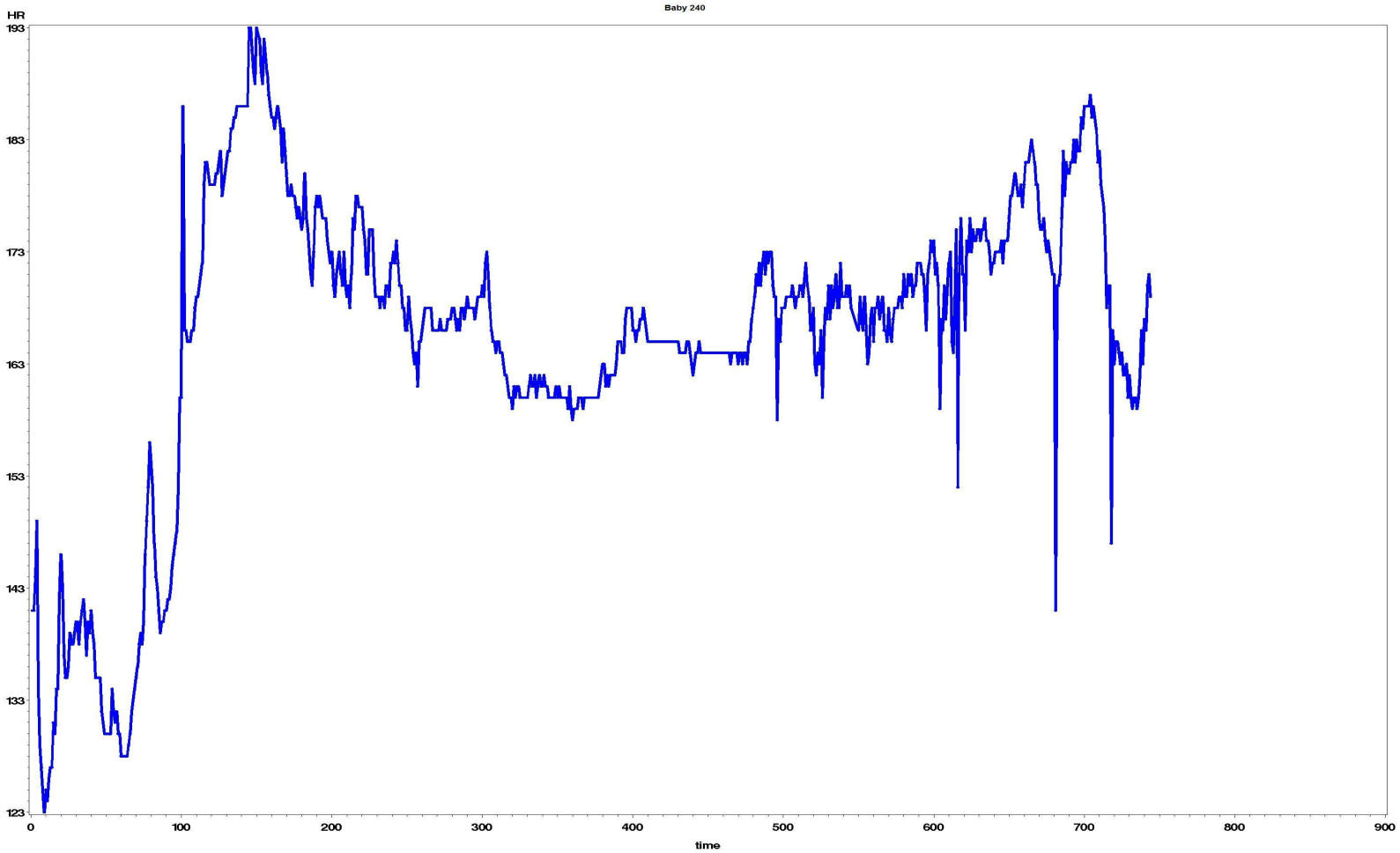
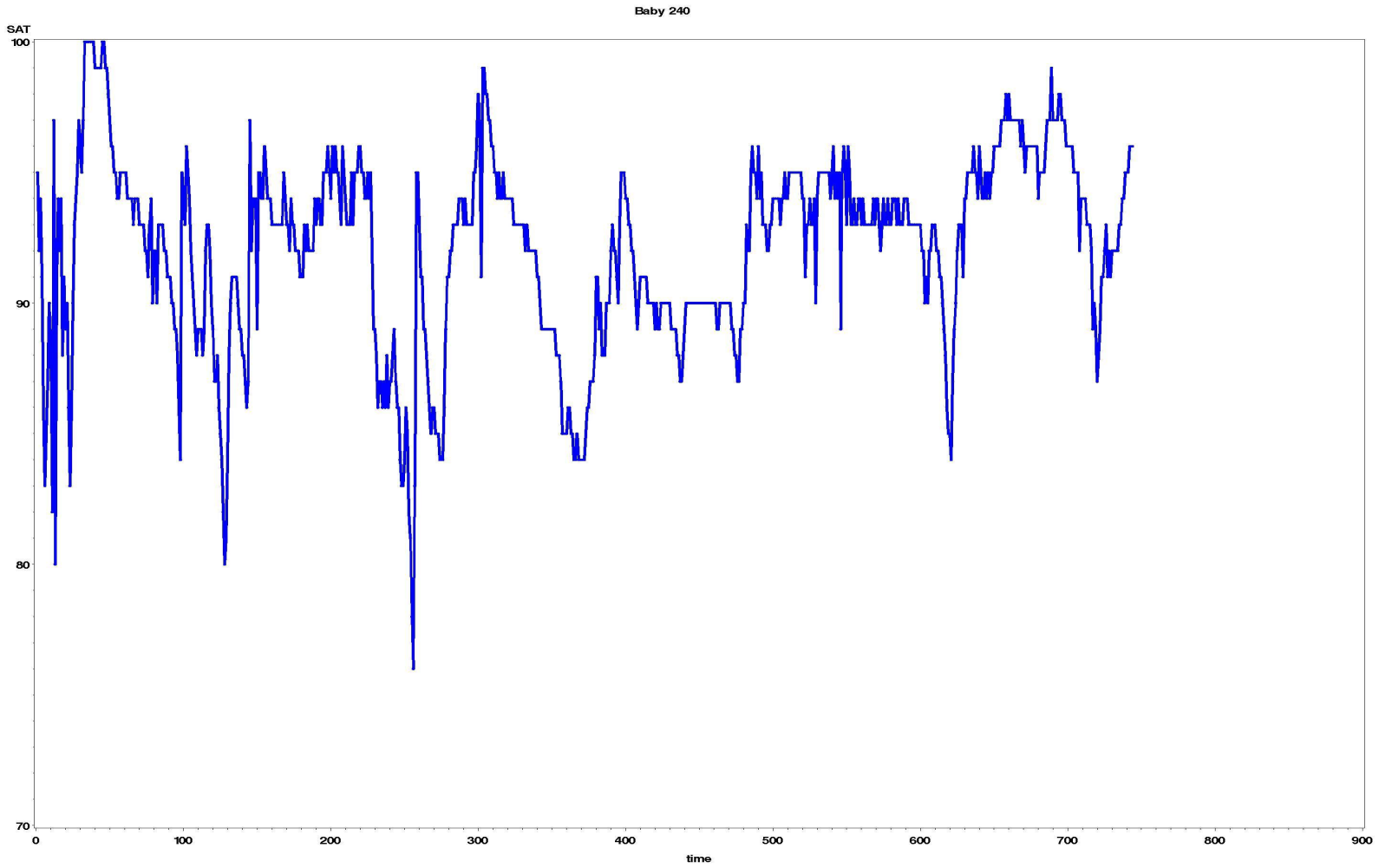


Figure 4.6 Oxygen Saturation for Infant 240 for Study Period



The infant was placed on a conventional ventilator upon admission to the NICU at 60% FiO_2 and was decreased to 21% FiO_2 by 1 ½ hours of age. The infant then increased to 30% FiO_2 and stayed between 30% FiO_2 and 45% FiO_2 for the remainder of the study period. Figure 4.6 presents the infant's oxygen saturations for the 12-hour study period.

Table 4.6 Secondary Variables from Medical Chart for Infant 240

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
30 min	35.4				
1 hr	33	130	7.23	-9	215
2 hr	35.3				
3 hr	35.9	43	7.18	-8.8	162
3 ½ hr	36.4				
4 hr		62	7.24	-9.7	133
5 ½ hr	36.1				
8 hr		56	7.04	-8.7	143
9 ½ hr	36.3				
10 hr		51	7.26	-7.9	130

The infant appeared to have a persistent metabolic acidosis (see Table 4.6). The infant was hypothermic and hypotensive much of the study period, as well as hypovolemic; any of these physiologic states (hypothermia, hypotension, and hypovolemia) might lead to acidosis.

Most likely, hypothermia, hypotension and hypovolemia combined to result in acidosis. Blood glucose measured at the bedside was elevated then trended downward as the infant became more stabilized than he was from the initial resuscitation.

Subject 311

This infant was a 550-gram White female delivered by cesarean section at 25-weeks gestation. The infant was attached to study monitors at 10 minutes of age, however the peripheral temperature probe would not register and had to be changed twice. Data collection did not start until approximately 2 hours of age for the peripheral temperature. Table 4.7 presents the descriptive data for the primary study variables. The rectal temperature at admission was 36.3˚ C which indicated the infant was fairly warm despite her size due to the use of a polyurethane bag in the delivery room. Her temperatures began to fall with stabilization and were still not stable at the desired 36.5˚ C (the temperature at which the nurses had set the computer set point for skin temperature) by 10 hours of age.

The infant's peripheral temperature remained higher than the abdominal temperature for the majority of the study period, until the last hour of the 12 hours under study, whereby the difference between the peripheral and abdominal temperatures became minimal and the abdominal temperature was slightly higher (see Figure 4.7). This infant spent more than half the 1-minute periods with a temperature spread of at least 1˚ C with the peripheral temperature higher than the abdominal temperature (see Table 4.8). Only 0.2% of the periods had the defined peripheral vasoconstriction.

During the initial stabilization period, heart rate fluctuated (see Figure 4.8) and oxygen saturations decreased (see Figure 4.9). The infant was placed on a ventilator upon admission

to the NICU at 30% FiO_2 then weaned down to room air (21%) by 2 hours of age, remaining there throughout the study period.

Table 4. 7 Descriptive Statistics of Primary Variables for Infant 311.

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	35.51 ˚ C	2.03	28.96˚ C	38.14˚ C
Peripheral Temperature (foott)	37.06˚ C	1.00	32.13˚ C	38.35˚ C
Adominal – peripheral temperature	-1.00˚ C	0.77	-2.5˚ C	2.3˚ C
Oxygen saturation	96.42%	2.39	80 %	100 %
Heart rate	127.54	9.32	104	164

The medical personnel were unable to place an arterial line therefore two venous gases were drawn during the study period. Because these gases were venous, the pO_2 levels are much lower than the levels obtained by arterial blood in the majority of the study subjects. The infant was more acidotic at 3 hours of age when she was colder, than at 8 hours. The glucose values increased as the infant became warmer and less acidotic. Table 4.9 presents secondary variables available for this subject during the study period.

Figure 4.7 Abdominal and Peripheral Temperature for Infant 311

Red = peripheral temperature Blue = abdominal temperature

Table 4.8 Abdominal – Peripheral Temperature Difference for Infant 311

Abdominal – Peripheral Temperature	% of observations
2˚ C	0.2%
1.5˚ C	0.4%
1˚ C	0.7%
-1˚ C	51.2%
-1.5˚ C	27.6%
-2˚ C	12.7%

Table 4.9 Secondary Variables from Medical Chart for Infant 311

Infant age	Axillary temps ˚C	pO_2 mm Venous	pH	Base deficit	Chemstrips
15 min	36.3				
2 hr	34.6				
3 hr	35.6	39	7.34	-9.5	98
4 hr	36.6				
6 hr	36.1				
8 hr	36.6	42	7.36	-4.5	153
10 hr	36.4				

Figure 4.8 Heart Rate for Infant 311 for Study Period

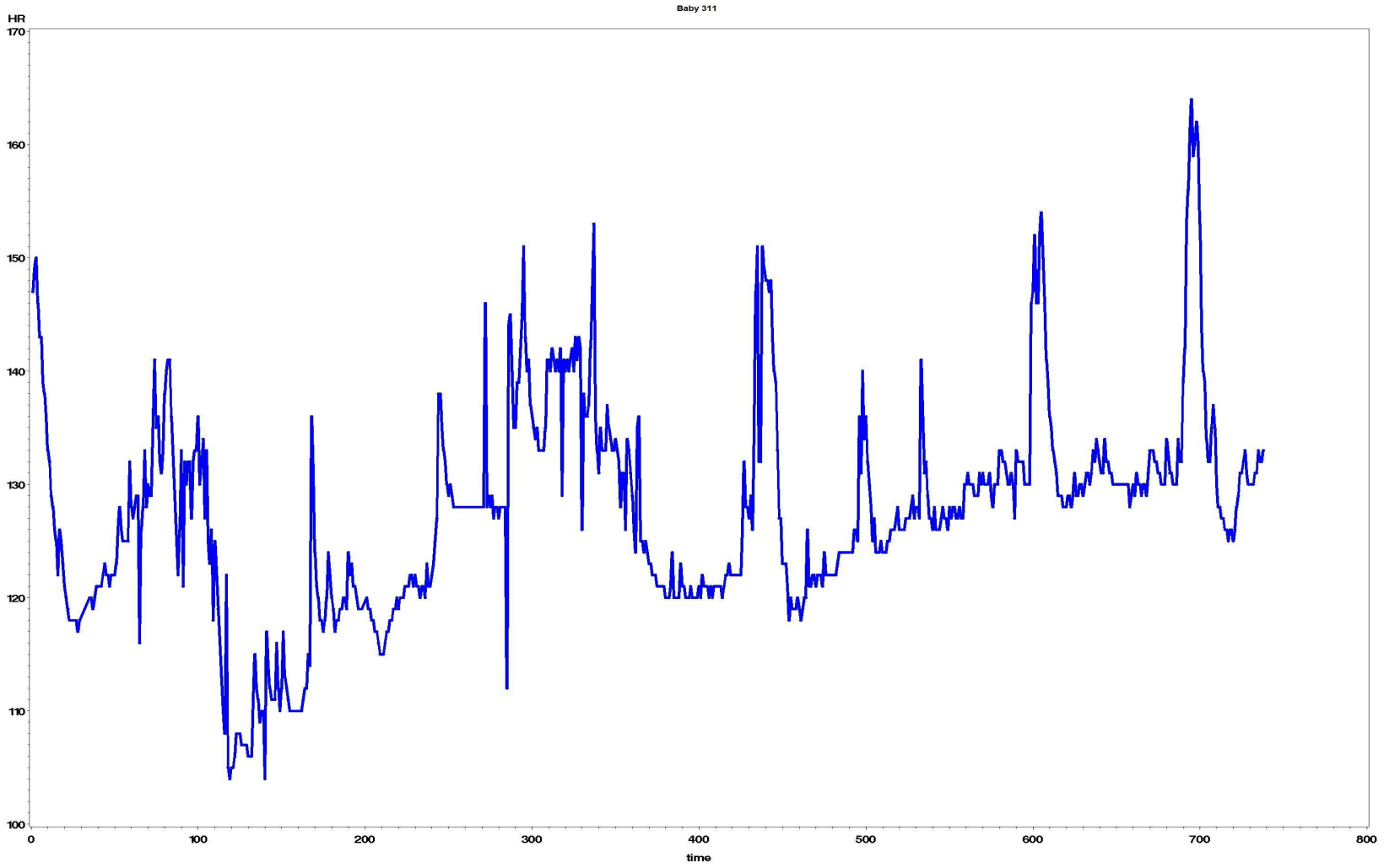
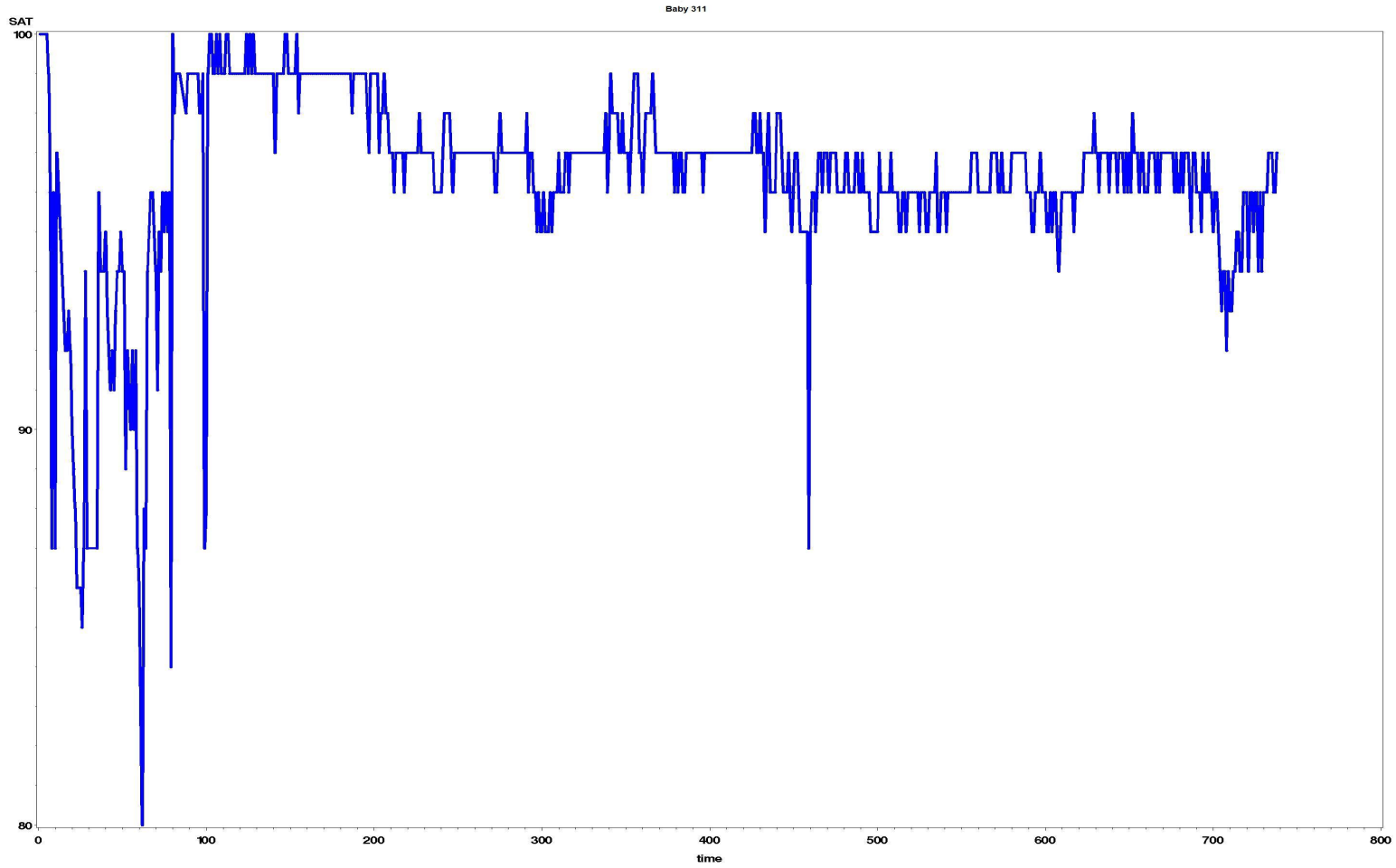


Figure 4.9 Oxygen Saturation for Infant 311 for Study Period



Subject 320

This infant was a 710-gram African American male delivered by cesarean section at 25 weeks-gestation. The infant was eliminated from analyses because the heart rate and oxygen saturation did not record for the entire 12-hour study period due to a malfunction of the monitoring system. An additional infant was enrolled to replace this infant in the analyses.

Subject 360

This infant was an 880-gram African American male delivered by vaginal delivery at 26-weeks gestation. The infant only required CPAP by Neopuff (not intubated) for the transfer to the NICU. Once the infant was admitted to the NICU, he was intubated and placed on a ventilator. The temperature monitors were attached at 1 hour of age and the limb leads for heart rate and oxygen saturation were not attached by medical personnel until 3 hours of age, once umbilical lines were placed. Therefore, the first 3 hours of heart rate and oxygen saturation data are missing. Table 4.10 gives the primary variable descriptive data for the 12-hour study period for infant 360.

Umbilical line placement took place over the first 3 hours of age. The infant was cold upon admission; however, his temperature increased fairly quickly. Neither the abdominal temperature nor the peripheral temperature was generally higher than the other as they alternated several times being the higher temperature (see Figure 4.10).

This infant spent 8.8% of the study period with peripheral vasoconstriction as defined by a temperature difference between abdominal and peripheral temperature of greater than 2˚ C (see Table 4.11). Many heart rate fluctuations occurred with clinical stimulation events; sometimes the heart rate increased during a clinical event and sometimes the heart rate

decreased (see Figure 4.11).

Table 4.10 Descriptive Statistics of Primary Variables for Infant 360

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	36.23˚ C	0.94	32.70˚ C	38.19˚ C
Peripheral Temperature (foot)	35.73˚ C	1.30	32.91˚ C	38.41˚ C
Adominal – peripheral temperature	0.50˚ C	0.92	-2.04˚ C	3.28˚ C
Oxygen saturation	93.42%	4.25	64.0 %	100.0 %
Heart rate	161.95	9.29	113.0	194.0

Table 4.11 Abdominal – Peripheral Temperature Difference for Infant 360

Abdominal – Peripheral Temperature	% of observations
2˚ C	8.8%
1.5˚ C	17.3%
1˚ C	28.5%
-1˚ C	2.2%
-1.5˚ C	0.7%
-2˚ C	0.1%

Figure 4.10 Abdominal and Peripheral Temperature for Infant 360

Red = peripheral temperature Blue = abdominal temperature

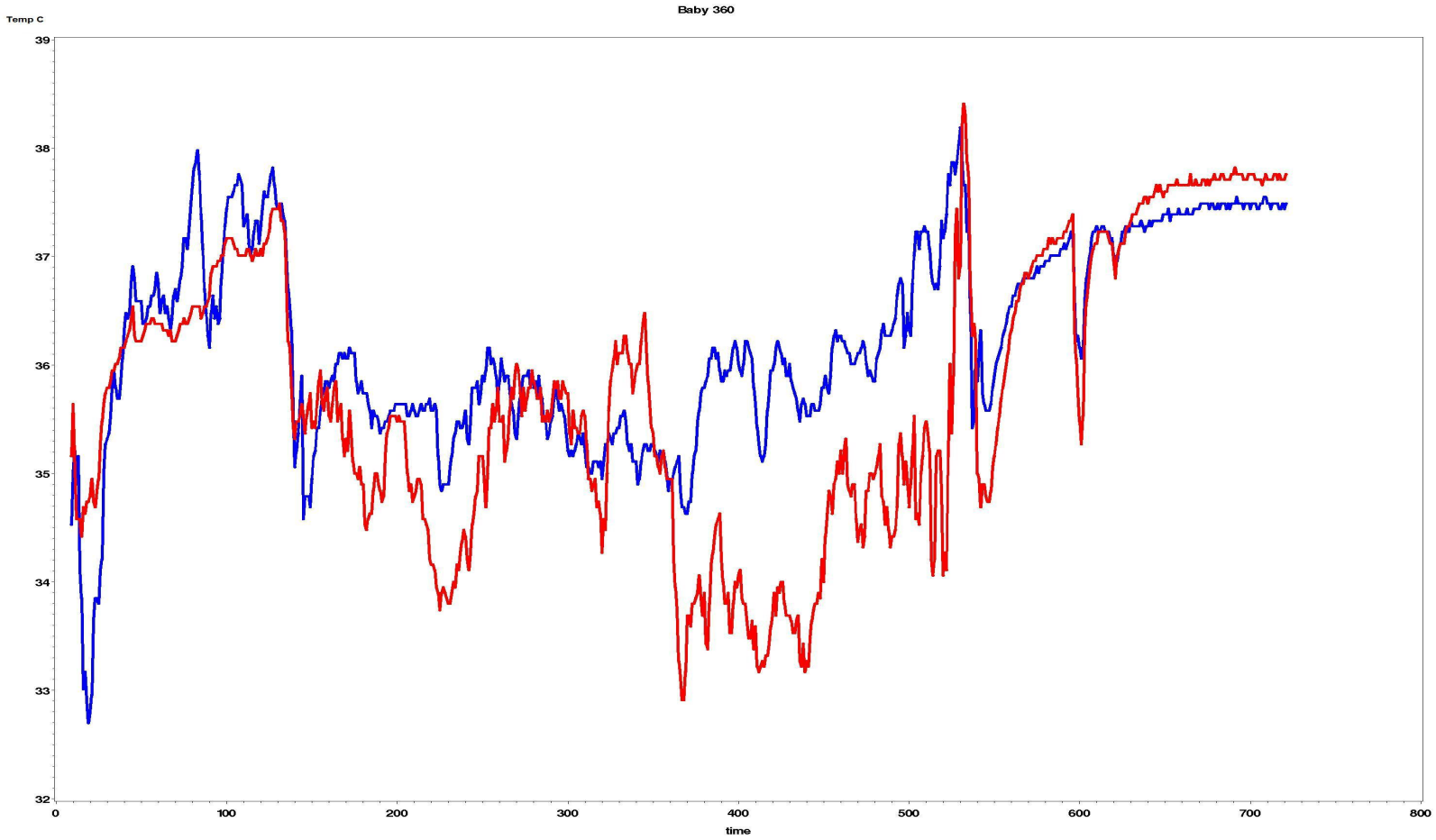
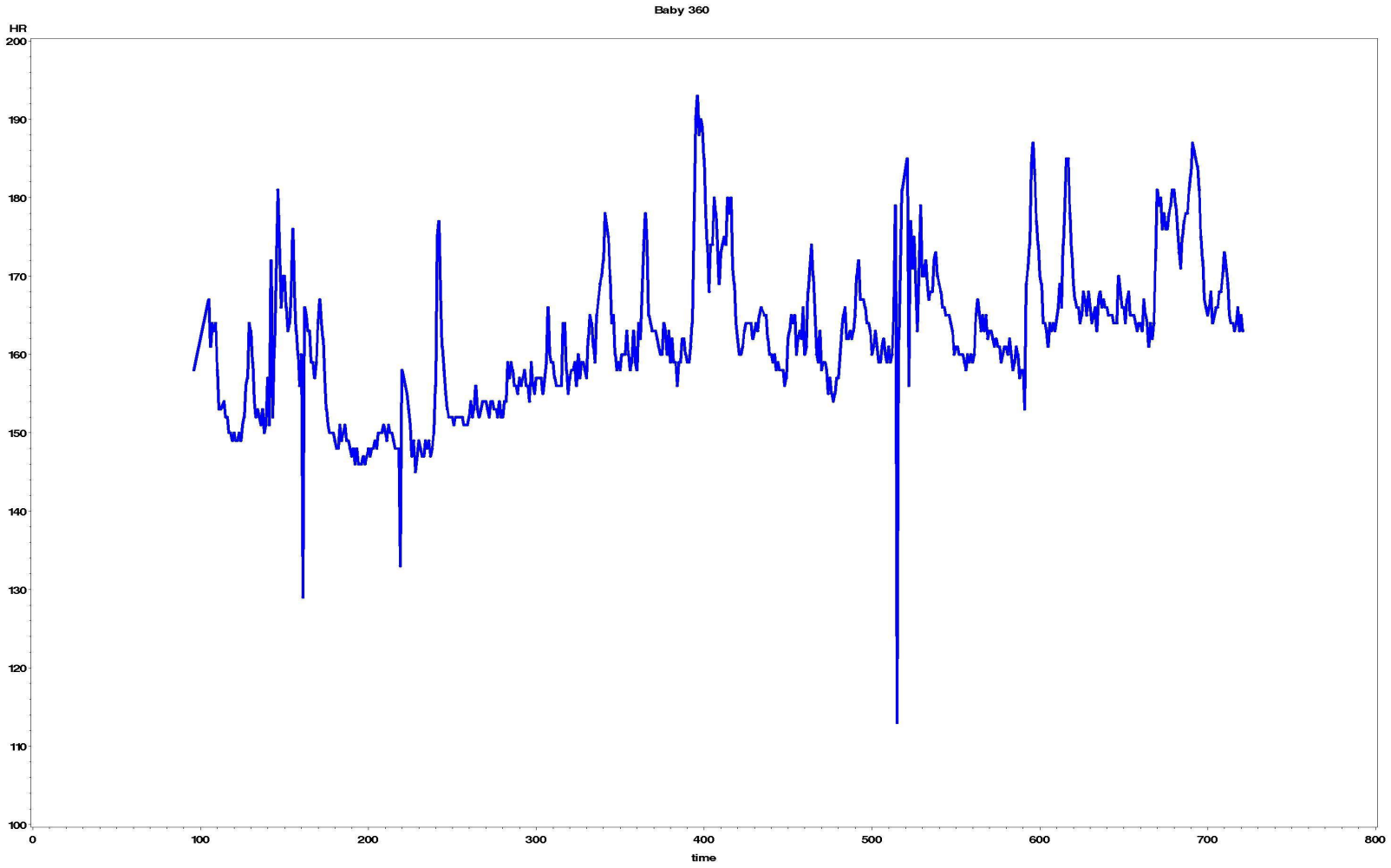


Figure 4.11 Heart Rate for Infant 360 for Study Period



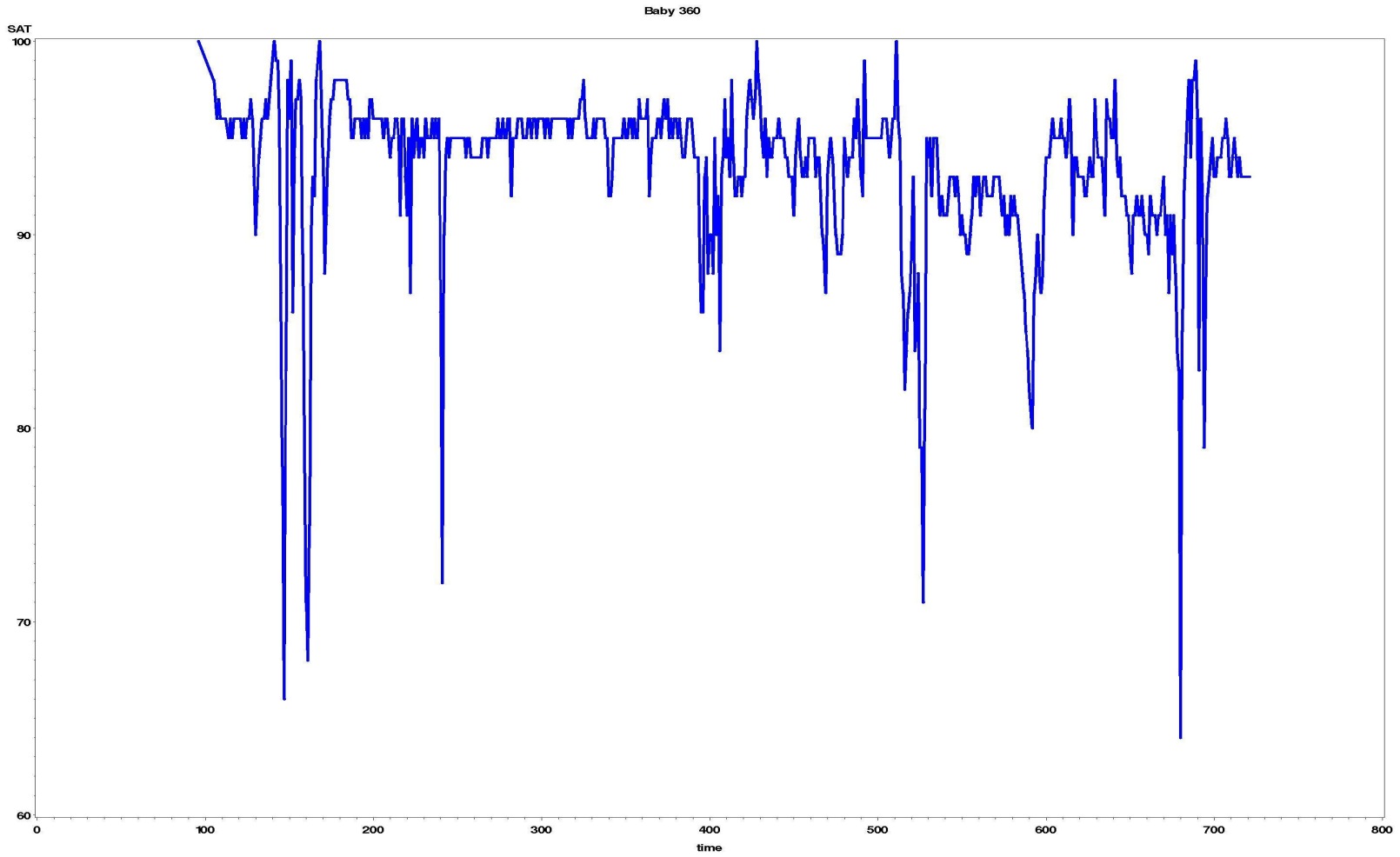
The infant was placed on a ventilator after he was admitted to the NICU at 21% FiO_2 (room air). The infant remained at 21%-26% FiO_2 through the entire study period, however visual inspection of the trends indicated that many desaturation episodes (see Figure 4.12) were associated with clinical events.

The infant had a slight metabolic acidosis signified by the negative base deficit, however, the pH was in the normal range therefore it was compensated (see Table 4.12). The initial bedside glucose value at 1 hour of age was low (36), however the remaining glucose measurements were normal and remained stable throughout the study period.

Table 4.12 Secondary Variables from Medical Chart for Infant 360

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
15 min	34.8				
1 hr		68	7.40	-2.2	36
1 ½ hr					82
2 ½ hr					94
5 ½ hr		116	7.42	-2.8	86
9 ½ hr		67	7.35	-4.9	94

Figure 4.12 Oxygen Saturation for Infant 360 for Study Period



Subject 410

This infant was a 720-gram White female delivered by cesarean section at 25-weeks gestation. This infant was transported to the NICU with positive pressure ventilation by bag and mask and intubated upon admission to the NICU. The study monitors were attached at approximately 1 hour of age. Table 4.13 presents the primary variable descriptive statistics for the 12 hours of the study.

Table 4.13 Descriptive Statistics of Primary Variables for Infant 410

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	35.28˚ C	0.99	32.49˚ C	37.92˚ C
Peripheral Temperature (foot)	36.36˚ C	0.96	32.91˚ C	37.82˚ C
Adominal – peripheral temperature	-1.13˚ C	0.67	-3.52˚ C	1.57˚ C
Oxygen saturation	94.0%	4.44	65.0 %	100.0 %
Heart rate	166.12	10.79	133.0	192.0

This infant received stimulation and medical procedures over the first 6 hours of age. The peripheral temperature remained higher than the abdominal temperature for the entire study period (see Figure 4.13). There was an obvious difference between peripheral and abdominal temperature the majority of the study. The abdominal and peripheral temperatures moved

closer together at approximately 10 hours of age when the Dopamine intravenous drip was increased to10 mcg/kg/min. This subject did not have any period that could be called peripheral vasoconstriction. However during the majority (68%) of the 1-minute periods, the difference in the abdominal and peripheral temperatures was greater than 1˚ C with the peripheral temperature higher (see Table 4.14).

Between 3 hours of age and 5 ½ hours of age, no heart rate data was collected because the limb leads were removed from the infant, then replaced when the observer noted missing heart rate information on the study computer (see Figure 4.14).

Table 4.14 Abdominal – Peripheral Temperature Difference for Infant 410

Abdominal – Peripheral Temperature	% of observations
2˚ C	0%
1.5˚ C	0.2%
1˚ C	1.4%
-1˚ C	68.4%
-1.5˚ C	28.8%
-2˚ C	5.1%

The infant was intubated and placed on the ventilator on admission to the NICU at 21% FiO_2. By 2 hours of age, the infant was increased to 27% FiO_2, was briefly on 100% FiO_2 for 1 hour at 3 hours of age, and then weaned back down to room air (21%) by 4 hours of age. She

remained at room air for the rest of the study period except for the last hour which was spent at 30% FiO_2. The oxygen saturations stayed relatively stable over the study period (see Figure 4.15) except with desaturations in association with clinical procedures. The infant became increasingly more acidotic as the study period progressed (see Table 4.15). Additionally the glucose values increased over time.

Table 4.15 Secondary Variables from Medical Chart for Infant 410

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
10 min	35				
1 hr		45	7.39	-3.2	73
2 hr	36.1				
3 hr	36.6				
4 hr		152	7.31	-7.6	
4 ½ hr	35.2				
5 ½ hr	35.8				
6 hr		48	7.31	-7.2	121
6 ½ hr	36.6				
8 hr		48	7.28	-5.1	
9 hr	36.9				
11 hr		55	7.27	-7.1	124
12 hr	37.1				

Figure 4.13 Abdominal and Peripheral Temperature for Infant 410

Red = peripheral temperature Blue = abdominal

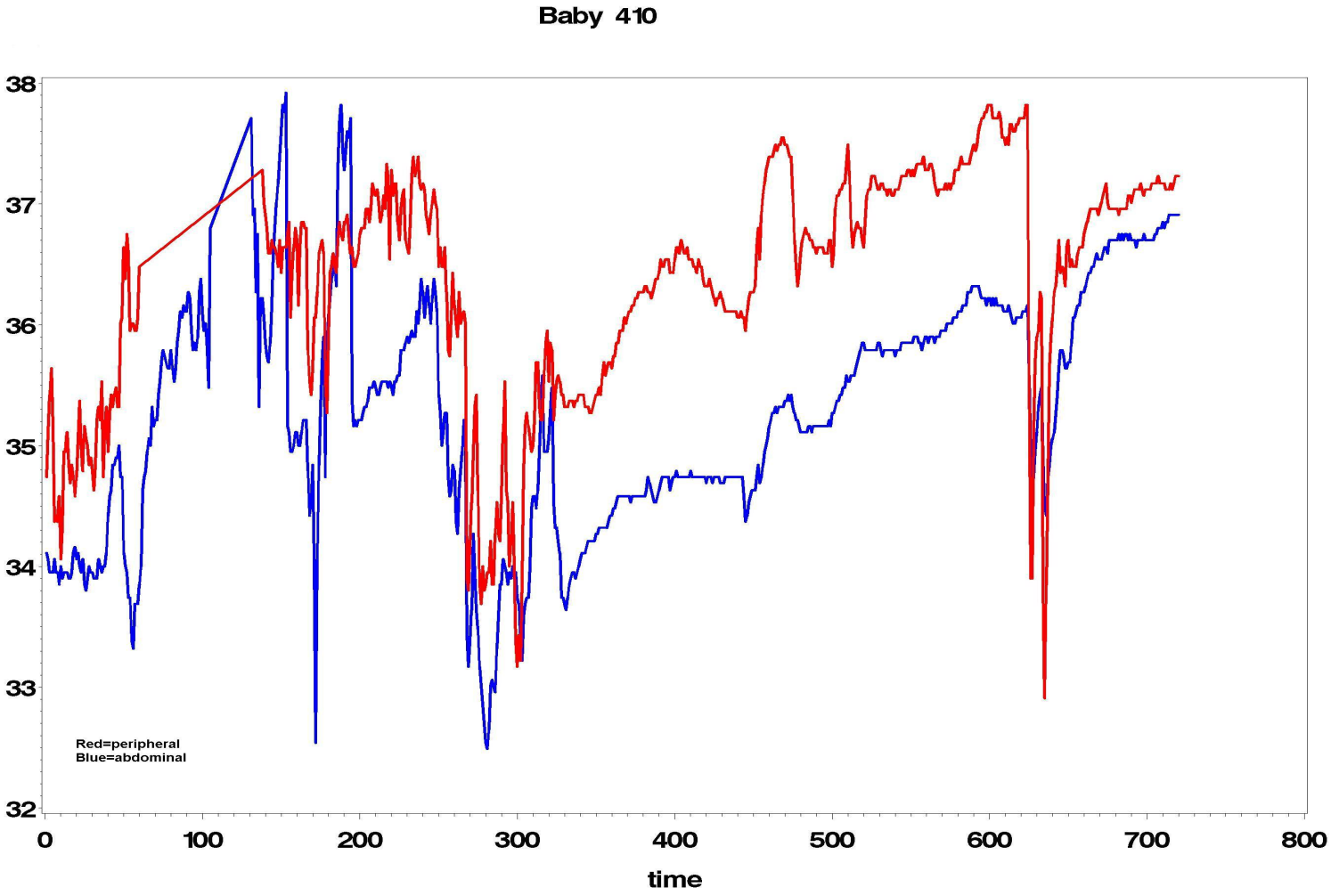


Figure 4.14 Heart Rate for Infant 410 for the Study Period

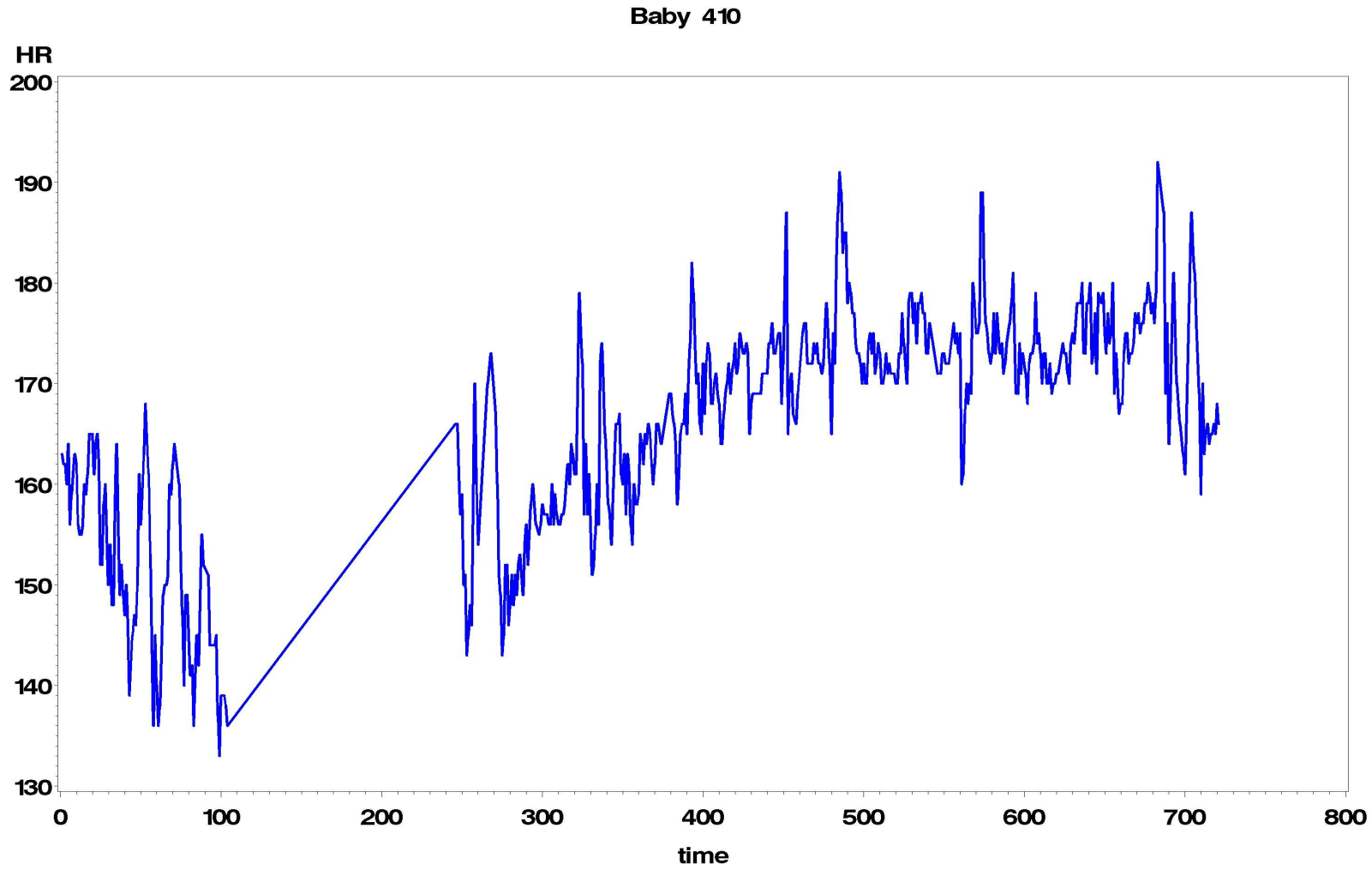
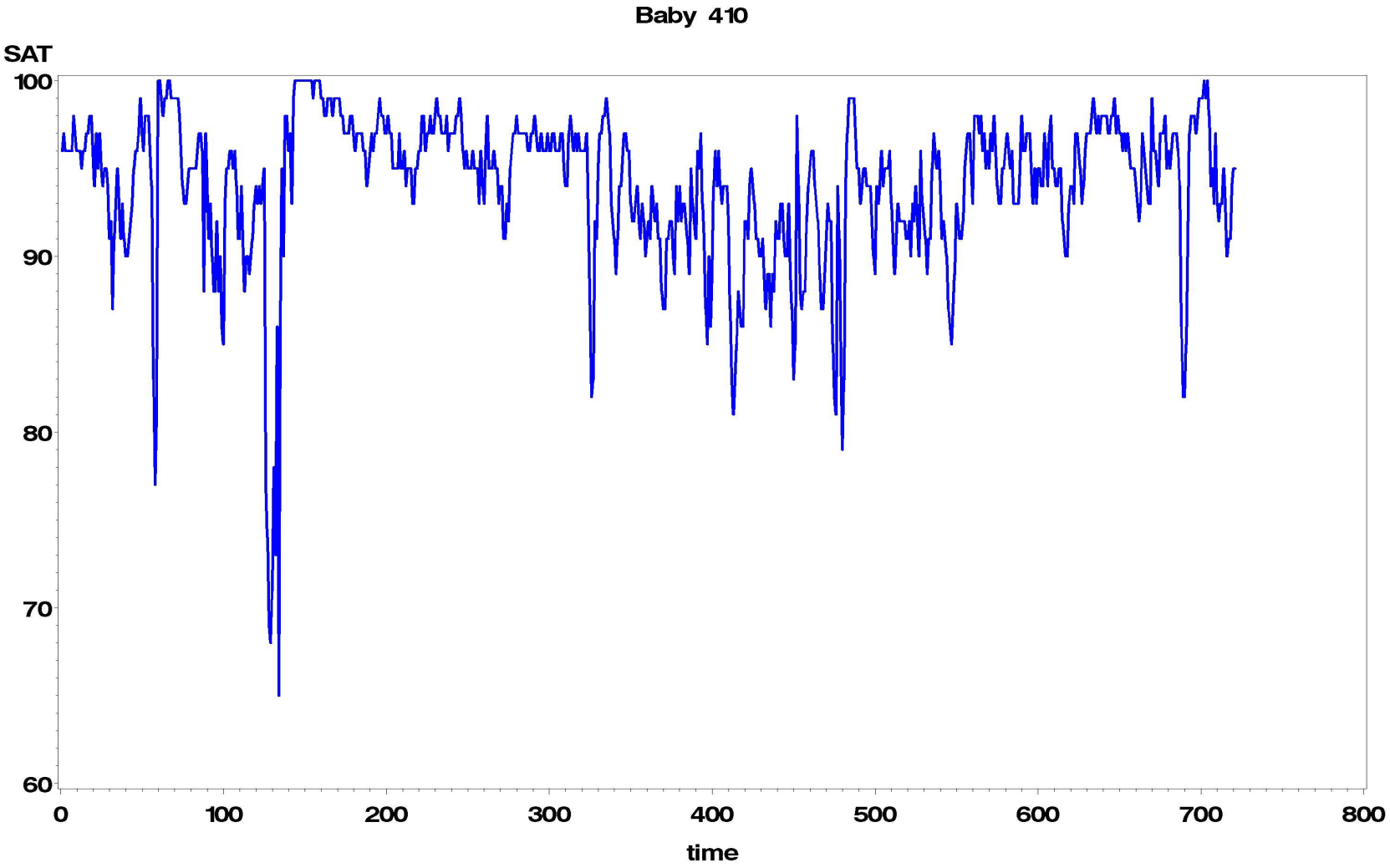


Figure 4.15 Oxygen Saturation for Infant 410 for Study Period



Subject 450

This infant was a 670-gram African American female delivered by vaginal delivery at 25-weeks gestation. The infant was not placed on study monitors until 2 hours of age because medical personnel were placing umbilical lines and I was unable to attach study monitors until that procedure was completed. The infant remained cold much of the study period (see Table 4.16).

Table 4. 16 Descriptive Statistics of Primary Variables for Infant 450

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	35.17˚ C	1.33	32.18˚ C	37.23˚ C
Peripheral Temperature (foot)	35.10˚ C	0.99	33.17˚ C	36.80˚ C
Adominal – peripheral temperature	0.07˚ C	0.89	-2.68˚ C	1.21˚ C
Oxygen saturation	93.79%	2.73	74.0 %	100.0 %
Heart rate	139.38	7.90	106.0	176.0

Visual inspection of the printed graphs revealed the infant's peripheral temperature was higher than the abdominal temperature for the first 5 ½ hours of life, then the temperatures came together and were nearly the same for a short period, afterwards, the abdominal temperature became higher until the end of the study (see Figure 4.16).

This infant did not have any observations defined as peripheral vasoconstriction. However,

16.3% of the observations had a 1˚ C difference in temperatures with the peripheral temperature higher than the abdominal temperature (see Table 4.17).

Table 4.17 Abdominal – Peripheral Temperature Difference for infant 450

Abdominal – Peripheral Temperature	**% of observations**
2˚ C	0%
1.5˚ C	1.5%
1˚ C	7.3%
-1˚ C	16.3%
-1.5˚ C	7.3%
-2˚ C	3.5%

From the visual trends, heart rate increases were associated with stressful clinical events (see Figure 4.17). The infant was placed on the ventilator at 35% FiO_2 upon admission and weaned down to room air (21%) on the ventilator by 5 ½ hours of age and remained there for the study period. Figure 4.18 presents the infant's oxygen saturations over the 12 hours of the study. The infant had a essentially normal blood gases with stable pH values throughout the study period. The glucose values increased as the hours progressed through the study period (see Table 4.18). This could be due to warming and/or glucose infusion.

Figure 4.16 Abdominal and Peripheral Temperature for Infant 450

Red = peripheral temperature Blue = abdominal temperature

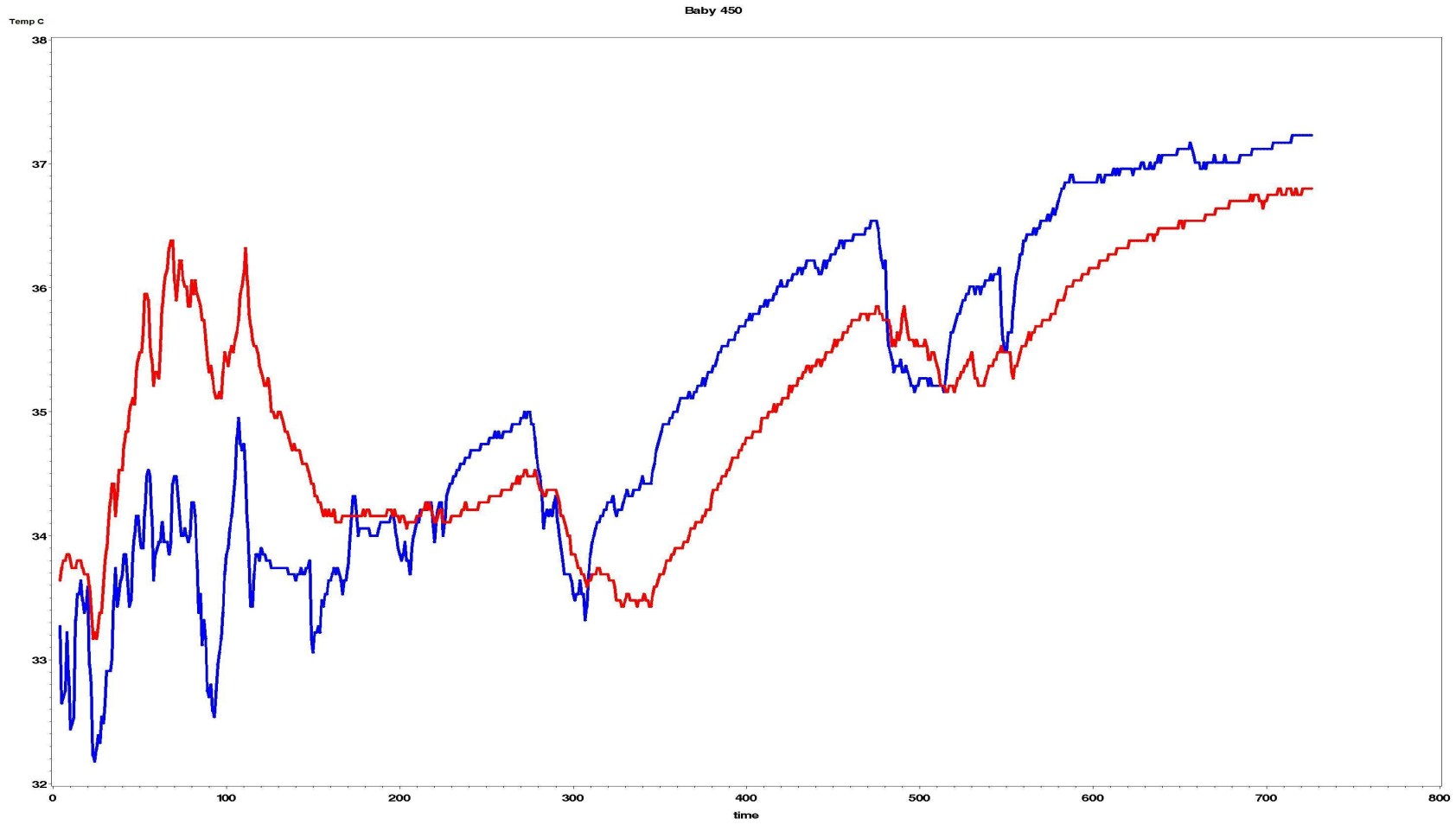


Figure 4.17 Heart Rate for Infant 450 for Study Period

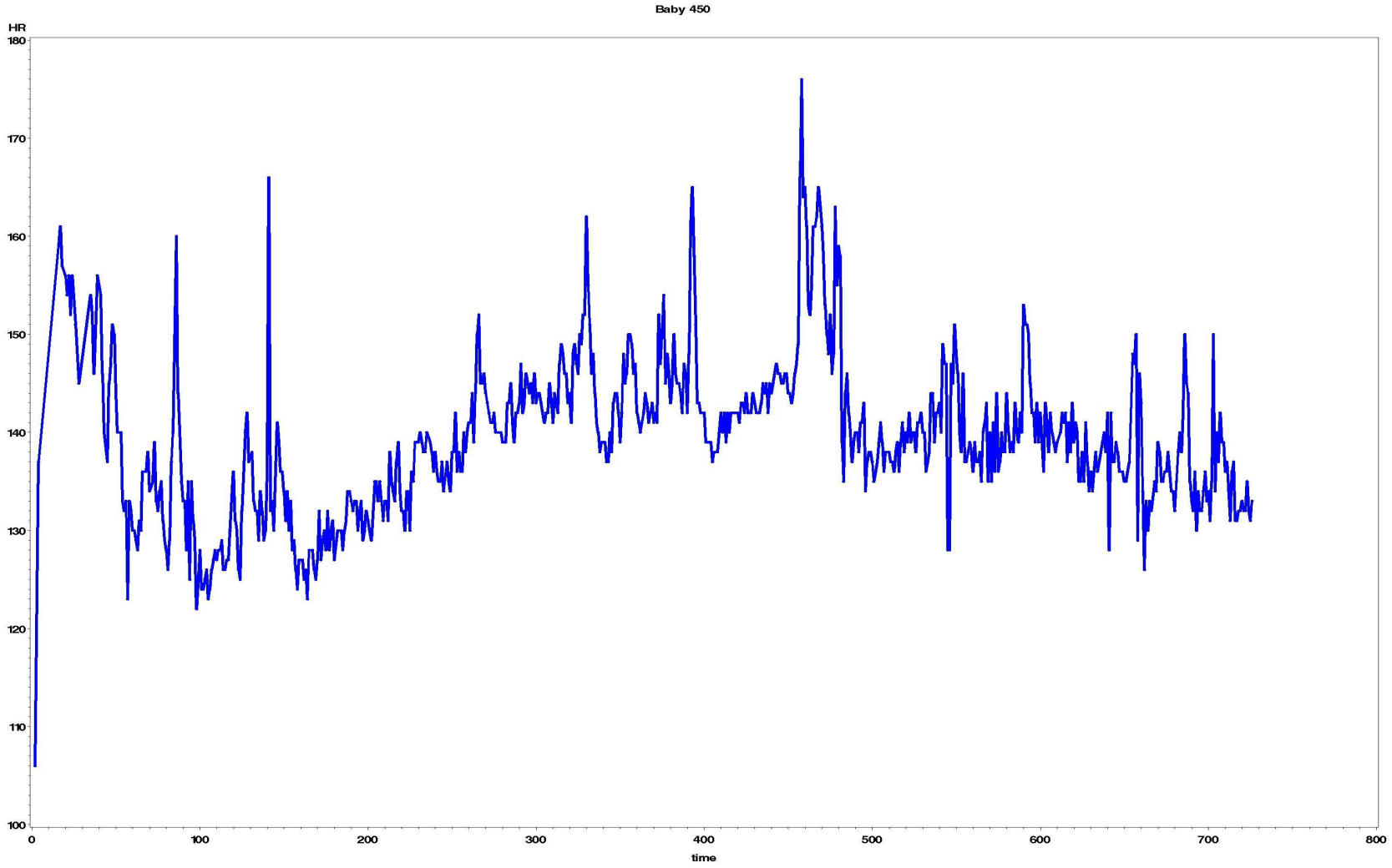


Figure 4.18 Oxygen Saturation for Infant 450 for Study Period

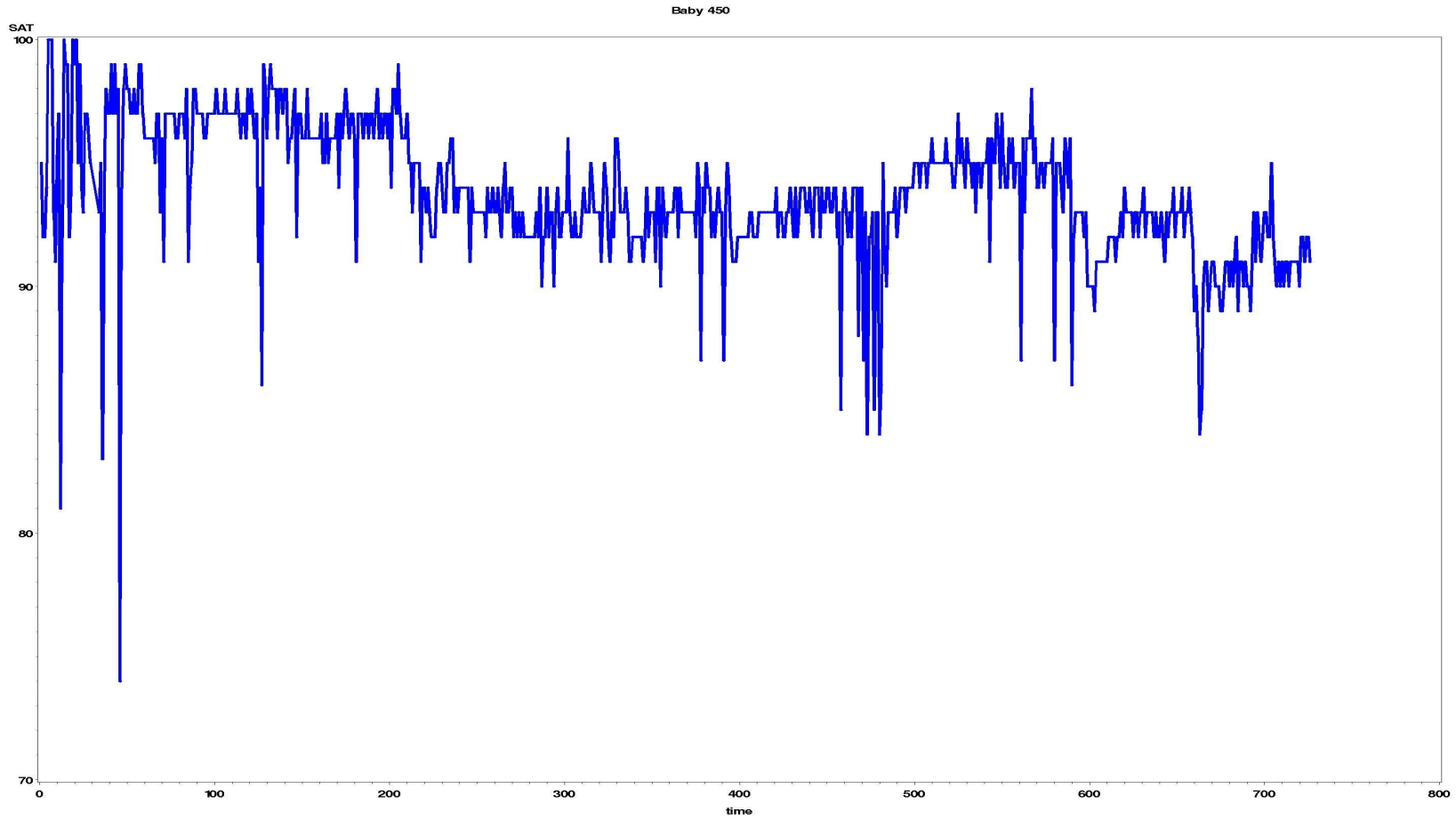


Table 4.18 Secondary Variables from Medical Chart for Infant 450

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
1 ½ hr		177	7.49	-4.9	
2 hr	34				
3 ½ hr	33				
4 hr		59	7.42	-1.8	67
4 ½ hr	34.8				
5 ½ hr	36.8				
7 ½ hr	37.1	78	7.45	-2.8	125
12 hr		54	7.43	-2.0	156

Subject 510

This infant was a 510-gram White female delivered by cesarean section at 26-weeks gestation. There was some trouble with the peripheral probe picking up a temperature. Therefore the temperature channels were changed and the probe replaced twice. The peripheral temperature began to register at 4 ½ hours of age. The infant underwent stabilization procedures during which her umibilical lines were placed, however, the umbilical arterial line had to be discontinued. A peripheral arterial line was placed but was subsequently discontinued due to arterial spasms. Three arterial blood gases and two venous blood gases obtained during the study period. Table 4.19 gives the descriptive statistics for

the primary variables over the 12 hours of the study for this infant.

Table 4.19 Descriptive Statistics of Primary Variables for Infant 510

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	35.79˚ C	0.88	31.61˚ C	38.25˚ C
Peripheral Temperature (foot)	36.71˚ C	0.91	29.44˚ C	37.78˚ C
Adominal – peripheral temperature	-0.52˚ C	1.12	-2.09˚ C	7.20˚ C
Oxygen saturation	94.34%	5.56	47 %	100 %
Heart rate	141.97	9.48	108.0	174.0

The computerized abdominal temperature probe on the incubator initially read 34.5˚ C and did not read 36.0˚ C until 2 hours of age. This probe was placed on the abdomen next to the study abdominal probe. The peripheral temperature did not record data until 4 ½ hours of age. After that time, the peripheral temperature remained higher than the abdominal temperature for the entire study period (see Figure 4.19).

This infant exhibited peripheral vasoconstriction for 6 % of the 1-minute periods. However, almost 20% of the periods had a temperature difference of 1˚ C with the peripheral temperature higher than the abdominal temperature (see Table 4.20).

Figure 4.19 Abdominal and Peripheral Temperature for Infant 510

Red = peripheral temperature Blue = abdominal temperature

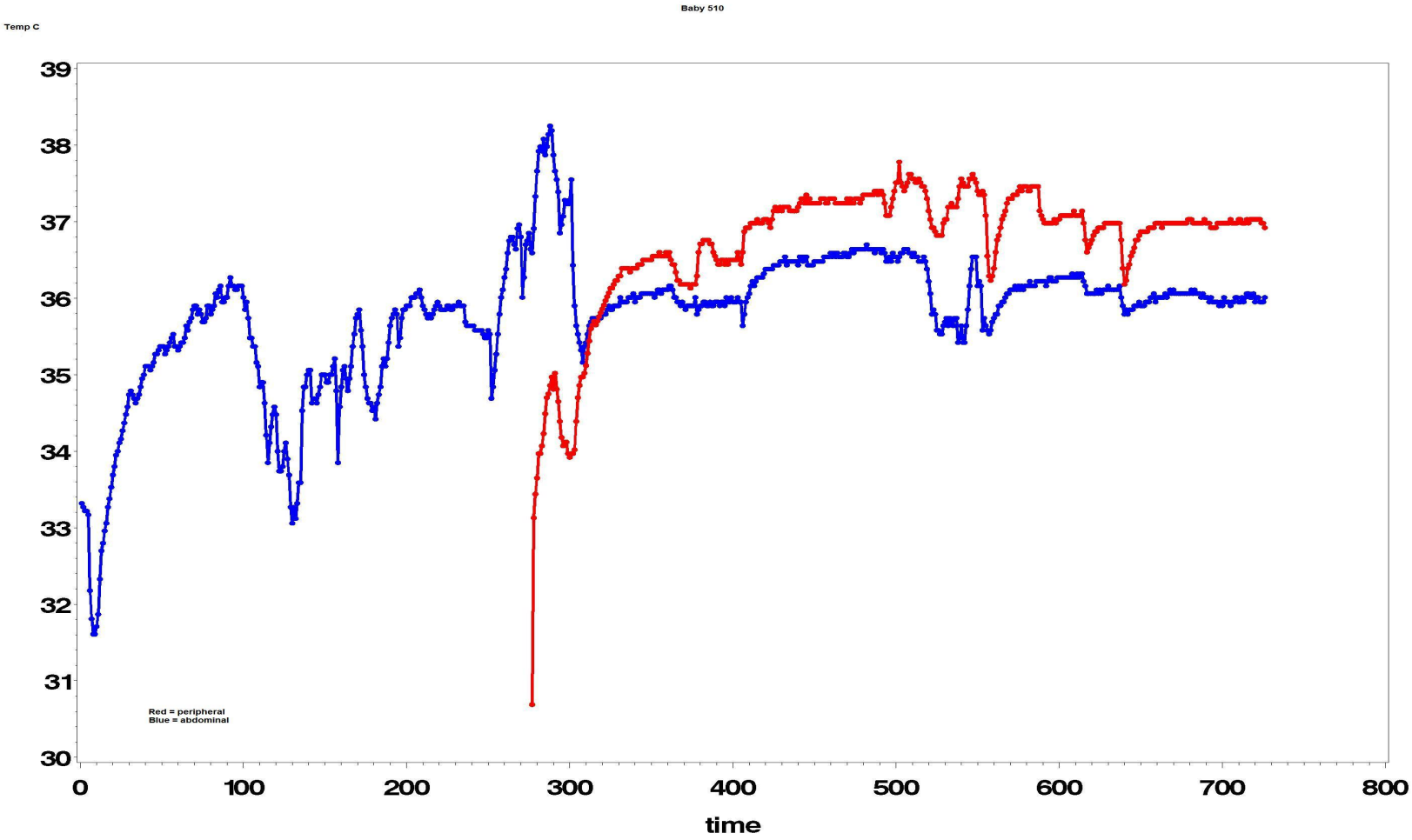


Table 4.20 Abdominal – Peripheral Temperature Difference for Infant 510

Abdominal – Peripheral Temperature	% of observations
2˚ C	6%
1.5˚ C	6.2%
1˚ C	6.4%
-1˚ C	19.7%
-1.5˚ C	2.7%
-2˚ C	0.4%

Visual inspection of the heart rate graph (Figure 4.20) shows higher heart rates in the beginning of the study period during stabilization with a large amount of fluctuation and a trend downward towards the middle of the study, ending with a more stable heart rate towards the end of the study. Heart rate fluctuations were associated with clinical stimulation to the infant. The infant was placed on the ventilator at 60% FiO_2 and increased up to 80% FiO_2 within the first hour of life. After surfactant administration, the FiO_2 weaned down to 21% or room air by 1½ hours of age. The infant remained between 21% and 26% FiO_2 for the remainder of the study, with two brief episodes at 100% FiO_2. Figure 4.21 shows the infant's oxygen saturations over the 12 hours of the study.

Although the pH values for this infant were mostly normal, the infant was compensating for a metabolic acidosis as shown by the base deficits and low CO_2 values. The CO_2 values

were in the low 20's in the beginning of the study period and slowly increased to 43. Therefore, there was a metabolic acidosis in the first 8 hours of the study (see Table 4.21). The glucose values were all within normal values and were variable. The values did not show a consistent trend or relationship with temperature.

Table 4.21 Secondary Variables from Medical Chart for Infant 510

Infant age	**Axillary temps ˚C**	**pO_2 mm**	**pCO_2**	**pH**	**Base deficit**	**Chemstrips**
15 min	36					86
30 min		219	26	7.45	-6	
2 hr						87
3 hr	36.6	110	29	7.42	-5.6	112
4 ½ hr	36.8					
6 hr		131	29	7.38	-7.5	66
8 ½ hr	36.8	42 venous	33	7.40	-4.1	94
11 hr		29 venous	43	7.30	-5.8	118

Figure 4.20 Heart Rate for Infant 510 for Study Period

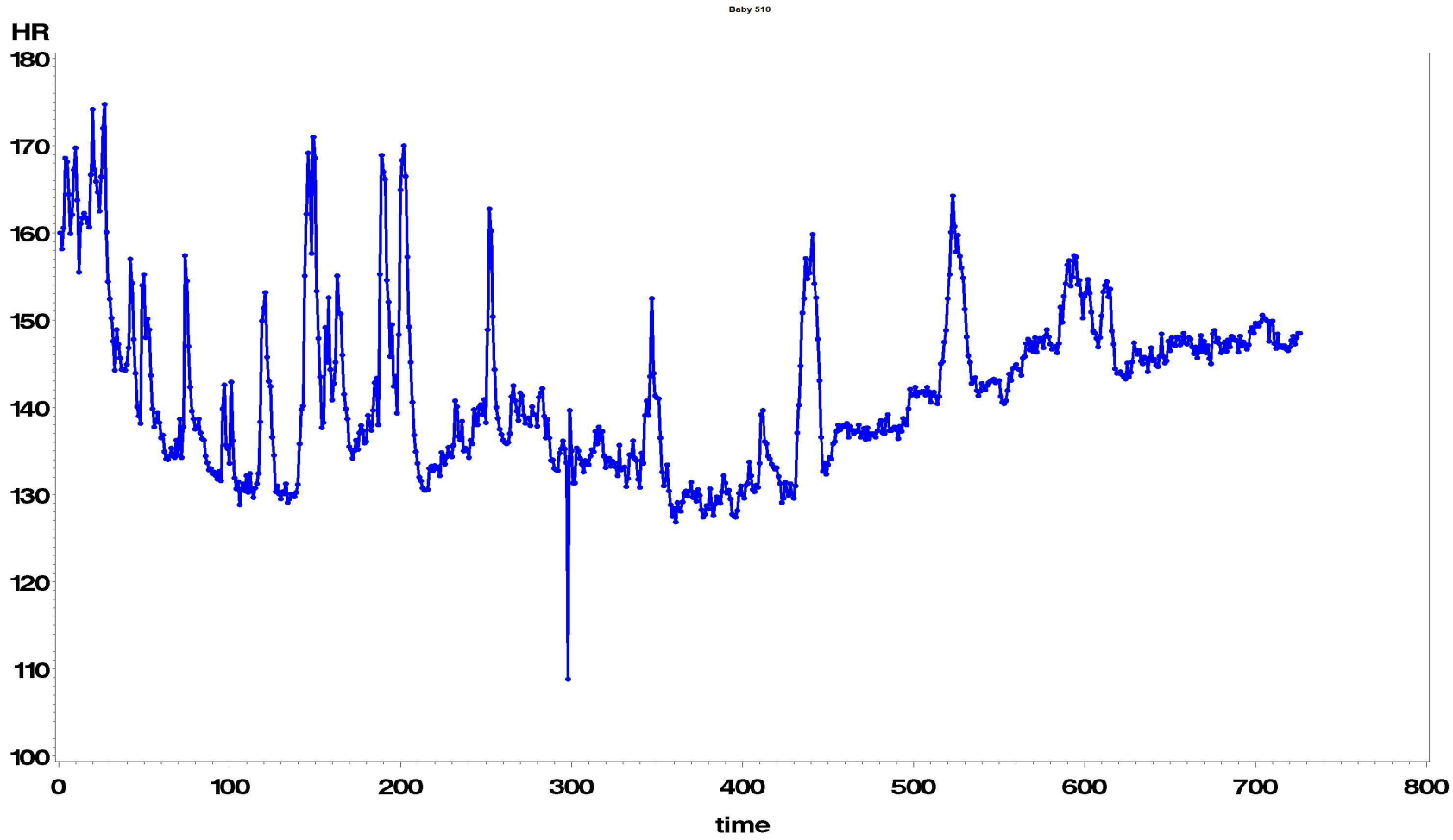
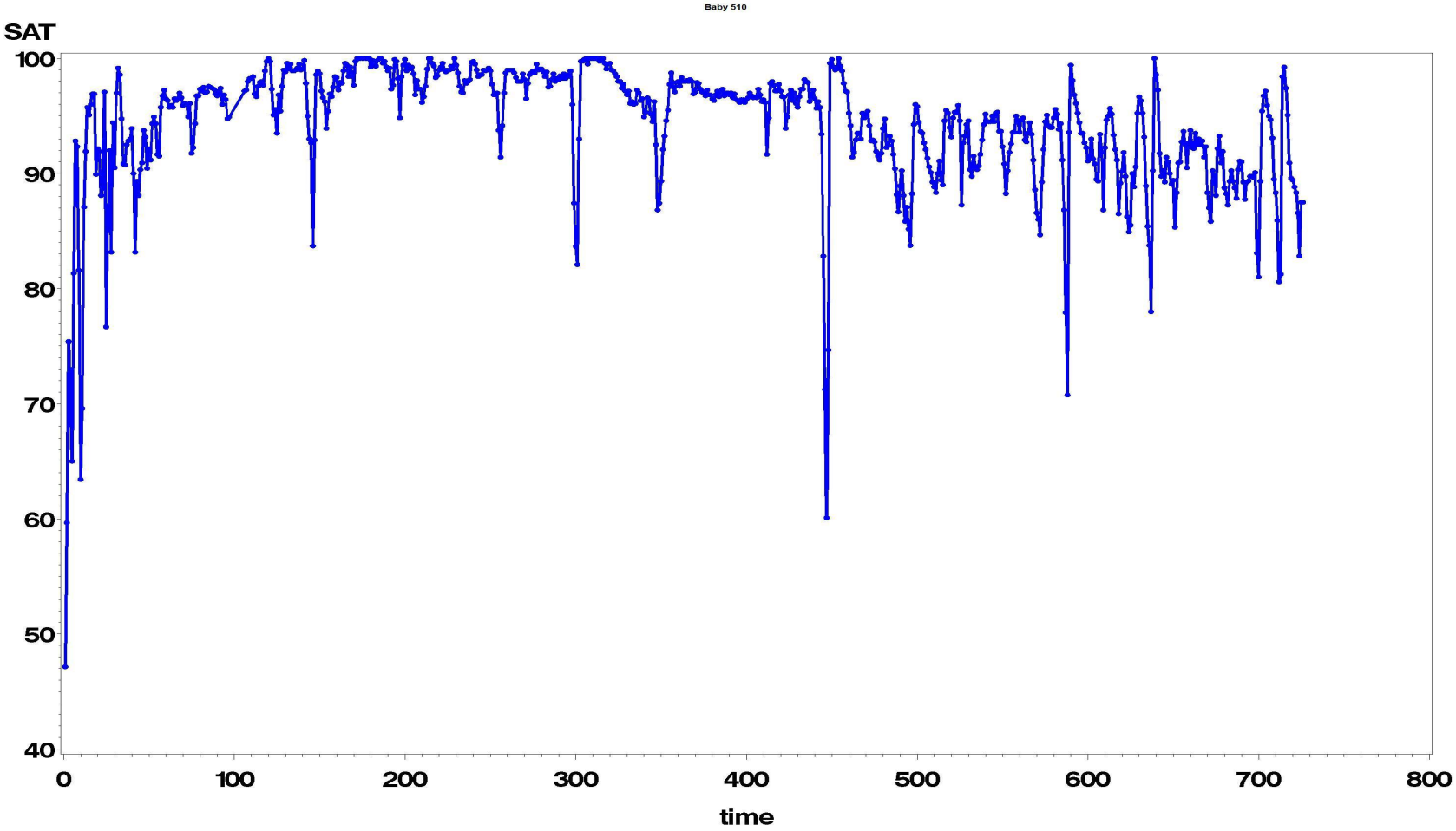


Figure 4.21 Oxygen Saturation for Infant 510 for Study Period



Subject 590

This was a 710-gram African American male delivered by vaginal delivery at 25-weeks gestation. The infant was enrolled in the study and study monitors were attached with data collection beginning at 20 minutes of age. Table 4.22 gives descriptive data for all primary variables.

Table 4.22 Descriptive Statistics of Primary Variables for Infant 590

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	36.44˚ C	1.17	32.80˚ C	37.92˚ C
Peripheral Temperature (foot)	36.75˚ C	0.95	33.17˚ C	38.14˚ C
Adominal – peripheral temperature	-0.32˚ C	0.57	-2.41˚ C	1.90˚ C
Oxygen saturation	94.17%	3.33	69.0 %	100.0 %
Heart rate	144.0	7.05	125.0	164.0

This infant had stabilization procedures during the first 4 ½ hours of life; the umbilical arterial line was connected at 4 ½ hours of age. Visual examination of the graphic trends revealed a difference between peripheral and abdominal temperatures over the first 5 hours of age, in which the peripheral temperature was higher than the abdominal temperature the majority of the time (see Figure 4.22).

Figure 4.22 Abdominal and Peripheral Temperature for Infant 590

Red = peripheral temperature **Blue = abdominal temperature**

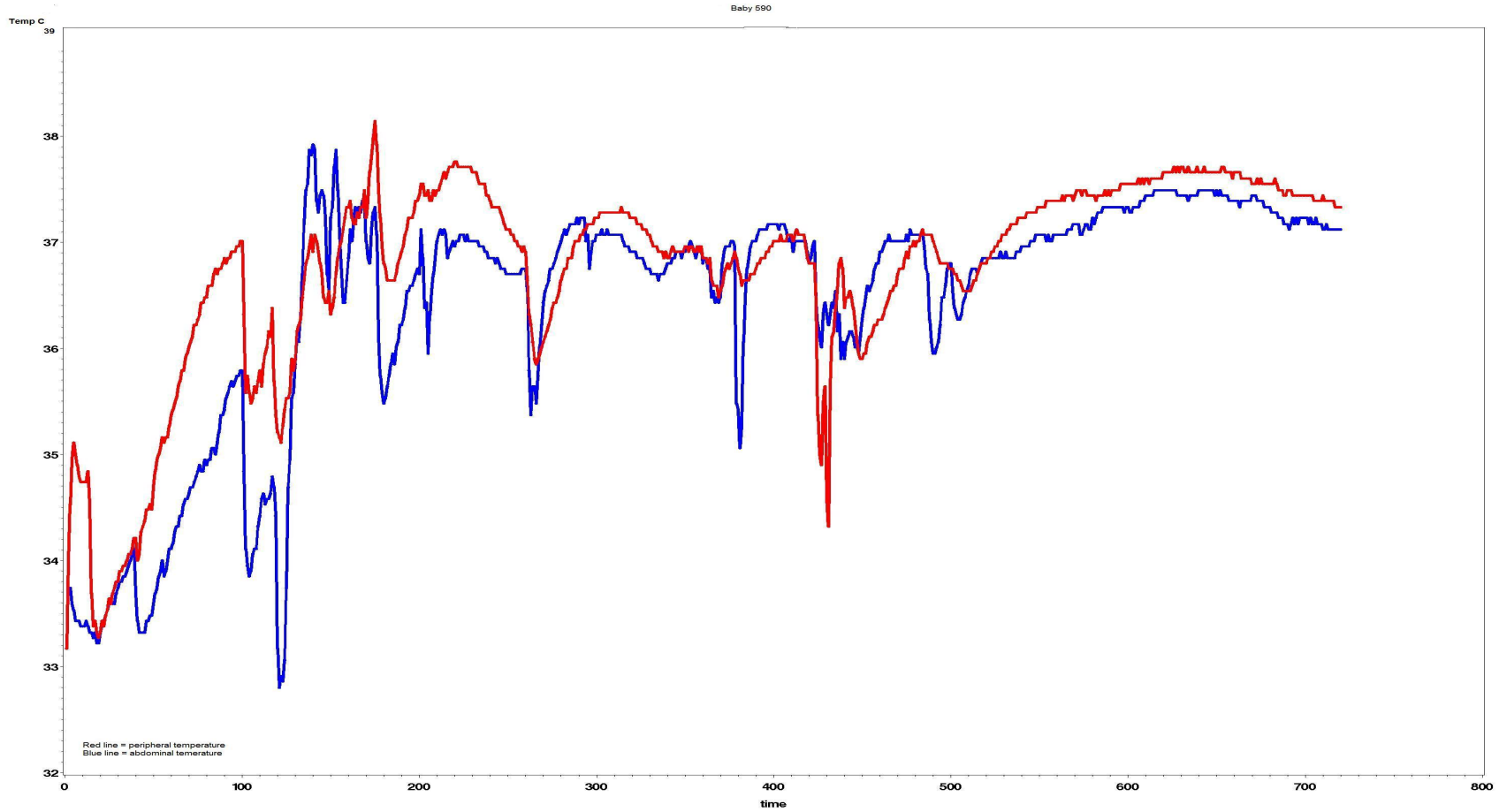


Figure 4.23 Heart Rate for Infant 590 for Study Period

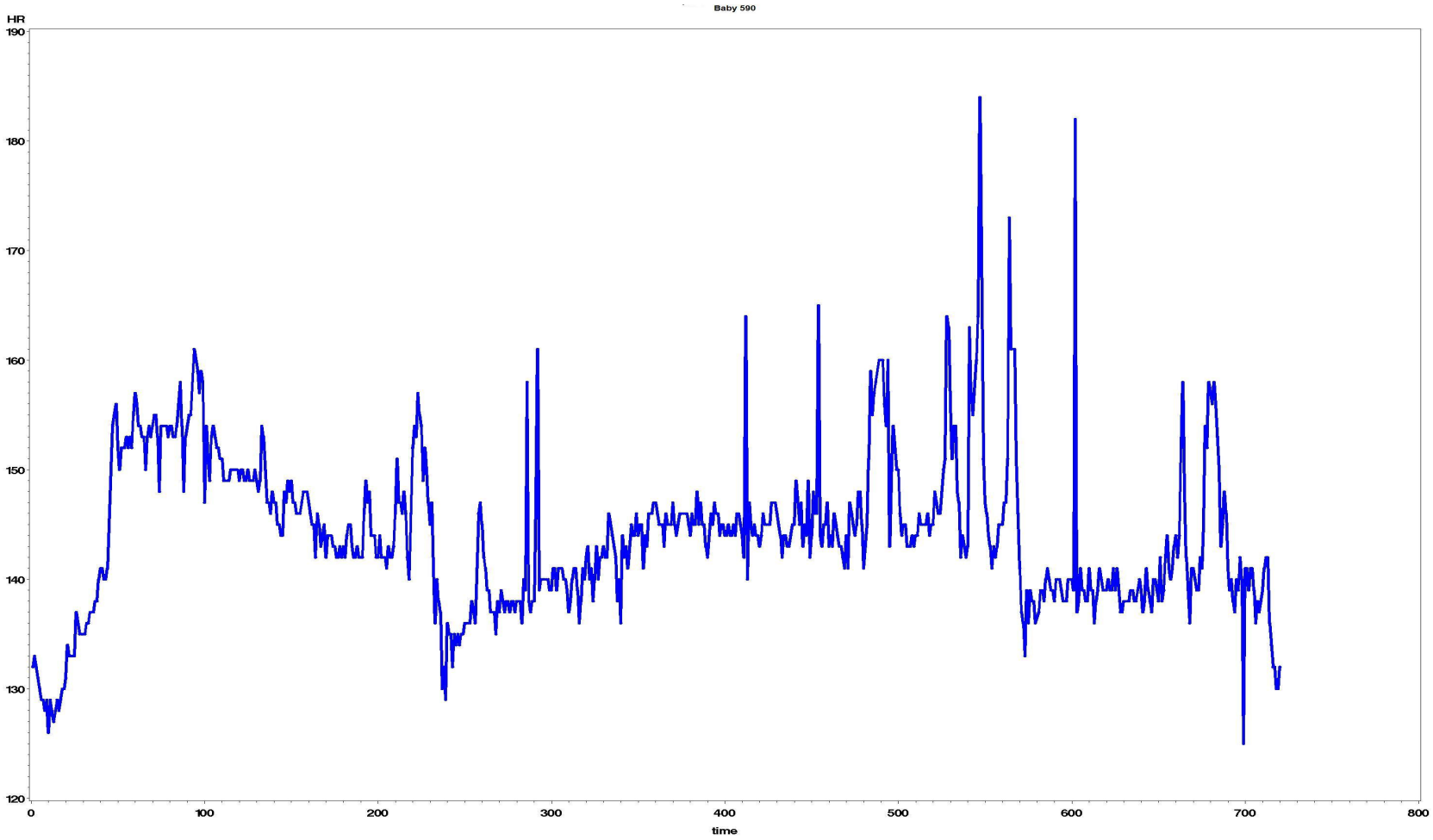
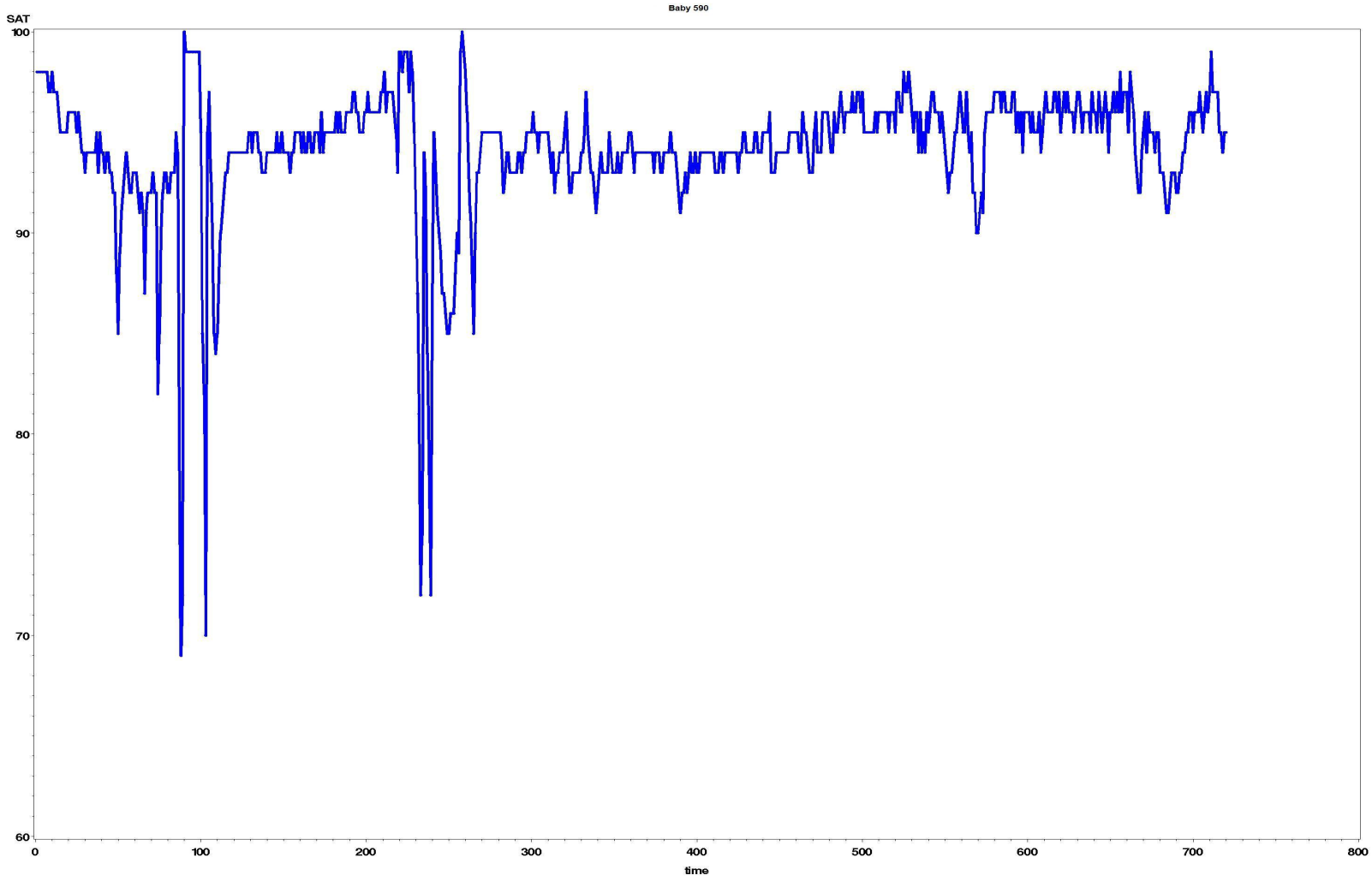


Figure 4.24 Oxygen Saturation for Infant 590 for Study Period



This infant did not have any 1-minute periods defined as peripheral vasoconstriction. However, 15.2% of the periods had a 1˚ C difference in temperatures with the peripheral temperature higher than the abdominal temperature (see Table 4.23).

This infant had increases in heart rate and temperature variability that occurred the 1 ½ hours prior to, during and after shift change. Shift change includes nurses talking at the bedside, entering the incubator to check the infant's intravenous sites, and assessments of the infant by the oncoming nurse. Heart rate trends are presented in Figure 4.23.

Table 4.23 Abdominal – Peripheral Temperature Difference for Infant 590

Abdominal – Peripheral Temperature	**% of observations**
2˚ C	0%
1.5˚ C	0.3%
1˚ C	1%
-1˚ C	15.2%
-1.5˚ C	3.7%
-2˚ C	0.4%

The infant was placed on the ventilator on admission to the NICU at 40% FiO_2 and was weaned down to room air on the ventilator by 2 hours of age. A small amount of time was spent at 28% to 45% during stabilization; however, the infant returned to room air (21%) by 5 ½ hours of age and remained there for the rest of the study period. Figure 4.24 presents the infant's oxygen saturations over the 12 hours of the study. The infant had a stable pH

throughout the study period (see Table 4.24). Although this infant went through several hours of stabilization procedures, acid-base balance remained stable. Glucose values started out low and increased with advancing age and stabilization.

Table 4.24 Secondary Variables from Medical Chart for Infant 590

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
1 hr		53	7.35	-1.5	36
2 hr					43
3 hr	36.7				
4 hr	36.8				
5 hr					107
5 ½ hr		61	7.37	-3.4	108
8 hr		62	7.35	-3.1	79

Subject 680

This infant was a 590-gram White male delivered by cesarean section at 24-weeks gestation. Study monitors were attached and began recording at 1 hour of age. Table 4.25 presents the descriptive statistics for the primary study variables over the 12 hour study period.

Stabilization of the infant (attachment of the ventilator, monitors and umbilical line placement) in the NICU took place for approximately 1 hour prior to beginning data

Table 4.25 Descriptive Statistics of Primary Variables for Infant 680

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	35.61˚ C	1.30	31.24˚ C	36.91˚ C
Peripheral Temperature (foot)	36.32˚ C	1.29	32.96˚ C	37.44˚ C
Adominal – peripheral temperature	-0.71˚ C	0.52	-3.07˚ C	0.95˚ C
Oxygen saturation	94.53%	2.43	72.0 %	100.0 %
Heart rate	129.10	9.62	106.0	165.0

Table 4.26 Abdominal – Peripheral Temperature Difference for Infant 680

Abdominal – Peripheral Temperature	% of observations
2˚ C	0%
1.5˚ C	0%
1˚ C	0%
-1˚ C	23.7%
-1.5˚ C	11.7%
-2˚ C	1.4%

Figure 4.25 Abdominal and Peripheral Temperature for Infant 680

Red = peripheral Blue = abdominal

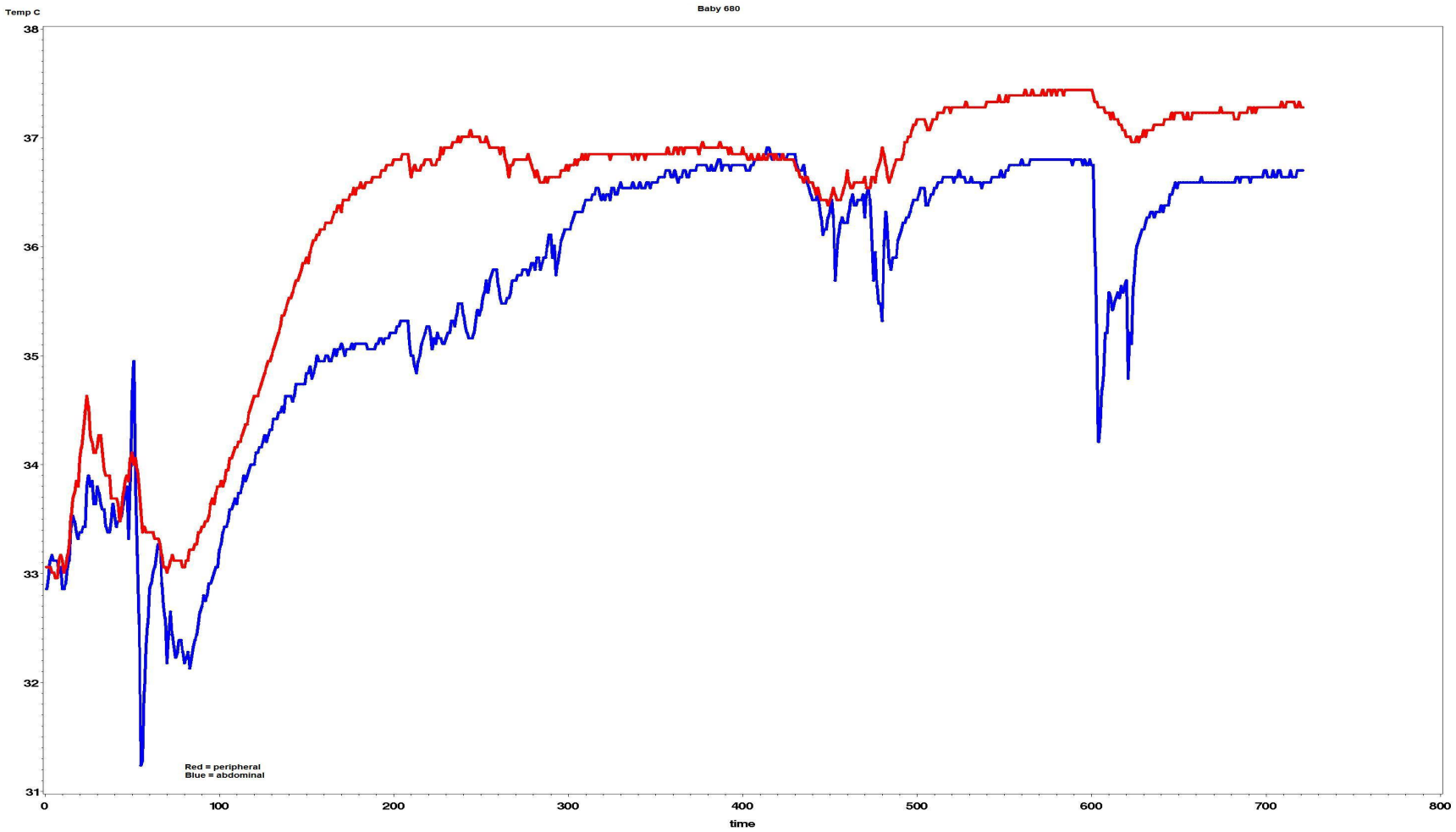


Figure 4.26 Heart Rate for Infant 680 for Study Period

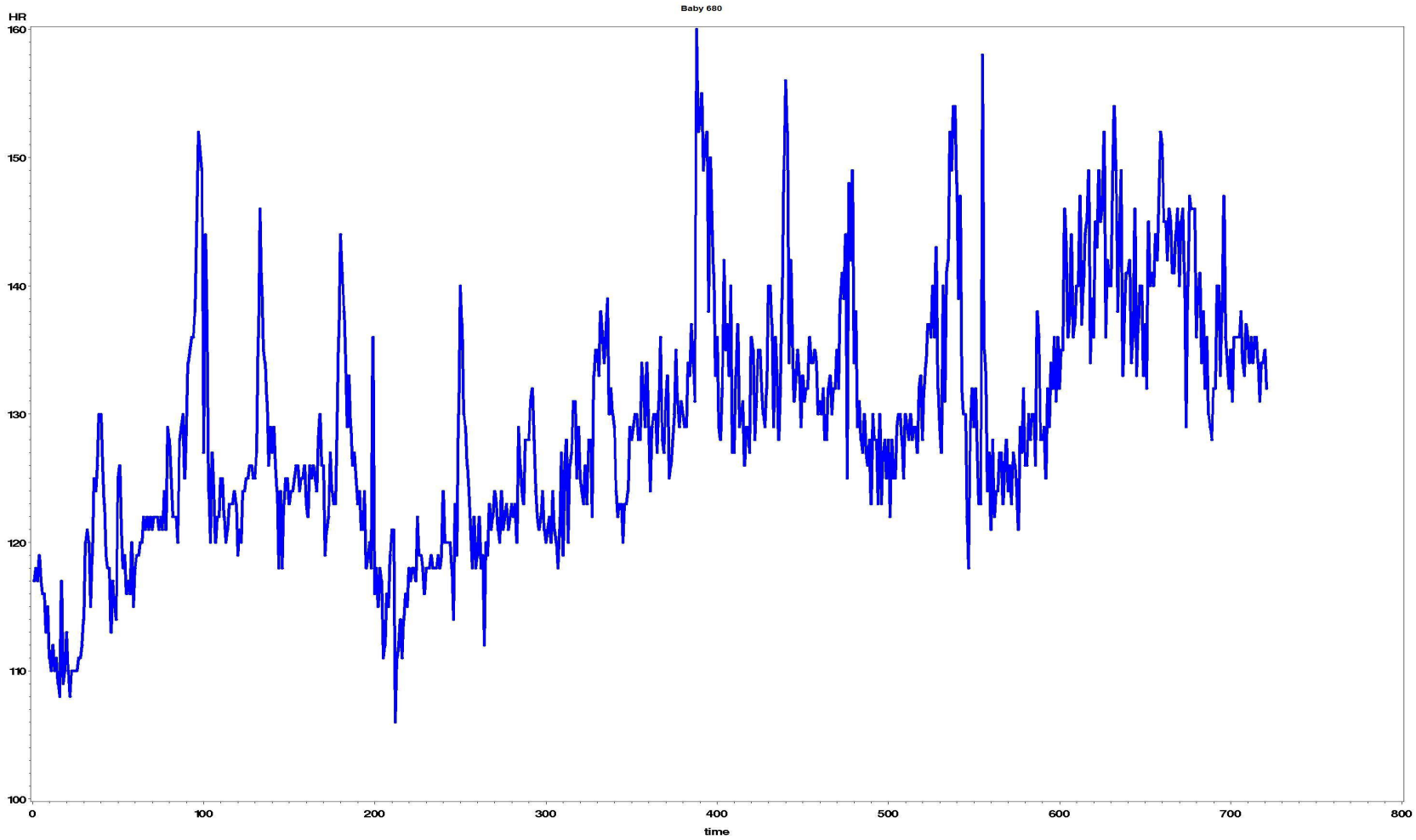
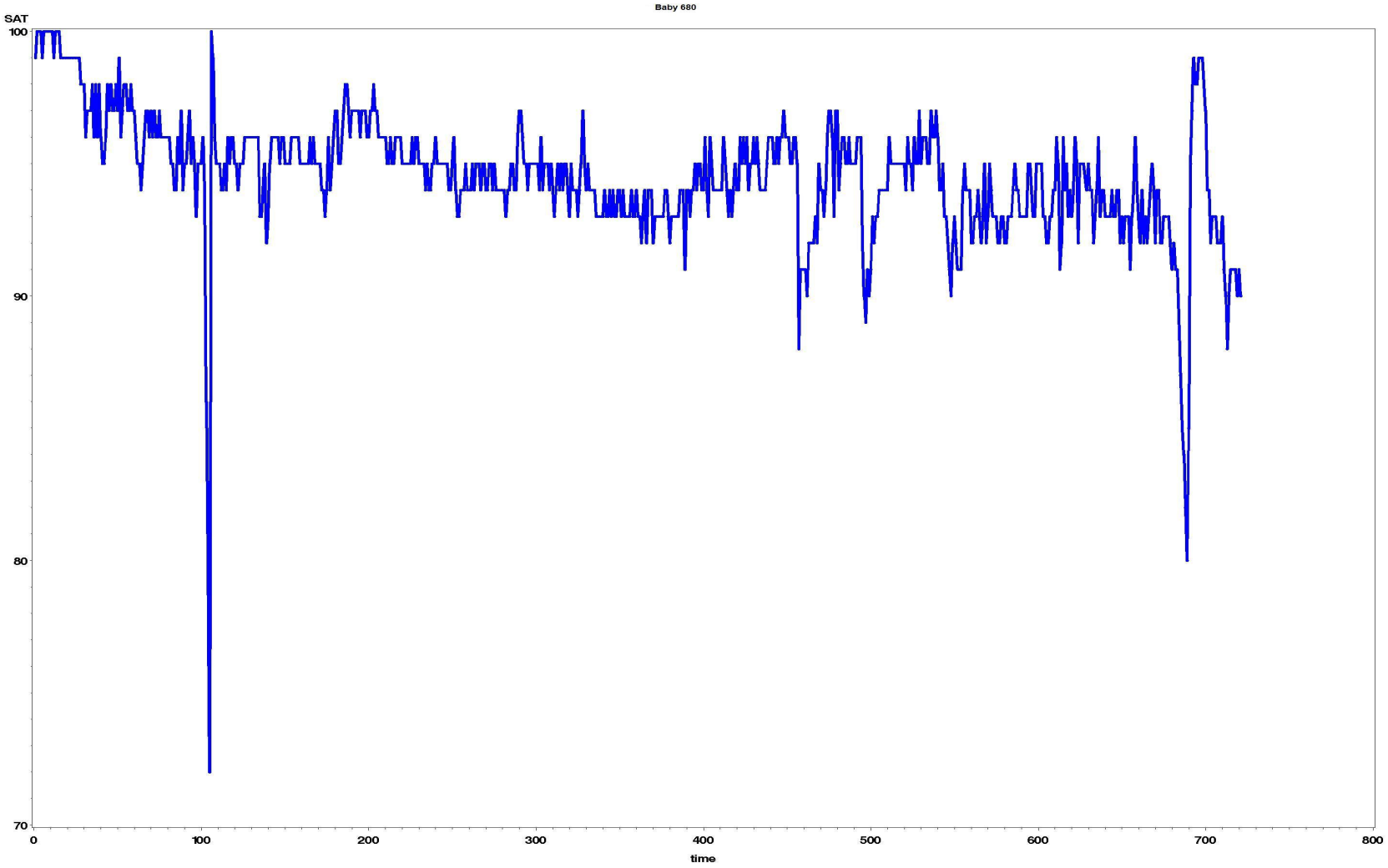


Figure 4.27 Oxygen Saturation for Infant 680 for Study Period



collection. Even though initial temperature was 35.4˚ C on admission, rectal temperature at 1 hour of age and post stabilization was too low to be read on the electronic IVAC thermometer and these low temperature trends are presented in Figure 4.25.

This infant did not have any 1-minute periods defined as peripheral vasoconstriction. However, 23.7% of the periods had a 1˚ C difference in temperatures with the peripheral temperature higher than the abdominal temperature and 11.7% of the periods had a temperature difference of 1.5˚ C (see Table 4.26). Figure 4.26 presents the infant's heart rate trend over the 12-hour study period. The mean heart rate increased over the study period and became stable by the end of the study period. The infant was placed on the ventilator on admission at 28% FiO_2 and weaned down to 21% FiO_2 (room air) on the ventilator by approximately 2 hours of age. He remained on room air for the remainder of the study period with a brief period of 35% FiO_2 at about 12 hours of age. Figure 4.27 presents the infant's oxygen saturations over the 12-hour study period. Table 4.27 shows the secondary variables for this infant over the 12-hour study period. Acidosis improved as the infant's temperature improved over time. Blood glucose values increased over time.

Subject 730

This infant was a 960-gram African American female delivered vaginally at 26-weeks gestation. The infant was reintubated after NICU admission and placed on the ventilator. Study monitors were attached after the infant was weighed. Monitors began recording at approximately 15 minutes of age. However, the abdominal temperature began recording at 30 minutes of age and the peripheral temperature began recording at almost 4 hours of age because of temperature probe malfunctions. Table 4.28 gives the descriptive statistics for the

primary variables for infant 730 over the 12 hours of the study. The abdominal temperature remained higher than the peripheral temperature throughout the study (see Figure 4.28).

Table 4.27 Secondary Variables from Medical Chart for Infant 680

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
15 min	35.4				
1 hr	Too low to register	137	7.39	-6.4	77
2 hr	34.6 axillary 33.9 rectal				
2 ½ hr		68	7.32	-3.9	92
3 hr	36.2				
4 ½ hr		86	7.33	-2.2	128
6 hr	36.3				
7 hr	36.4				
10 hr		68	7.37	-3.7	148
11 hr		57	7.36	-3.1	143
12 ½ hr		60	7.30	-3.4	121

This infant exhibited peripheral vasoconstriction for 1.4% of the 12 hour study period (see Table 4.29). The majority of the infant's 1-minute periods (62.5%) exhibited a temperature difference between the abdominal and peripheral temperatures of 1˚ C, which may have been an attempt at peripheral vasoconstriction. Figure 4.29 presents the infant's heart rate trends over the 12 hours of the study. A large amount of fluctuation in the heart rate was visible

Table 4.28 Descriptive Statistics of Primary Variables for Infant 730

Variable	Mean	SD	Minimum	Maximum
Abdominal temperature	36.60˚ C	0.34	33.95˚ C	37.28˚ C
Peripheral Temperature (foot)	35.50˚ C	0.49	33.53˚ C	36.91˚ C
Adominal – peripheral temperature	1.08˚ C	0.35	-1.37˚ C	2.58˚ C
Oxygen saturation	91.26%	4.40	51.0 %	100.0 %
Heart rate	140.57	9.65	76.0	174.0

Table 4.29 Abdominal – Peripheral Temperature Difference for Infant 730

Abdominal – Peripheral Temperature	% of observations
2˚ C	1.4%
1.5˚ C	8.8%
1˚ C	62.5%
-1˚ C	0%
-1.5˚ C	0%
-2˚ C	0.2%

Figure 4.28 Abdominal and Peripheral Temperature for Infant 730

Red = peripheral temperature Blue = abdominal temperature

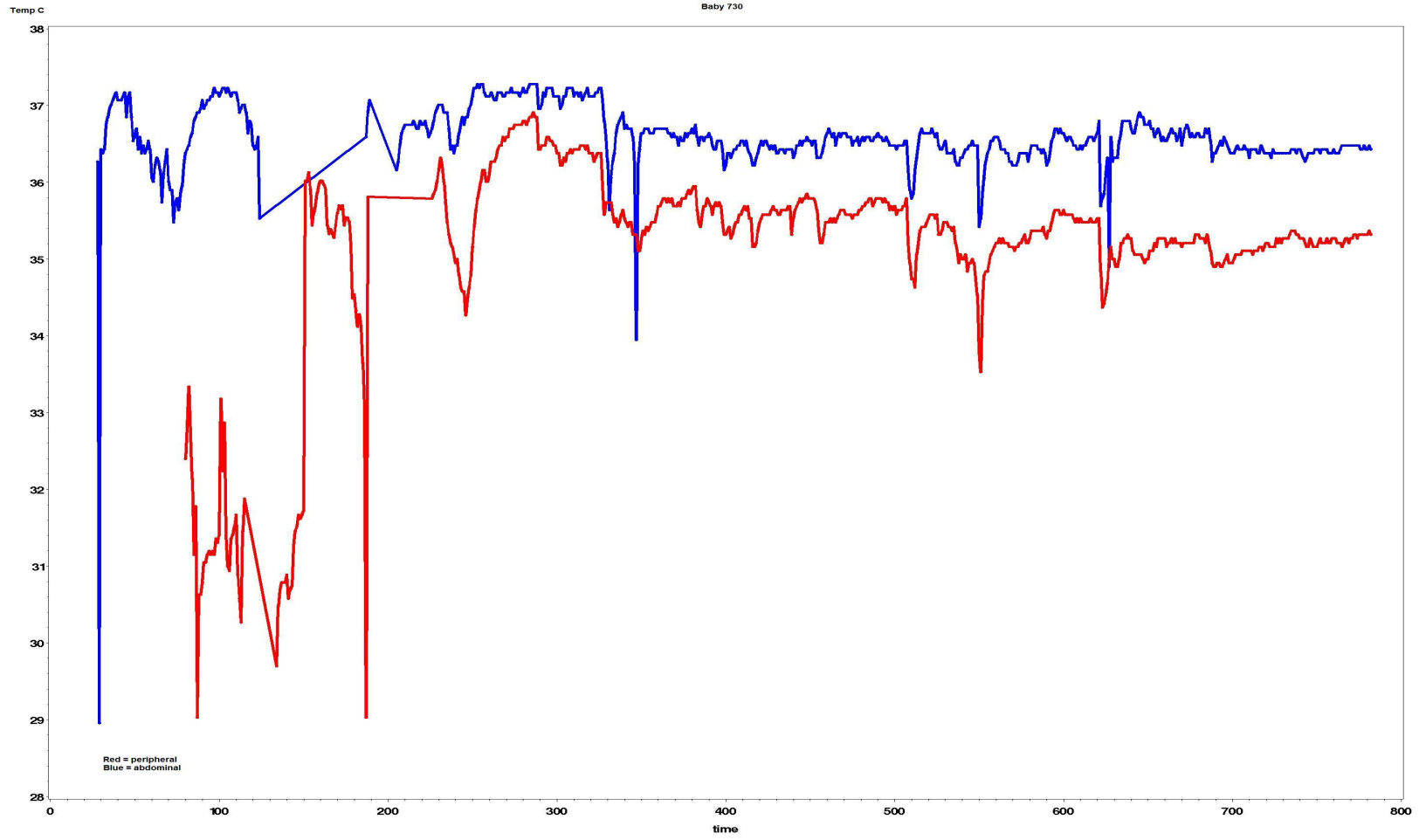


Figure 4.29 Heart Rate for Infant 730 for Study Period

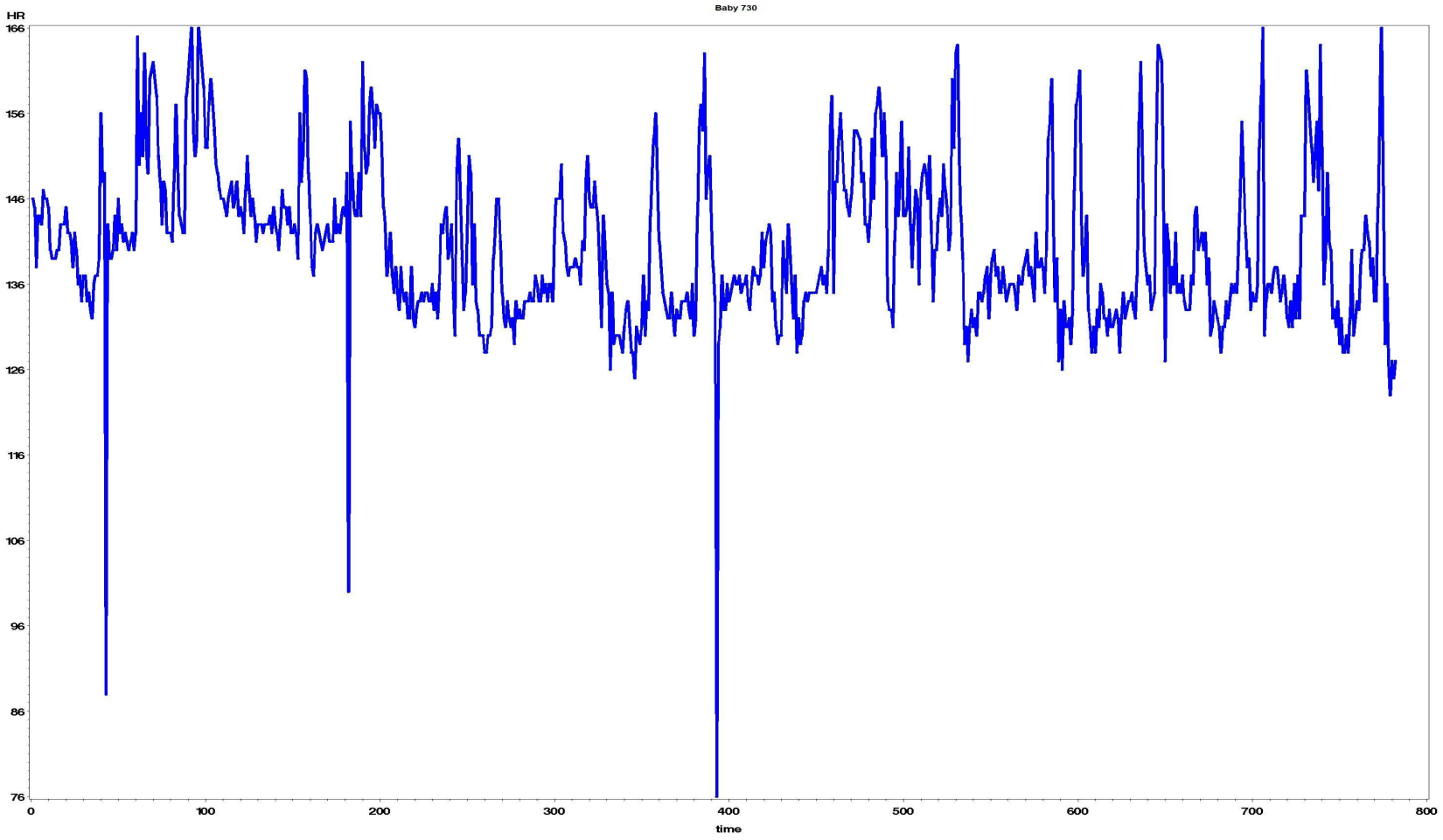
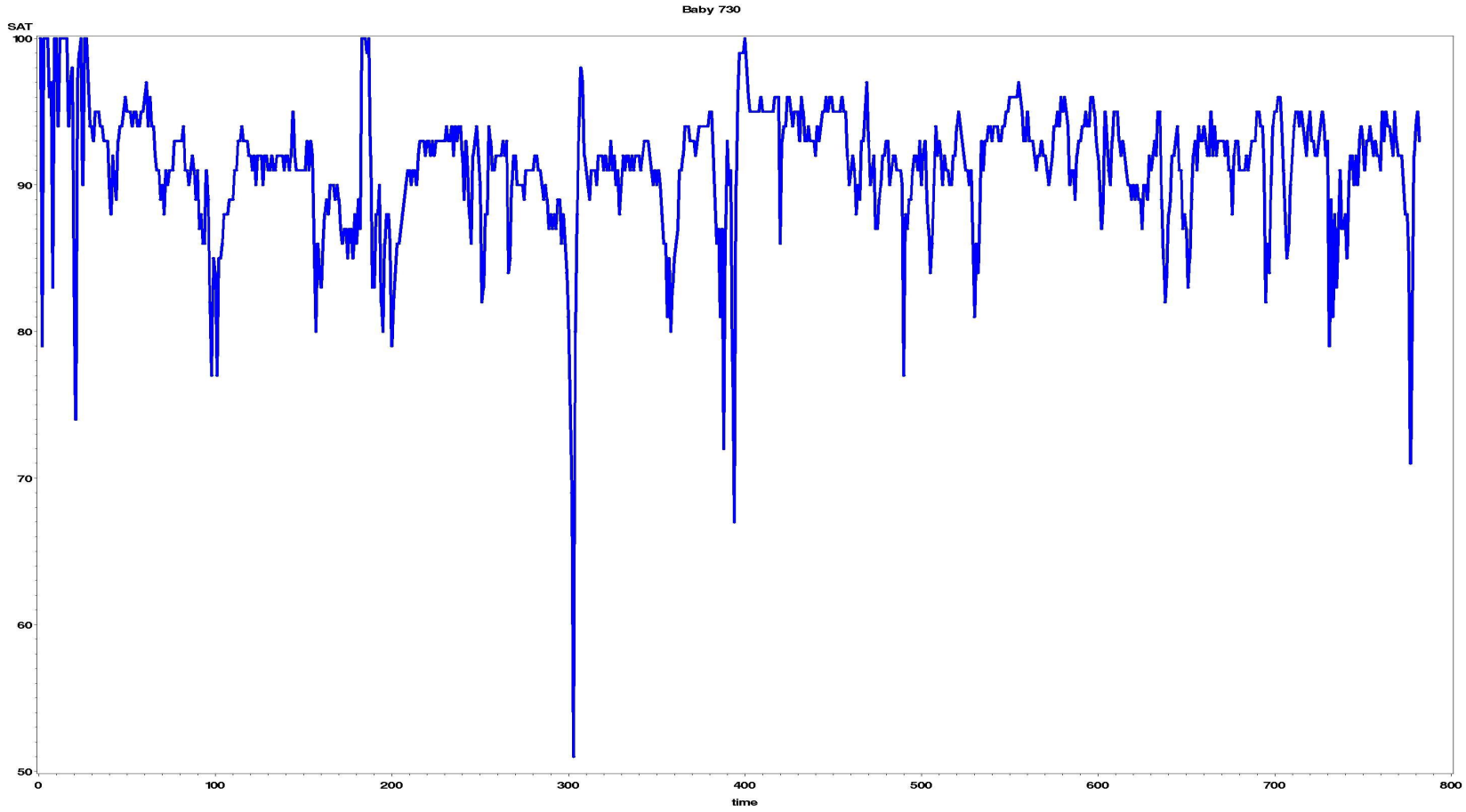


Figure 4.30 Oxygen Saturation for Infant 730 for Study Period



on the graphic trend. Of all study subjects, this infant had the greatest variation in oxygen saturations over the study period in addition to the widest variation in heart rate (see Figure 4.30). The infant was placed on a ventilator at 40% FiO_2 on admission and weaned to room air (21% FiO_2) by 30 minutes of age. Her oxygen level remained between 21% and 26% FiO_2 for the remainder of the study period. She was extubated to nasal pharyngeal CPAP at 8 hours of age. The infant had a slight metabolic acidosis over the study period (see Table 4.30). The glucose values increased over the study period.

Table 4.30 Secondary Variables from Medical Chart for Infant 730

Infant age	Axillary temps ˚C	pO_2 mm	pH	Base deficit	Chemstrips
30 min	37.1				
1 hr					31
2 hr		56	7.32	-3.9	71
2 ½ hr	37.7				
4 hr	36.8	90	7.34	-5.2	104
4 ½ hr	36.7				
7 ½ hr		55	7.38	-4.8	
9 hr		94	7.34	-5.5	

Similarities in Primary Variables Over Infants

Minimum abdominal temperatures for the 10 subjects ranged from 28.96˚ to 33.95˚ C and their maximums ranged from 36.91˚ C to 38.25˚ C (see Appendix IV). The range of mean abdominal temperatures over the 12-hour study periods for each infant ranged from 35.17˚ to 36.68˚ C. Seven of ten subjects had a mean abdominal temperature for the study period less than the 36.4˚ C defined cut point for hypothermia.

Peripheral temperatures ran slightly higher. The minimum peripheral temperature for each infant ranged from 32.13˚ to 35.12˚ C and the maximum ranged from 36.8˚ to 39.6˚ C. The mean peripheral temperature range for all 10 study infants was 35.10˚ to 37.06˚ C. Five of the ten infants had mean peripheral temperatures that were less than the cut point for hypothermia.

I examined the graphs of abdominal and peripheral temperature for all study subjects; 7 of 10 infants had peripheral temperatures greater than abdominal temperatures for most of the study period. The mean abdominal temperature for all 10 study subjects was 35.93˚ C which is 0.38˚ C lower than the mean peripheral temperature for all 10 study subjects (36.31˚ C).

The heart rate range was individual to each infant. Minimum heart rate for the 10 study subjects ranged from 76 to 133. Maximum heart rate ranged from 164 to 194. The mean heart rates ranged from 127 to 166. Thus, at least one infant had a mean heart rate greater than the maximum heart rate of another and at least one infant had a mean heart rate lower than the minimum of another.

Oxygen saturation minimum ranged from 47% to 80% for the study subjects. All infants had a maximum oxygen saturation of 100%, regardless of whether or not they were on supplemental oxygent. The mean oxygen saturation for the 10 infants ranged from 91.26%

to 96.42%.

Correlations of abdominal temperature lags with heart rate and oxygen saturation

Abdominal temperature at simultaneous timing through 5 minute lags was examined at 1-minute increments in relationship to each infant's heart rate and oxygen saturation to determine if there was a stronger relationship between abdominal temperature and heart rate or oxygen saturations prior to the observation compared to simultaneously with the observation. Abdominal temperature was correlated with heart rate (Table 4.31) and oxygen saturation. This analysis is limited in that it only addresses lag times through 5 minutes and different results may be obtained if lag times are extended past 5 minutes.

Table 4.31 Pearson Correlations for Abdominal Temperature and Heart Rate at Lags (0-5 minutes)

Infant #	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4	Lag 5
170	0.278*	0.270*	0.258*	0.247*	0.231*	0.217*
240	0.717*	0.727*	0.711*	0.708*	0.697*	0.694*
311	0.039	0.048	0.058	0.067	0.074*	0.076*
360	0.337*	0.336*	0.342*	0.336*	0.336*	0.334*
410	0.441*	0.444*	0.451*	0.456*	0.454*	0.451*
450	0.166*	0.171*	0.174*	0.177*	0.180*	0.177*
510	-0.318*	-0.316*	-0.313*	-0.314*	-0.315*	-0.319*
590	-0.038	-0.048	-0.060	-0.073	-0.084*	-0.094*
680	0.444*	0.446*	0.444*	0.442*	0.442*	0.441*
730	0.036	0.048	0.0.46	0.030	0.012	0.013

* $p < .05$

Lag 0 = simultaneous timing

Table 4.32 Pearson Correlations for Abdominal Temperature and Oxygen Saturation at Lags (0-5 minutes)

Infant #	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4	Lag 5
170	0.315*	0.307*	0.294*	0.286*	0.282*	0.276*
240	-0.071	-0.070	-0.074*	-0.079*	-0.082*	-0.079*
311	0.503*	0.509*	0.515*	0.521*	0.539*	0.531*
360	0.337*	0.336*	0.342*	0.336*	0.336*	0.334*
410	0.054	0.060	0.075*	0.075*	0.095*	0.097*
450	-0.500*	-0.490*	-0.486*	-0.492*	-0.500*	-0.502*
510	0.131*	0.101*	0.076*	0.056	0.029	-0.009
590	0.165*	0.162*	0.158*	0.153*	0.155*	0.159*
680	-0.433*	-0.427*	-0.422*	-0.414*	-0.407*	-0.403*
730	-0.229*	-0.226*	-0.242*	-0.233*	-0.235*	-0.225*

* $p < .05$

Lag 0 = simultaneous timing

(Table 4.32) at a lag 0 (simultaneous timing), lag 1 (1 minute prior to the heart rate or oxygen saturation), lag 2 (2 minutes prior to the heart rate or oxygen saturation), lag 3 (3 minutes prior to the heart rate or oxygen saturation), lag 4 (4 minutes prior to the heart rate or oxygen saturation) and lag 5 (5 minutes prior to the heart rate or oxygen saturation). No apparent patterns developed between the abdominal temperature's correlation at simultaneous timing or at lag time of 1 through 5 minutes with heart rate or oxygen saturation. Essentially no correlations between abdominal temperature and heart rate and oxygen saturation occurred in 3 of 10 infants and the correlation was essentially the same at all the lag times in 6 of 10 infants for heart rate and oxygen saturation. Only one infant, # 170, had a significant correlation between the abdominal temperature and heart rate and oxygen saturation at simultaneous timing and the correlation became weaker as the timing of the abdominal temperature observation moved each minute previous to the heart rate and oxygen saturation. This pattern did not repeat in any of the others infants. Therefore, lag

time does not appear to be associated with the correlation between abdominal temperature and heart rate or oxygen saturation.

Correlations of Primary Variables

Pearson correlations were examined for each primary variable pair using abdominal temperature (AbT), peripheral temperature (Ft), heart rate (HR) and oxygen saturation (Sat) for each infant. Table 4.33 presents the correlations.

Abdominal and peripheral temperature. Five infants had a moderate (r = 0.64 to 0.77) and three infants had a strong (r = 0.87 to 0.92) correlation between abdominal and peripheral temperature. Figure 4.31 gives an example of a typical regression plot of abdominal temperature correlated with peripheral temperature.

Infant # 510 was the only subject with a negative correlation with abdominal temperature and peripheral temperature (r = -0.28). Because of an approximately 1 ½ hour period when the abdominal temperature reading was increased to the 37-38˚ C range, the correlation was possibly skewed in the negative direction by outliers (see Figure 4.32). At that time the air temperature in the incubator was recorded as 37-38˚ C by the observer and the axillary temperature was recorded as 36.8˚ C by the nurse. Adequate adhesion of the temperature probes to the skin of an ELBW infant can be a problem in the clinical setting because of the high humidity in the incubators. Because I could not go into the incubator frequently, I could only assume the temperature probe was closely adhered to the infants' skin and recording skin temperature instead of picking up air temperature. If the outliers were not in the analyses, then the correlation would be positive. Abdominal temperature was clearly closely and generally positively related to peripheral temperature in all 10 infants.

Figure 4.31 Scatterplot with Regression Line of Abdominal and Peripheral Temperatures for Infant 590

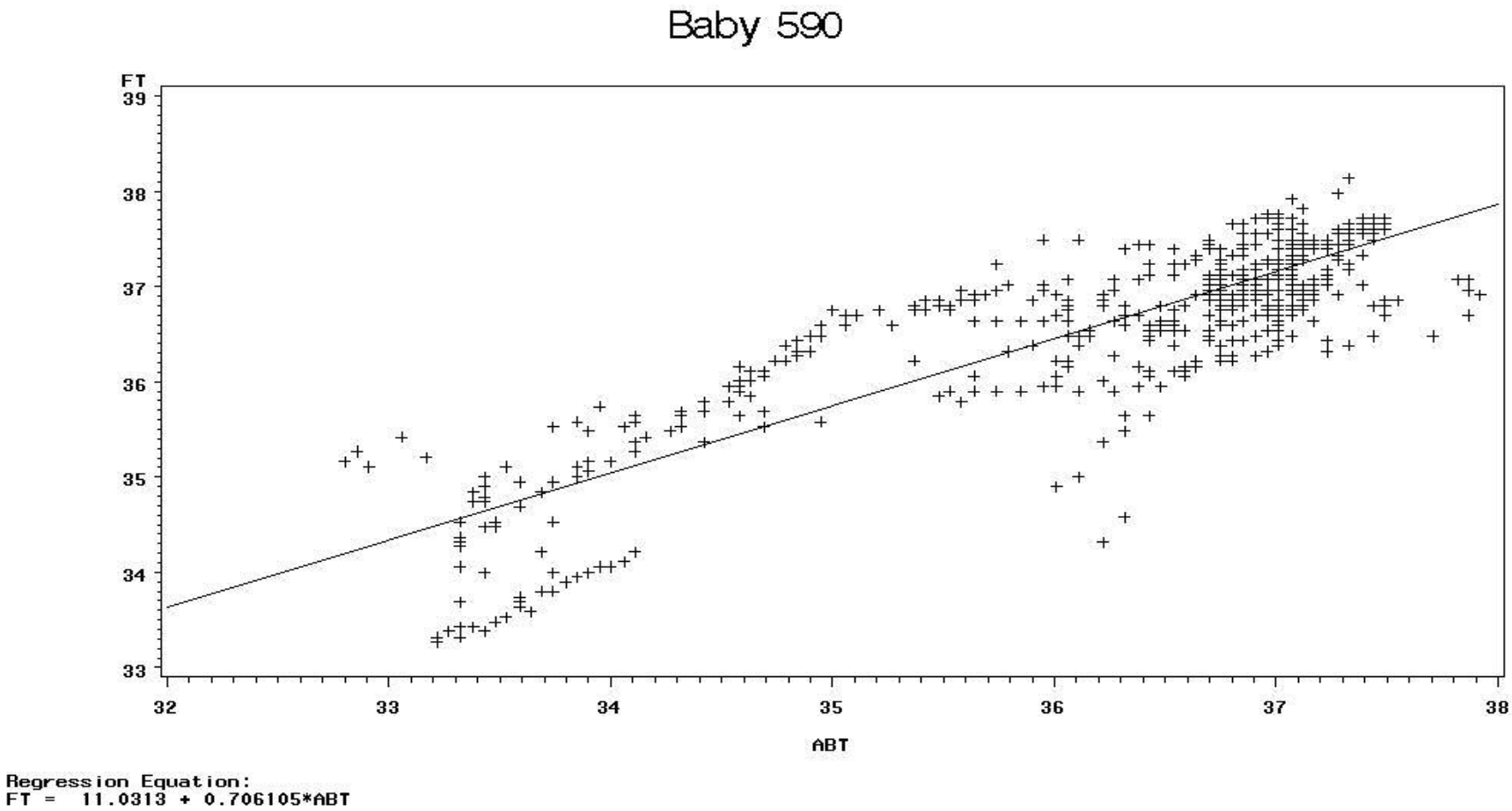


Figure 4.32 Scatterplot with Regression Line of Abdominal and Peripheral Temperatures for Infant 510

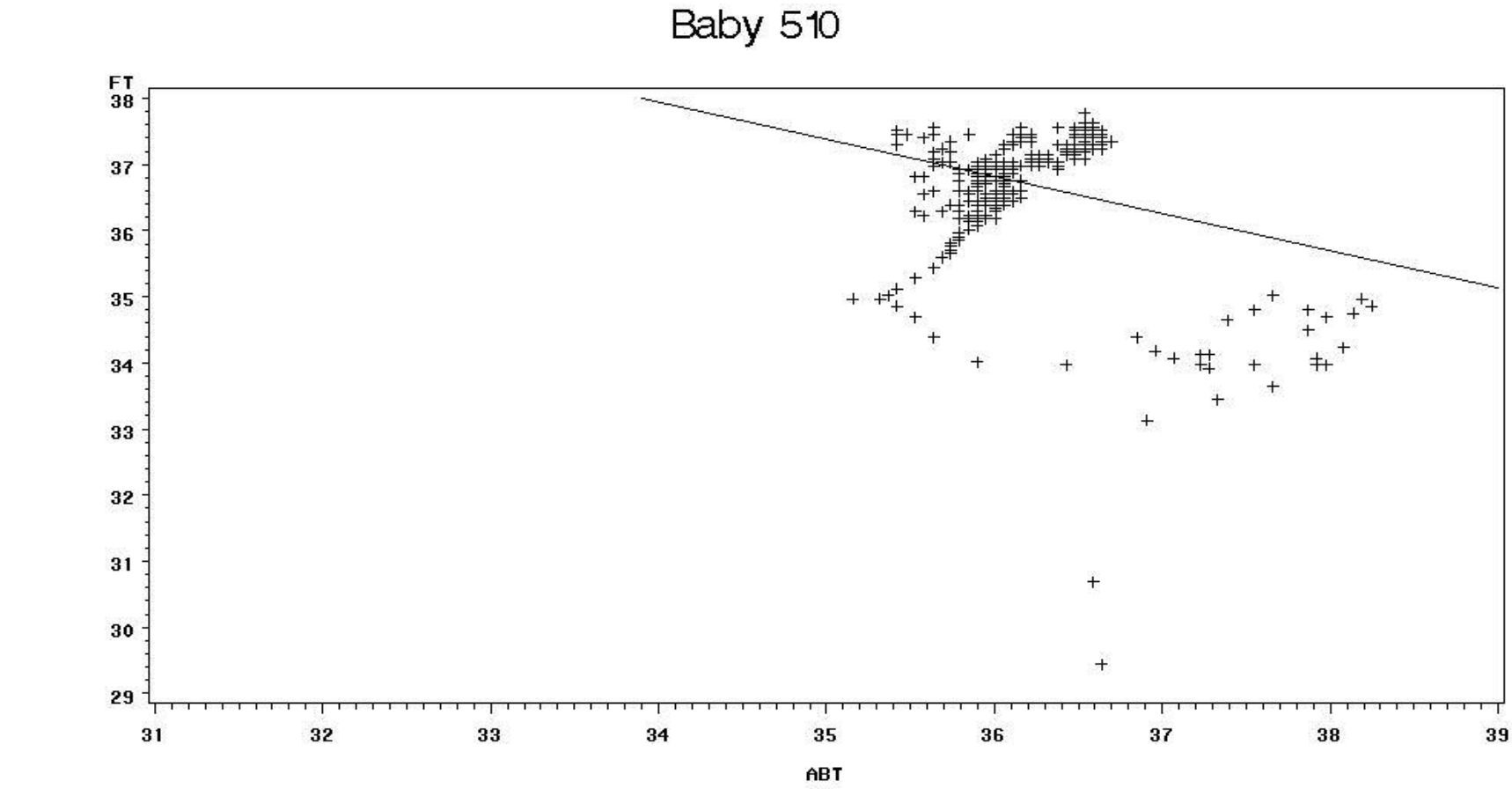


Table 4.33 Pearson Correlations (*r*) Between Study Variables

Infant #	AbT/Ft	AbT/HR	AbT/Sat	Ft/HR	Ft/Sat	HR/Sat
170	0.22*	0.28*	0.32*	-0.06	-0.06	-0.07
240	0.87*	0.72*	-0.07	0.67*	-0.00	0.06
311	0.68*	0.04	0.50*	0.23*	-0.12*	-0.13*
360	0.71*	0.34*	-0.22*	0.22*	-0.16*	-0.29*
410	0.77*	0.44*	0.05	0.60*	-0.07	0.03
450	0.75*	0.17*	-0.50*	-0.14*	-0.24*	-0.30*
510	-0.28*	-0.32*	0.13*	0.33*	-0.34*	-0.39*
590	0.87*	-0.04	0.16*	0.09*	0.10*	0.01
680	0.92*	0.44*	-0.43*	0.40*	-0.42*	-0.27*
730	0.64*	0.04	-0.23*	-0.06	-0.17*	-0.26*

*$p < .05$

AbT: Abdominal temperature Sat: Oxygen Saturation
Ft: Peripheral temperature HR: Heart rate

Temperature and heart rate. **S**even infants had significant correlations between heart rate and abdominal temperature at the $p < .05$ level (r = -0.32 to 0.72). Infant #510 alone had a significant correlation (r = -0.32) that was in the negative direction (see Figure 4.33). Because most of the very low abdominal temperatures for this infant were associated with high heart rates and the high temperatures were associated with normal to low heart rates, the correlation is in a negative direction. Infant #240 had the strongest correlation between heart rate and abdominal temperature (r = 0.72). This infant was a 680-gram 24-week infant who was unstable most of the 12 hours of the study and needed inotropic drugs of dopamine, dobutamine, and then an epinephrine intravenous infusion. During two episodes of clinical stressors, the infant's heart rate increased. Figure 4.34 presents an example of the relationship between the infant's abdominal temperature and the heart rate. Interestingly, the heart rate trended to decline as temperatures decreased and heart rate increased as the infant's temperature increased. This phenomenon is seen often clinically. This infant was very

unstable and did not compensate well metabolically by raising his heart rate with a low abdominal temperatures. Because the infant was colder during the first few hours of stabilization, and became hypotensive as the study period progressed, inotropic drugs were added to his care. As the infant warmed over the study period, concurrently there were more and more inotropic intravenous infusions given to the infant, with a side effect being an increased heart rate. Therefore, it appears that warmer abdominal temperatures were associated with higher heart rates; however, the inotropic infusions could contribute to that association.

Table 4.34 Relationships of the Significant ($p < 0.05$) Pearson Correlations Between Heart Rate and Abdominal Temperature with Infant Demographic Characteristics

Correlation *r* value	Subject #	Gestation (weeks)	Weight (grams)	Gender	Ethnicity
-0.32	510	26	510	F	W
0.17	450	25	670	F	AA
0.28	170	25	630	F	AA
0.34	360	26	880	M	AA
0.44	680	24	590	M	W
0.44	410	25	720	F	W
0.72	240	24	680	M	AA

F = Female, M = Male, AA = African American, W = White

Demographic characteristics of each infant were tabulated to compare with the Pearson correlations between abdominal temperature and heart rate (Table 4.34). No pattern

Figure 4.33 Scatterplot with Regression Line of Heart Rate and Abdominal Temperature for Infant 510

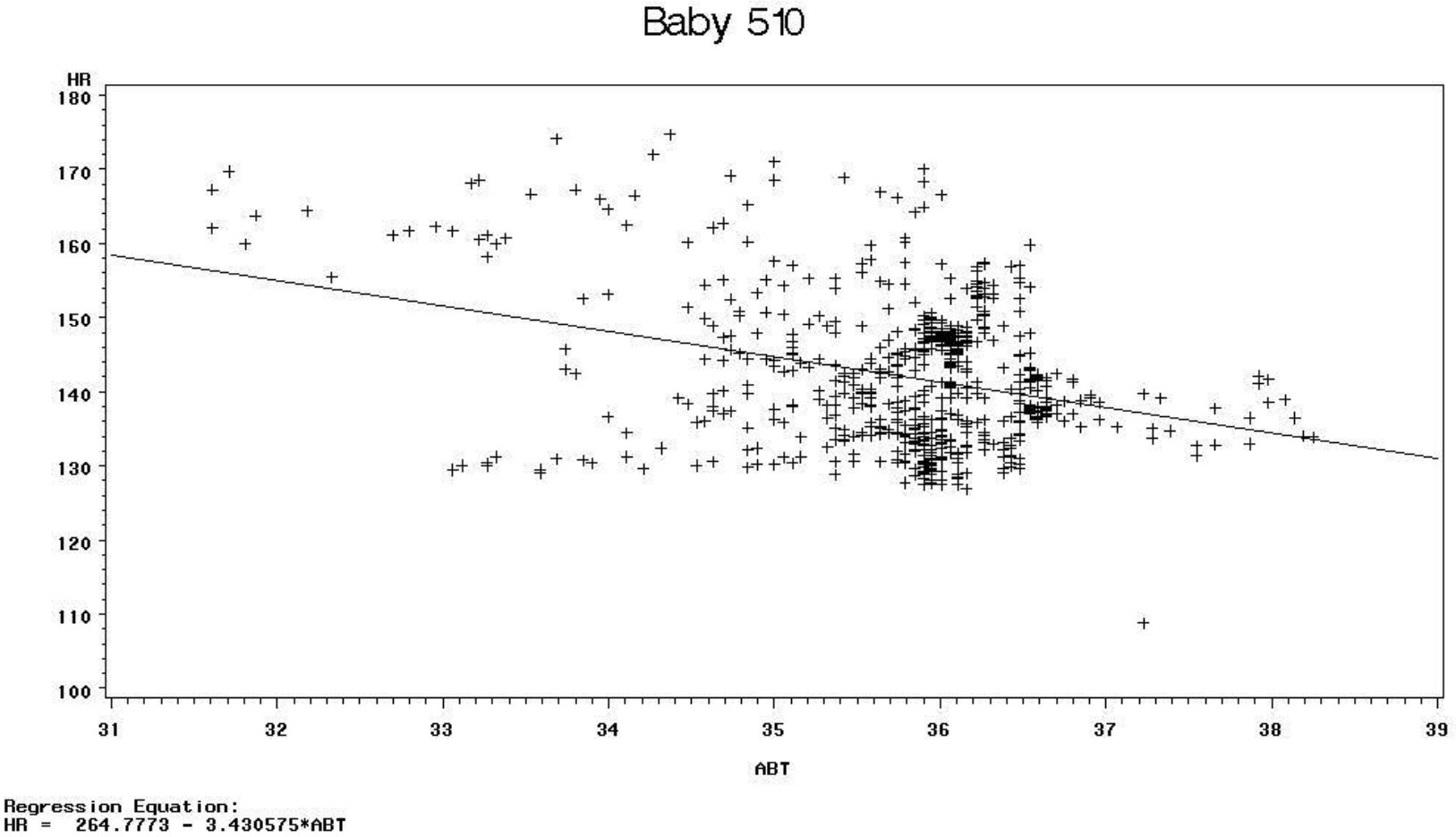
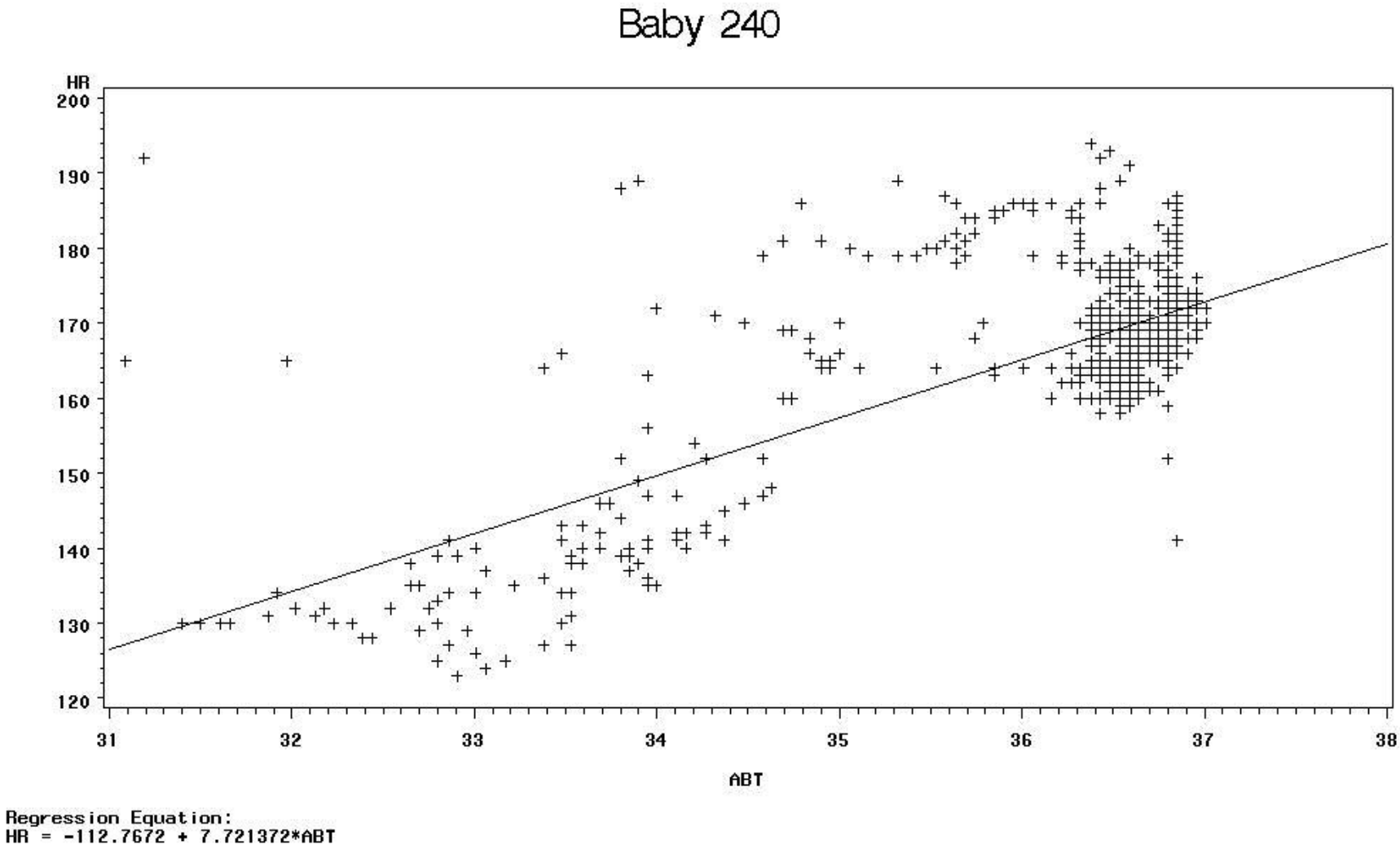


Figure 4.34 Scatterplot with Regression Line of Heart Rate and Abdominal Temperature for Infant 240



appeared in the table regarding the relationship of demographics with strength of correlation between heart rate and abdominal temperature. I attempted to classify infants according to stability over the study period to compare stability with correlation strength. However, delineating clear categories of stability for the 12-hour study period was difficult. Infants had varying degrees of acidosis, abdominal temperature stability, amounts of clinical procedures, and degrees of oxygen delivery. The only definitive classification I could make was infants who received and did not receive inotropic drips. Two infants were on Dopamine drips, #240 and #410. Infant #240 was clearly the most unstable infant because this infant received Dopamine, Dobutamine, and Epinephrine drips, had many procedures and had a persistent acidosis. This infant had the strongest correlation with heart rate. Infant #410 was on a Dopamine drip, had metabolic acidosis as the study period progressed, and had procedures for the first 6 hours with the second strongest correlation at 0.44. However, infant #680 had stabilization procedures for only 1 hour and an improved acidosis over time with the same correlation strength of 0.44. Seven infants had significant correlations between abdominal temperature and heart rate. Higher heart rates were associated with low and high abdominal temperatures however, low heart rates were associated with very low abdominal temperatures. Instability and inotropic intravenous infusions were associated with a moderate correlation between abdominal temperature and heart rate in these study infants. The correlations between peripheral temperature and heart rate were very similar to those of abdominal temperature and heart rate. Correlation *r* values ranged from 0.09 to 0.67 in the positive direction for six infants, with these correlations significant at $p < .05$. One negative correlation ($r = -0.14$) for infant 450 was also significant. As with abdominal temperature and heart rate, infant 240 had the strongest correlation for peripheral temperature and heart

Table 4.35 Relationships of the Significant ($p < 0.05$) Pearson Correlations Between Heart Rate and Peripheral Temperature with Infant Demographic Characteristics

Correlation *r* value	Subject #	Gestation (weeks)	Weight (grams)	Gender	Ethnicity
-0.14	450	25	670	F	AA
0.22	360	26	880	M	AA
0.23	311	25	550	F	W
0.33	510	26	510	F	W
0.40	680	24	590	M	W
0.60	410	25	720	F	W
0.67	240	24	680	M	AA

F = Female, M = Male, AA = African American, W = White

rate ($r = 0.67$). The scatterplot looked very similar to the plot of abdominal temperature and heart rate. Additionall, no relationships between demographic characteristics and strength of correlations for peripheral temperature and heart rate appeared when demographic characteristics were examined visually in tabular form (Table 4.35) against correlations. The association between peripheral temperature and heart rate was essentially the same as that between abdominal temperature and heart rate.

Temperature and oxygen saturation. Eight Pearson correlations reached significance at $p < 0.05$ between the abdominal temperature and oxygen saturation. However, four correlations were in the positive direction ($r = 0.13$ to 0.50) and four were in the negative direction ($r = -0.23$ to -0.43). The strongest positive correlation ($r = 0.50$) was for infant 311 and is presented in Figure 4.35. Outliers may have caused the regression line to have a slight

Figure 4.35 Scatterplot with Regression Line of Oxygen Saturation and Abdominal Temperature for Infant 311

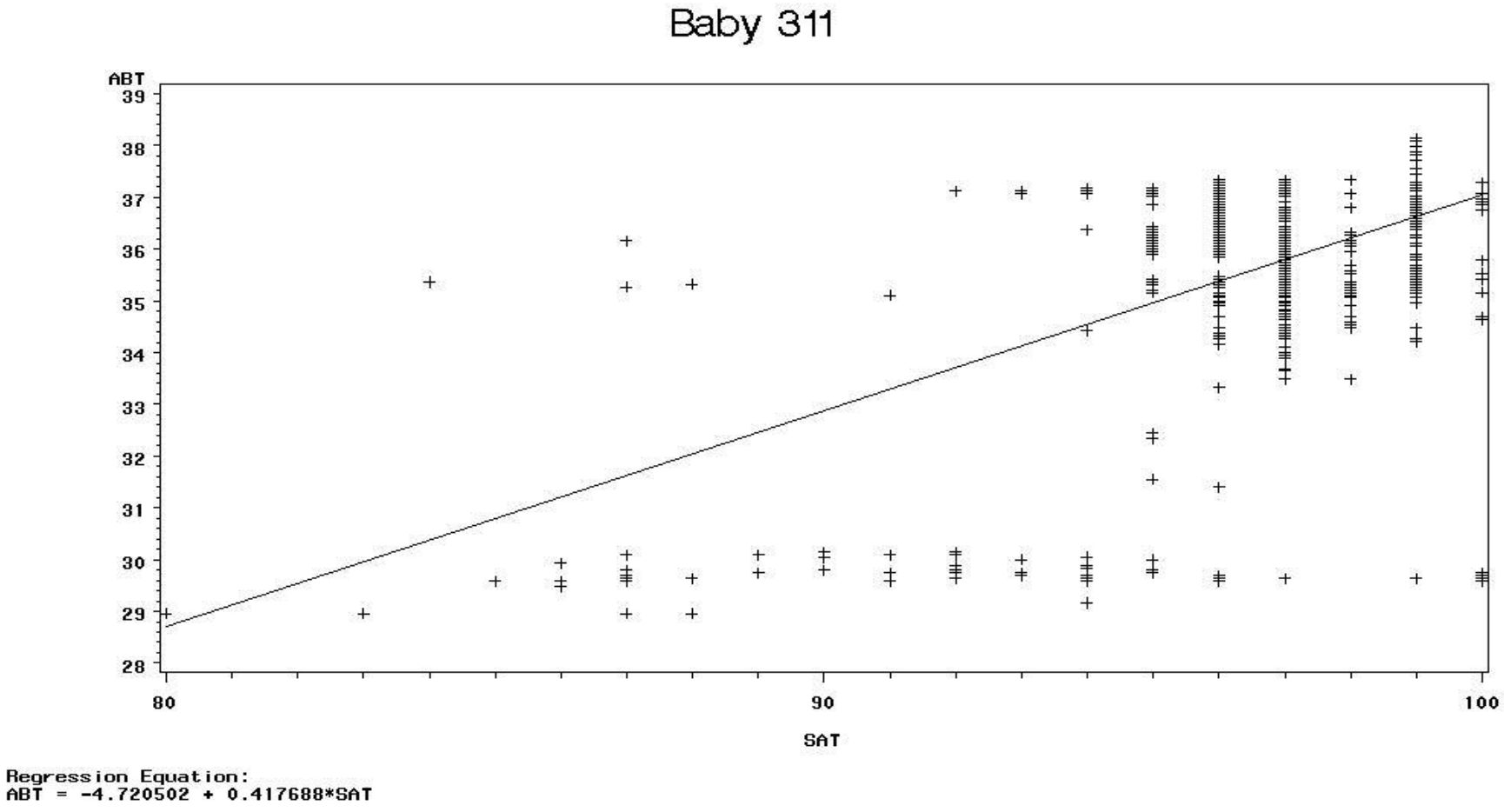
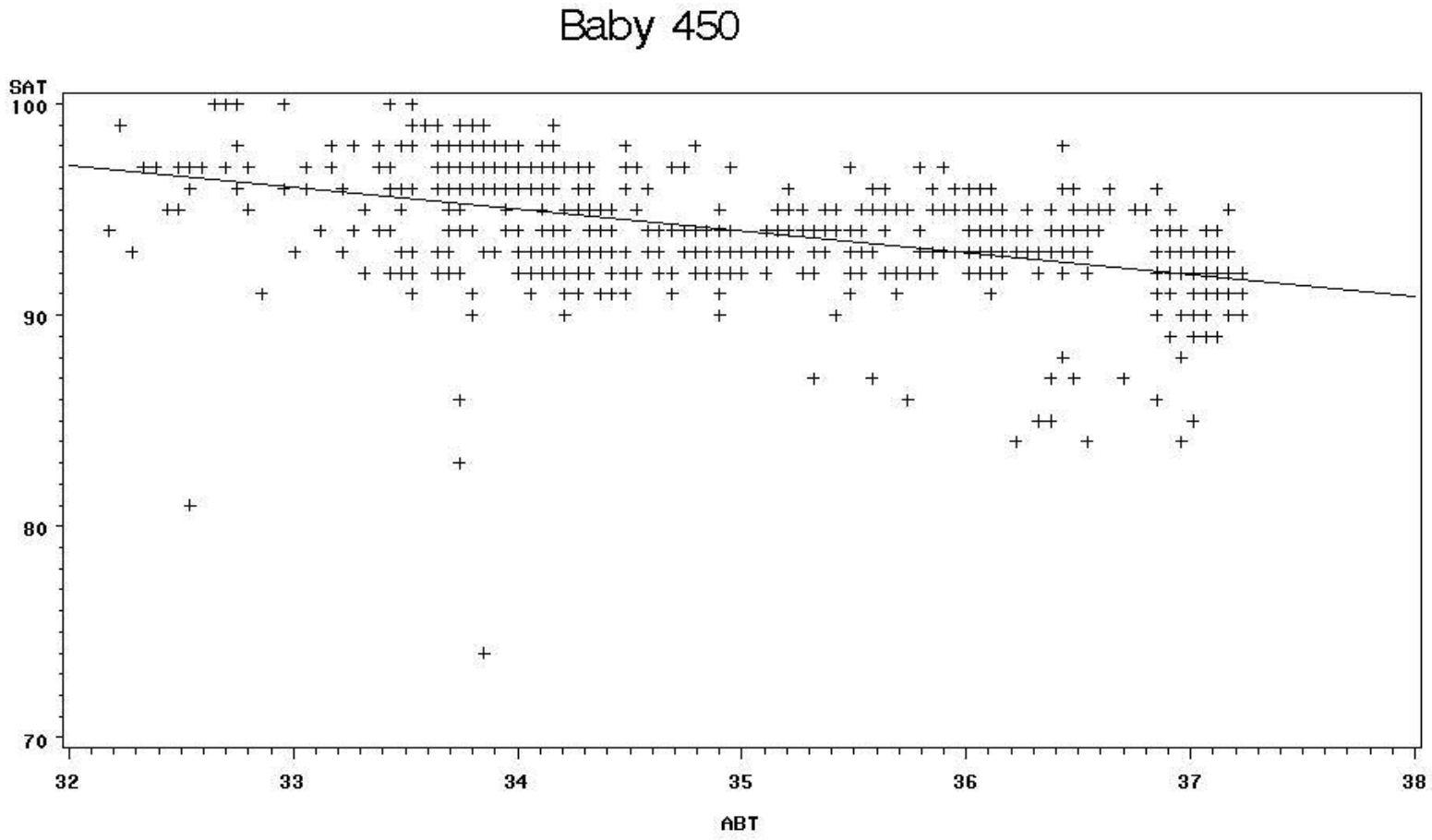


Figure 4.36 Scatterplot with Regression Line for Oxygen Saturation and Abdominal Temperature for Infant 450



negative direction for the strongest correlation in the negative direction as shown in Figure 4.36 for infant 450.

Demographic data were not related to the strength of the oxygen saturation and abdominal temperature correlation as shown in Table 4.36. No patterns were evident in the strength of correlation, direction of correlation, mean abdominal temperatures, oxygen delivery to the infant or demographic characteristics of the infants. Seven of the eight infants who had significant correlations between abdominal temperature and oxygen saturation were mostly on room air (21%) for the study period. Infants with mean abdominal temperatures that were

Table 4.36 Relationships of Significant ($p < 0.05$) Pearson Correlations Between Oxygen Saturation and Abdominal Temperature to Infant Demographic Characteristics

Correlation (*r* value)	Subject #	Gestation (weeks)	Weight (grams)	Gender	Ethnicity
-0.50	450	25	670	F	AA
-0.43	680	24	590	M	W
-0.23	730	26	960	F	AA
-0.22	360	26	880	M	AA
0.13	510	26	510	F	W
0.16	590	25	710	M	AA
0.32	170	25	630	F	AA
0.50	311	25	550	F	W

F = Female, M = Male, AA = African American, W = White

lower (35.17˚ to 35.79˚ C) had abdominal temperatures that were correlated with oxygen saturation in positive and negative directions, as well as weakly (.13) and strongly (-0.5, -0.43, 0.50) correlated. Neither weight, gender nor ethnicity was associated with correlation strength or direction.

Seven correlations reached significance at $p < .05$ for peripheral temperature and oxygen saturation which ranged between $r = -0.12$ and -0.42. One r value was in a positive direction at 0.10. The strongest correlation was $r = 0.42$ for infant 680 shown in Figure 4.37. No patterns were evident between the demographic data and the strength of the correlation. Although eight infants had significant correlations between temperature and oxygen saturation, the relationship was not apparently influenced by oxygen delivery to the infant or demographic characteristics.

Table 4.37 Relationships of Significant ($p < 0.05$) Pearson Correlations Between Oxygen Saturation and Heart Rate to Infant Demographic Characteristics

Correlation (r value)	Subject #	Gestation (weeks)	Weight (grams)	Gender	Ethnicity
-0.39	510	26	510	F	W
-0.30	450	25	670	F	AA
-0.29	360	26	880	M	AA
-0.27	680	24	590	M	W
-0.26	730	26	960	F	AA
-0.13	311	25	550	F	W

F = Female, M = Male, AA = African American, W = White

Figure 4.37 Scatterplot with Regression Line for Oxygen Saturation and Peripheral Temperature for Infant 680

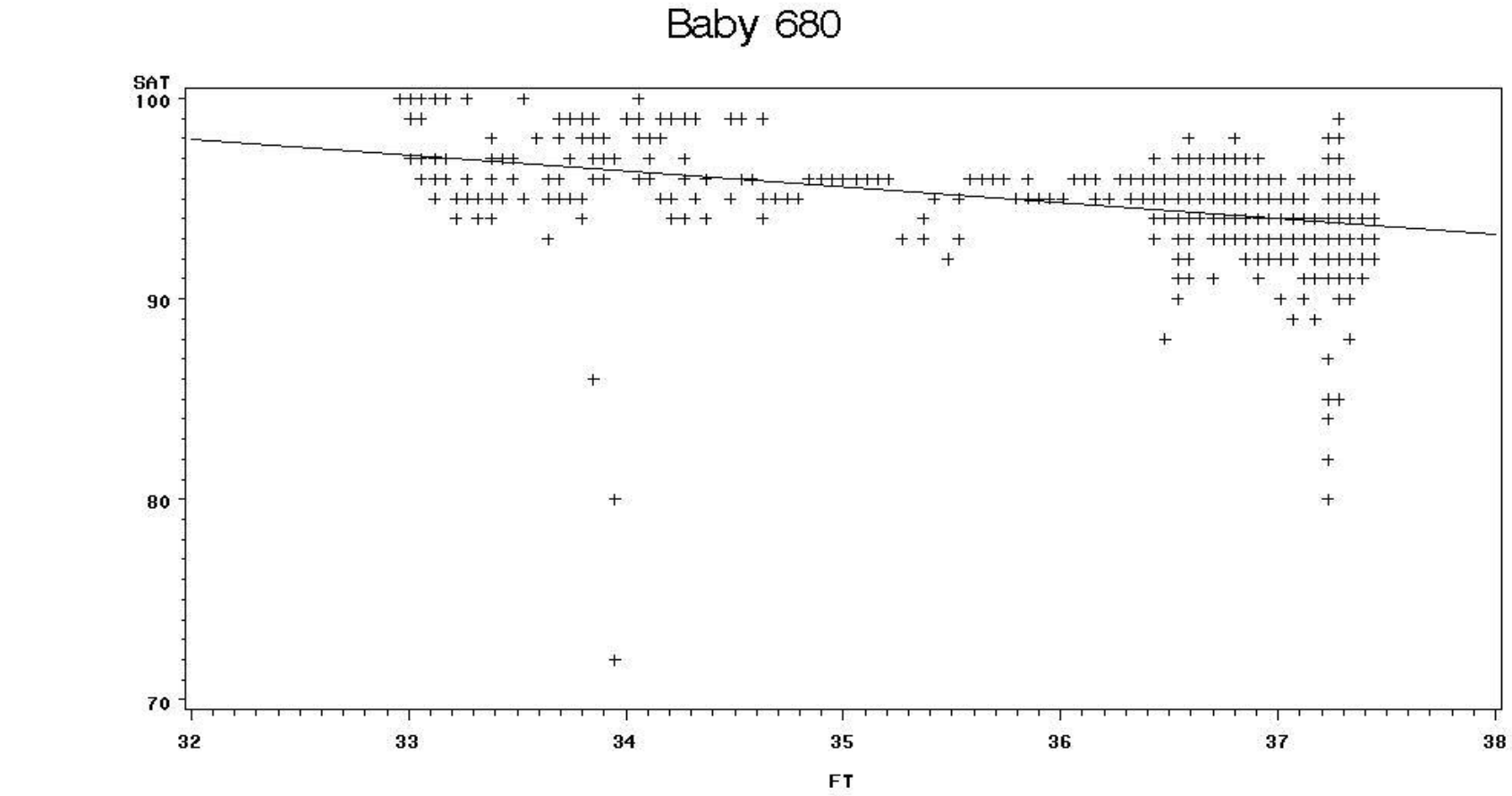
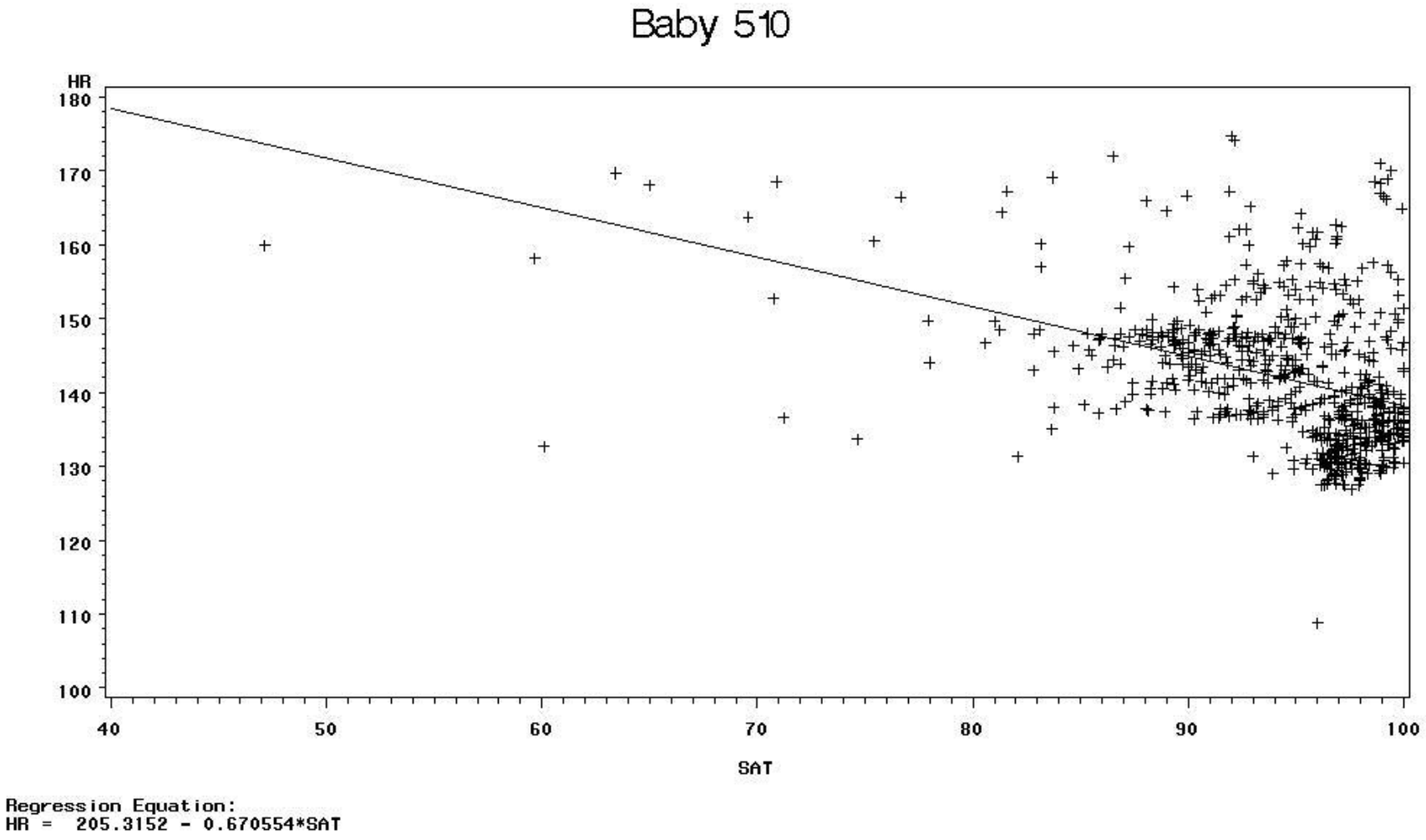


Figure 4.38 Scatterplot with Regression Line for Heart Rate and Oxygen Saturation for Infant 510



Heart rate and oxygen saturation. Six correlations reached significance at $p < .05$ between heart rate and oxygen saturation, all in the negative direction (r = -0.13 to -0.39). The strongest correlation between heart rate and oxygen saturation was for infant 510. However, the majority of the heart rate data and oxygen saturation data were grouped in one area as seen in the scatterplot in Figure 4.38. Demographic characteristics for each infant and r values for Pearson correlations between heart rate and oxygen saturation data were tabulated (Table 4.37) and examined. No pattern was evident between the demographic data and strength of correlations between heart rate and oxygen saturation.

Peripheral vasoconstriction

Table 4.38 presents percentages of observations for each infant with a temperature difference between -2˚ C and 2˚ C. Only 2 infants had greater than 2% of their observations meeting the definition of peripheral vasoconstriction (abdominal minus peripheral temperature being greater than 2˚ C). Infant # 360 spent the most time with peripheral vasoconstriction at almost 9% of the observations. This infant was an 880-gram 26-week, African American male. Infant # 510 spent 6% of the 1-minute periods with peripheral vasoconstriction. However, this infant had elevated abdominal temperature for approximately 1 ½ hours, which was most likely due to a false temperature reading of incubator air temperature. Therefore, it was unlikely that this 510-gram infant displayed peripheral vasoconstriction. The only other infant (#730) with a large amount of 1-minute periods approaching peripheral vasoconstriction was a 960-gram 26-week, African American female who spent 62.5% of the study period with a 1˚ C difference between her abdominal and peripheral temperatures.

Seven infants spent at least 15% of their study period with the peripheral temperature 1˚ C

higher than their abdominal temperature and five infants kept their peripheral temperature higher than their abdominal temperature by 2˚ C for at least 3% of the study period. Two infants had more than 20% of their temperature observations with their peripheral temperature greater than their abdominal temperature by 1.5˚ C and one infant had 12.7% of the temperature observations with the peripheral temperature greater than the abdominal temperature by 2˚ C. In this study, only the infants with birthweights over 800-grams and gestational age of 26 weeks showed peripheral vasoconstriction at the previously defined limit. Smaller (500-710 grams) and more premature infants (24-25 weeks) reacted differently with their peripheral temperatures higher than their abdominal temperatures during the study period.

Table 4.38 Percentage of Observations at Each Abdominal – Peripheral Temperature Level for Each Infant

Sub. # tdiff	170	240	311	360	410	450	510	590	680	730
2˚ C	0	0	0.2	8.8	0	0	6	0	0	1.4
1.5˚ C	0.9	0	0.4	17.3	0.2	1.5	6.2	0.3	0	8.8
1˚ C	4	0	0.7	28.5	1.4	7.3	6.4	1	0	62.5
- 1˚ C	24.5	6.8	51.2	2.2	68.4	16.3	19.7	15.2	23.7	0
- 1.5˚ C	15.9	4	27.6	0.7	28.8	7.3	2.7	3.7	11.7	0
- 2˚ C	6.8	3	12.7	0.1	5.1	3.5	0.4	0.4	1.4	0.2

Comparison of Physiological Data to Observer Data on Clinical Stimulation

Graphs of all primary variables (abdominal and peripheral temperature, heart rate and

oxygen saturation) over time were printed for each infant with a scale of 10 minutes equaling one inch. Each graph spanned 8-9 sheets of 8 x 11 inch paper. Clinical observation events were marked on the graphs. The curves were visually inspected to identify relationships between the physiological variable and the clinical events happening over the study period that were recorded by the observer as stimulation to the infant. Figures below are a condensed version of graphic trends using a much smaller scale.

Infant # 170 had a wide difference between the abdominal and peripheral temperatures at approximately 4 to 5 ½ hours of age when the infant received various nursing and medical procedures (a fluid bolus, change of linens, a chest radiograph, dressing to bleeding at the umbilical line site) (see Figure 4.39). At this time, the axillary temperature decreased to 34.9˚ C. Another clinical stimulation episode during which the umbilical line was pulled back was associated with an increase in heart rate, decrease in oxygen saturations, and an increase in the temperature difference between the abdominal and peripheral temperatures. A similar episode occurred when the infant had the hiccoughs.

Infant # 240 received two blood transfusions at 2 and 4 hours of age. Both transfusions were associated with a simultaneous decrease in temperature (see Figure 4.40). In addition, the infant received two infusions of normal saline given using a syringe and pump, both of which were associated with decreases in abdominal temperature, heart rate and oxygen saturation.

Graphs of all primary variables for infant 311 were printed and visually inspected for relationships between the clinical events happening over the time and the physiological variables during the study period that were recorded from the medical chart and the nurses notes recorded after the study period. No observer was available to collect data on this

Figure 4.39 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 170

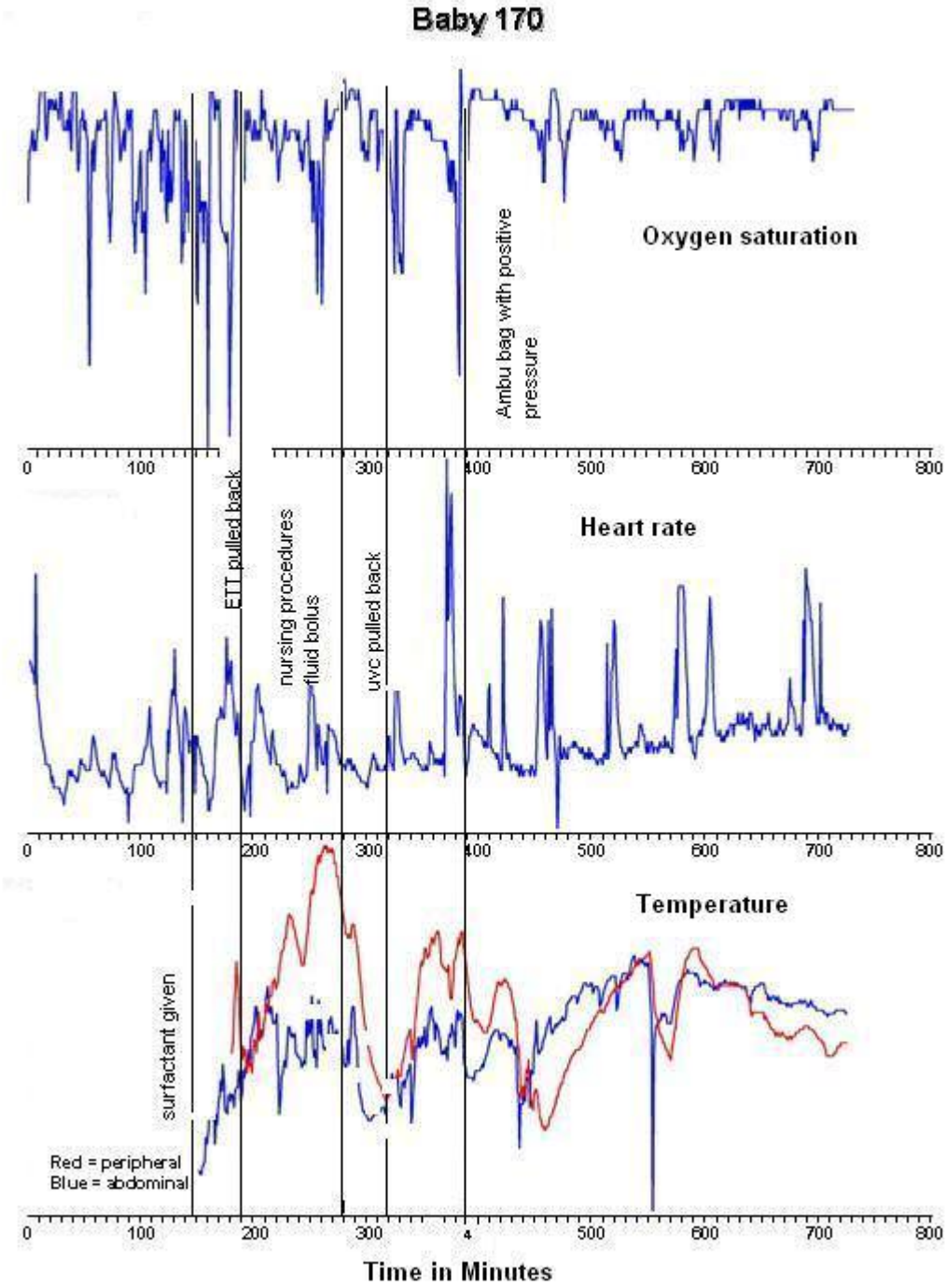
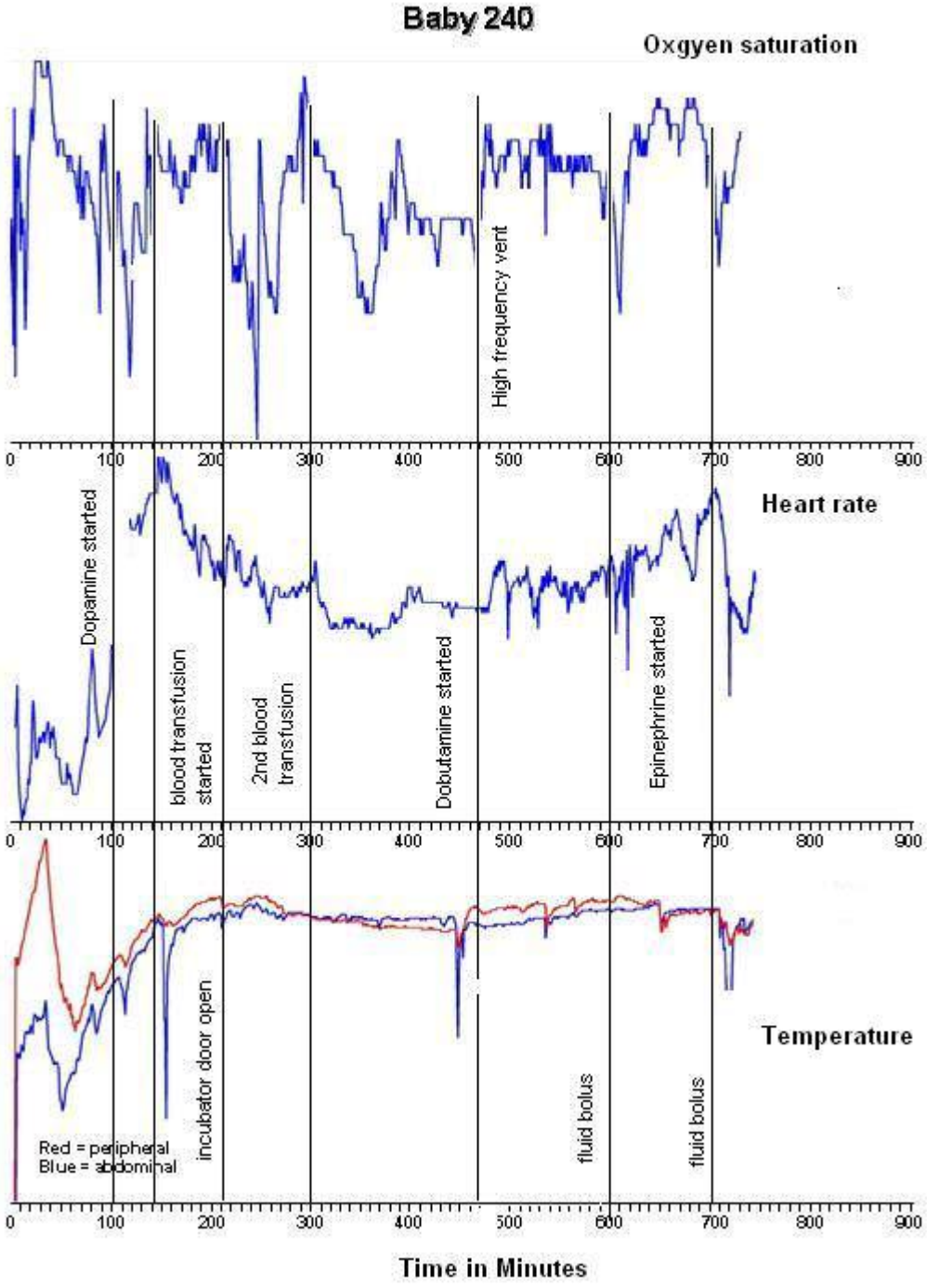


Figure 4.40 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 240



infant. Because time for infant enrollment was nearing completion, the infant was enrolled and the data collection proceeded by computer. Therefore, clinical information was not as detailed as it would have been had an observer been sitting at the bedside. Visual inspection of the data trends revealed a temperature drop and increase in the temperature differences when a chest radiograph was obtained (see Figure 4.41). Additionally, heart rate and temperature differences increased associated with the replacement of the umbilical venous line about 6 hours of age.

The abdominal temperature for infant 360 decreased once in association with the start of intravenous fluids (see figure 4.42). There were approximately nine instances when the infant was suctioned through the endotracheal tube and all of these events were associated with heart rate decreases or increases, oxygen saturation decreases, and an increase in the difference between the abdominal and peripheral temperatures, and occasionally with drops in temperature.

Infant 410 received stimulation and medical procedures over the first 6 hours of age including intubation, umbilical line placement, Xrays, an extubation and reintubation and having Dopamine started at about 4 hours of age. One clinical procedure episode at approximately 2 hours of age was associated with an increase in heart rate, decrease in oxygen saturation and an increase in the abdominal and peripheral temperature difference (see Figure 4.43). From approximately 5 hours of age to 7 hours of age, great variability in temperature readings, an increase in heart rate and a decrease in oxygen saturations occurred. During this time, the nurses entered the incubator twice to obtain blood gases.

Episodes of clinical stimulation (drawing blood gases) were associated with a larger difference in the abdominal and peripheral temperature for infant 450 (see Figure 4.44).

Figure 4.41 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 311

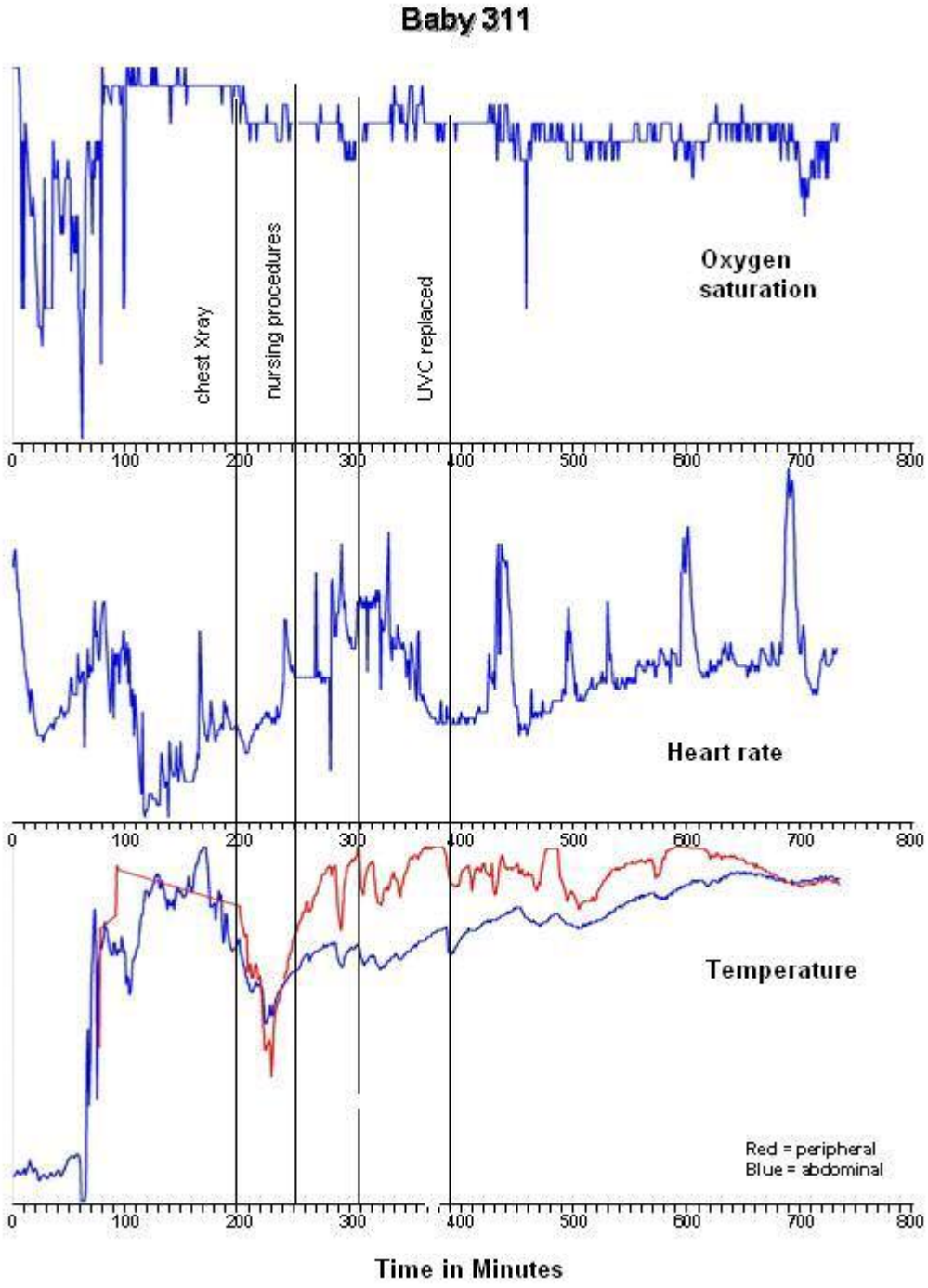


Figure 4.42 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 360

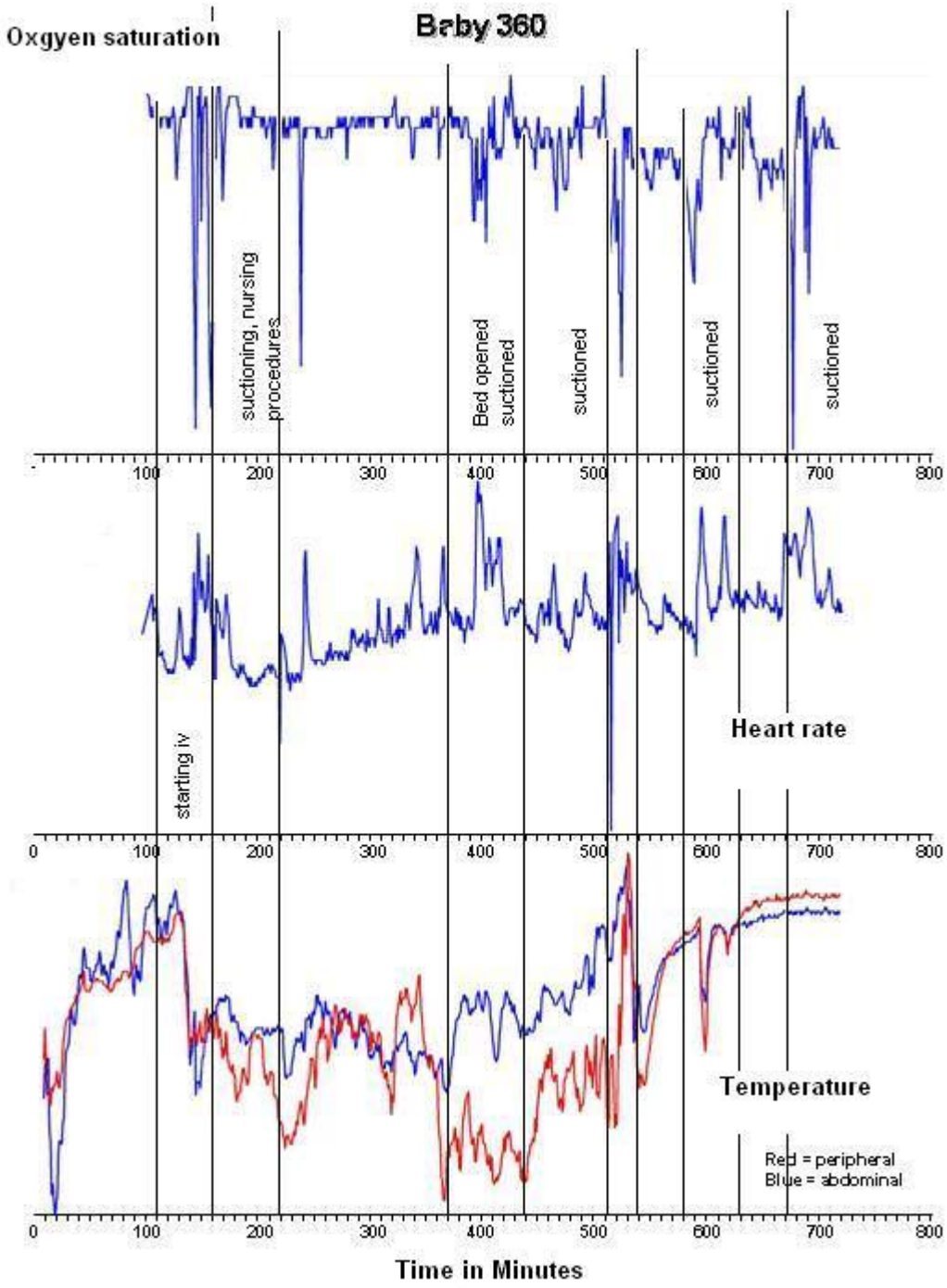


Figure 4.43 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 410

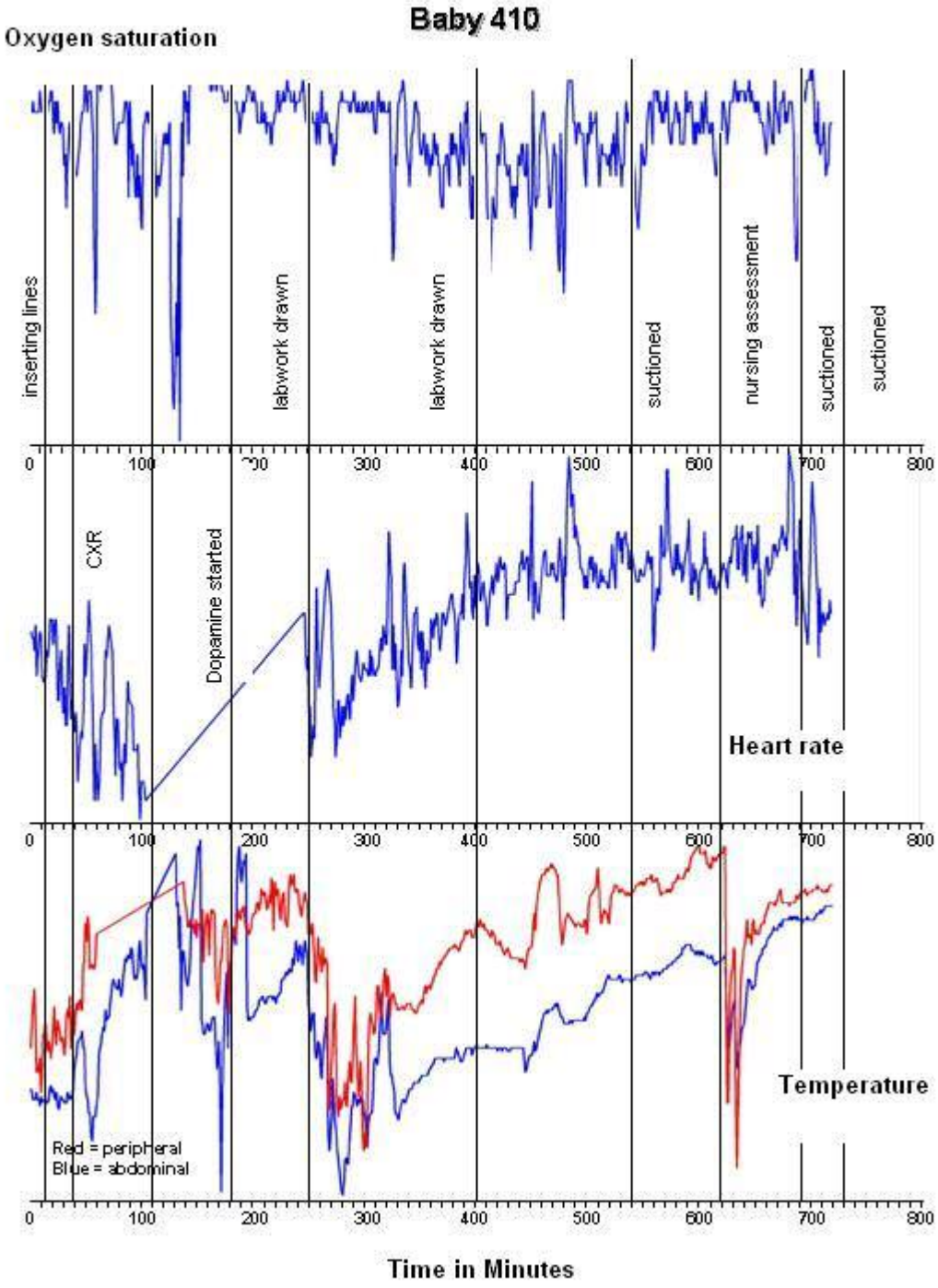
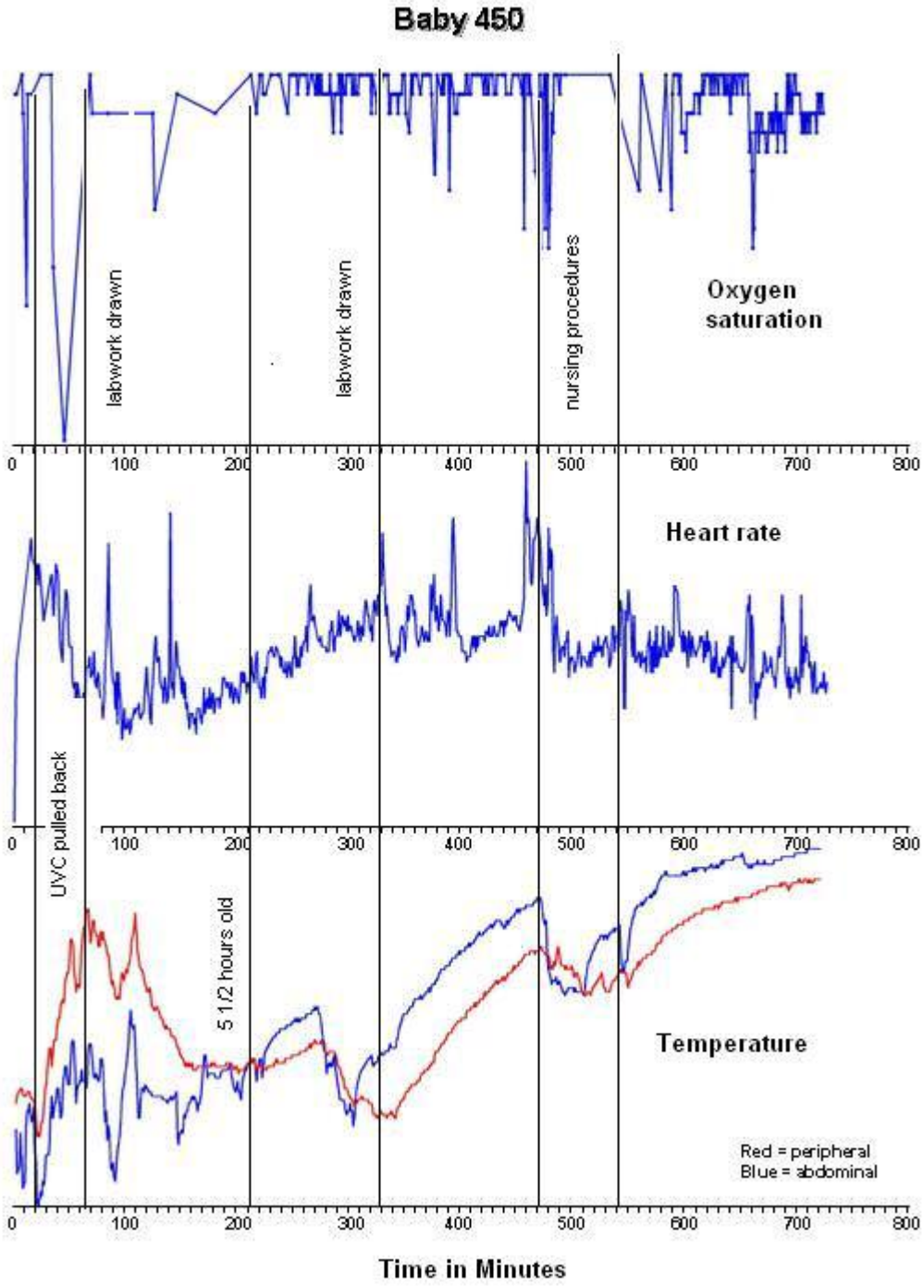


Figure 4.44 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 450



Instability occurred during the first 5 hours of the study period with many fluctuations of the heart rate, low temperatures and a large difference between the abdominal and peripheral temperatures.

Infant 510 had several episodes of heart rate increases, oxygen saturation decreases, and increases in the difference between abdominal and peripheral temperatures, along with abdominal temperature decreases which were associated with stimulation by the medical personnel (drawing blood gases, repositioning, suctioning) (see Figure 4.45). Additionally, one episode in which the infant spontaneously dropped his heart rate to 33 occurred while the oxygen saturation decreased and the difference between the abdominal and peripheral temperatures increased.

Graphic trends for infant 590 showed increases in heart rate, slight decreases in oxygen saturations, and a larger difference in the two temperatures during a time period when the infant received a fluid bolus and a chest Xray and had questionable seizures (see Figure 4.46). Later in the study period, the infant underwent umbilical line placement again, which was associated with another increase in the peripheral and abdominal temperature difference, a heart rate increase and a slight desaturation. During the three instances of stimulation to infant # 680 by medical personnel obtaining blood gases, repositioning infant, reattaching probes, and giving fluid boluses, the infant exhibited an increased difference between the abdominal and peripheral temperature along with an increase in heart rate and decrease in oxygen saturations (see Figure 4.47). On two other instances, clinical stimulation was associated with an increased difference in abdominal and peripheral temperatures and an increase in heart rate, but no obvious change in oxygen saturation. As the infant became warmer later in the study period, clinical stimulation did not seem to be associated with a

Figure 4.45 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 510

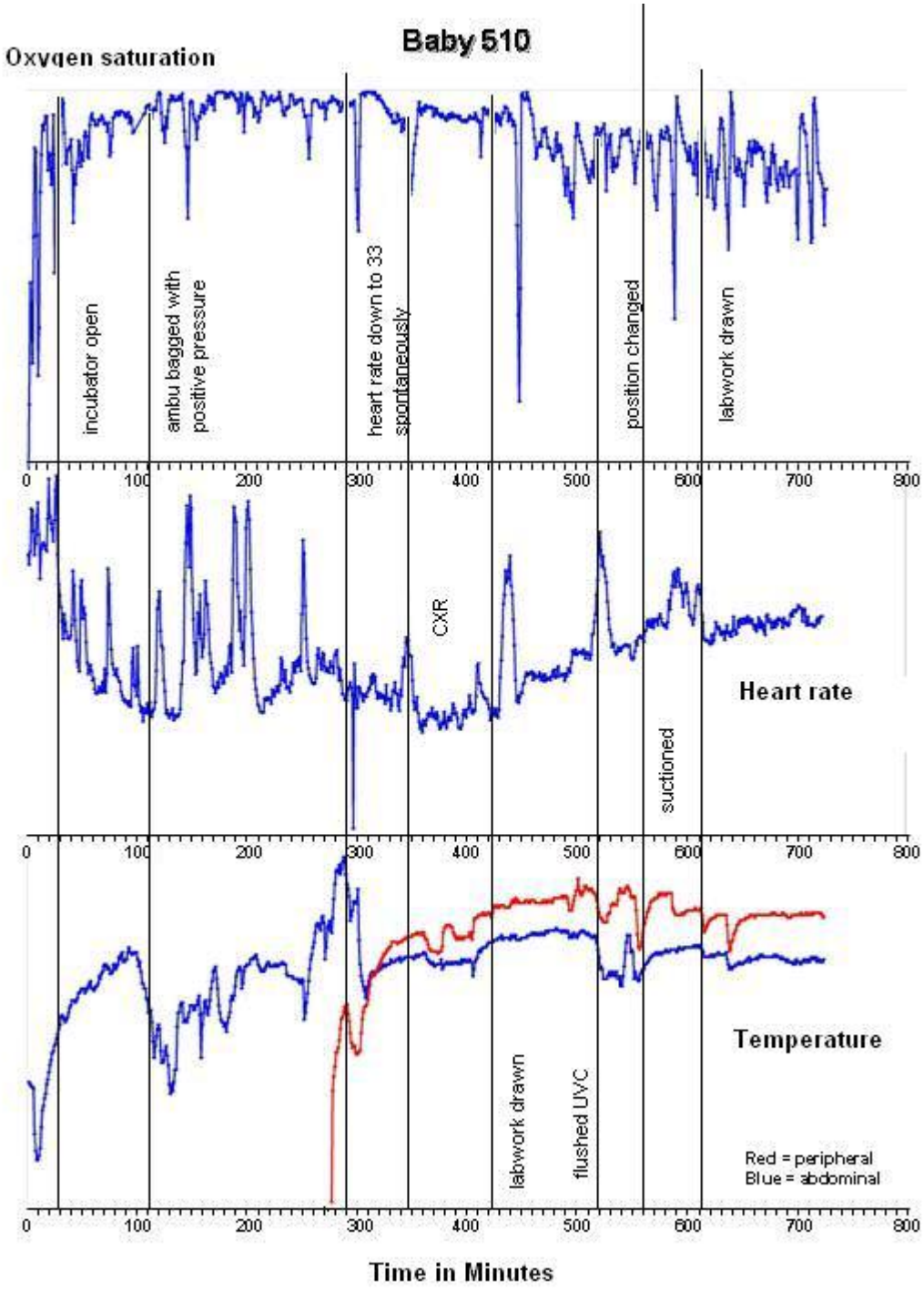


Figure 4.46 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 590

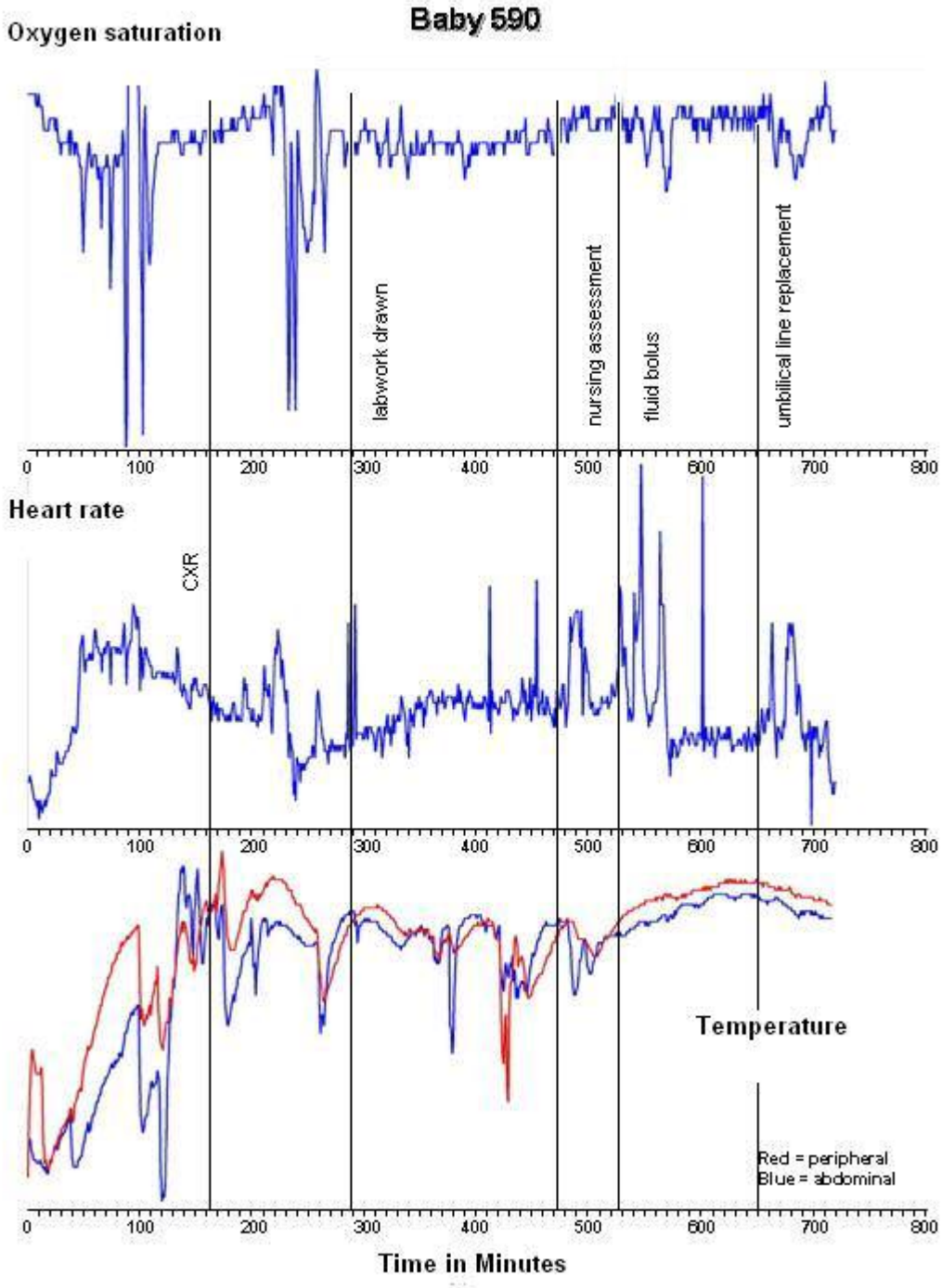
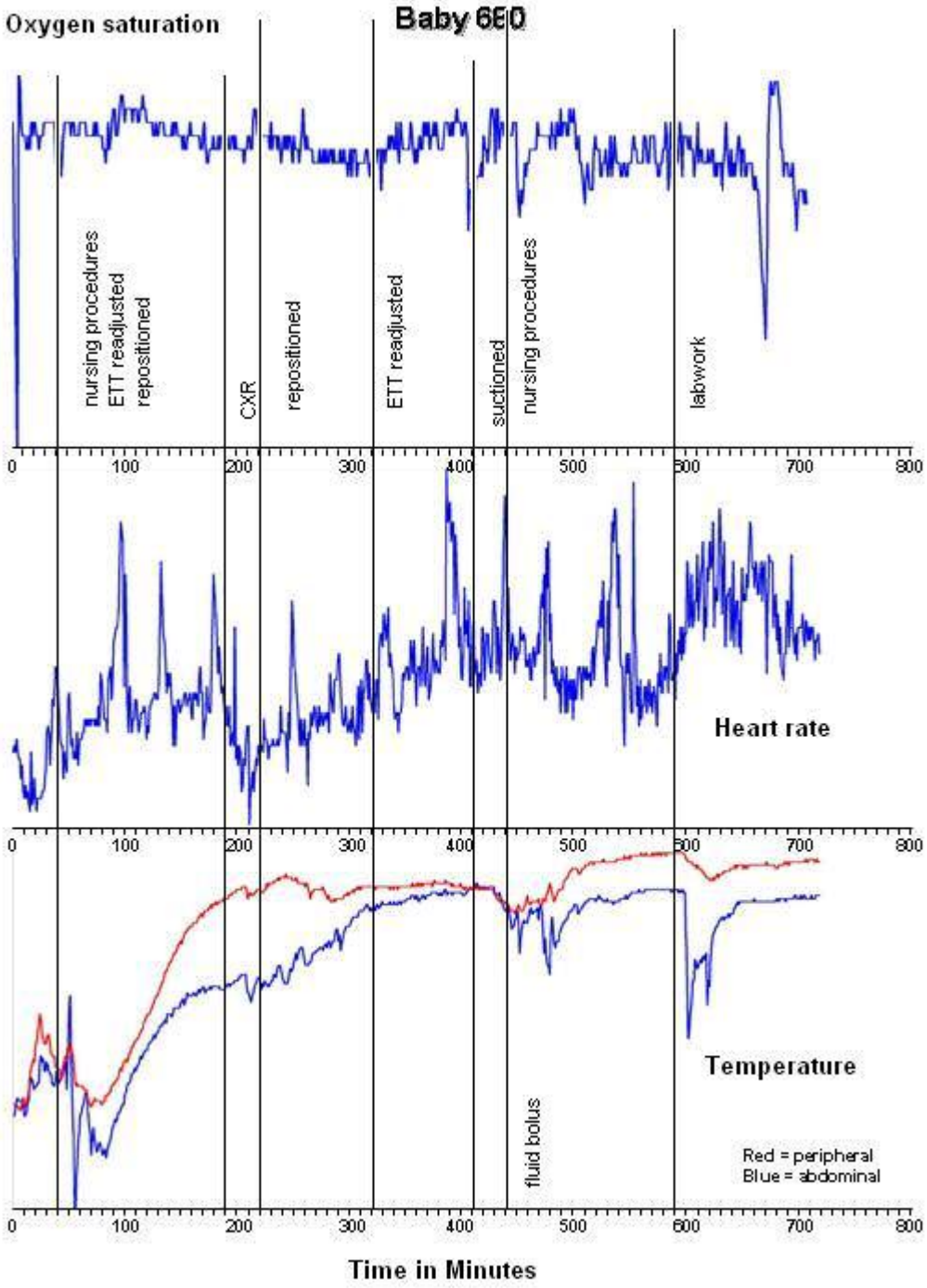


Figure 4.47 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 680



change in the difference between abdominal and peripheral temperatures.

Infant # 730 experienced several episodes of clinical stimulation including suctioning, blood draws, visitors touching the infant, and extubation, during which the heart rate decreased episodically, oxygen saturations decreased, temperatures decreased, and the difference between abdominal and peripheral temperatures increased (see Figure 4.48).

Table 4.39 presents a summary of the responses (temperature, heart rate, and oxygen saturation) to clinical stimulation of each infant. Nine of ten infants exhibited an increased difference between the abdominal and peripheral temperatures associated with caregiver handling and medical procedures. In two of the infants, the abdominal temperature was greater than the peripheral temperature and seven infants exhibited higher peripheral temperatures than abdominal temperatures. Seven infants had an increase in heart rate associated with caregiver handling and eight infants showed a decrease in oxygen saturation with caregiver handling. Two infants had a decrease in abdominal temperature associated with infusion of fluids through the umbilical venous catheter. Therefore, caregiver handling as well as nursing and medical procedures clearly increased the difference between abdominal and peripheral temperatures and increased infants' heart rate. Additionally, infusion of fluids at room temperature was associated with a drop in abdominal temperature when infused through the umbilical venous catheter. Most likely, infants were becoming colder centrally (abdominal temperature) and the peripheral temperature was staying warmer or closer to air temperature.

Figure 4.48 Plot of Temperature, Heart Rate and Oxygen Saturation with Noted Clinical Observations for Infant 730

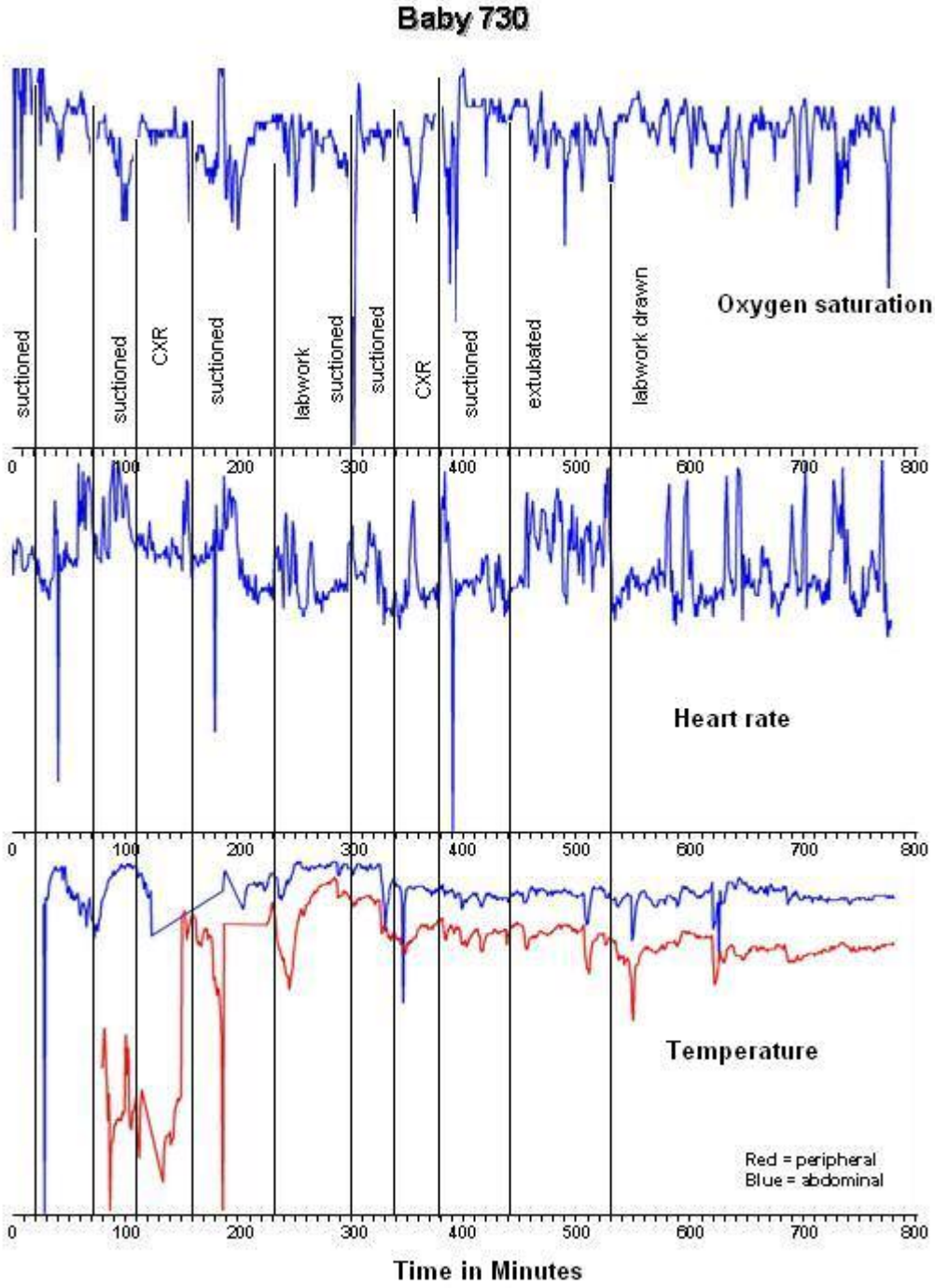


Table 4. 39 Clinical observations related to temperature, heart rate, and oxygen saturation

Infant Number	Difference between abdominal and peripheral temperatures with handling	Heart rate with handling	O_2 saturations with handling	Abdominal temperature with infusions through umbilical catheter
170	↑	↑	↓	
240		↓	↓	↓
311	↑	↑		
360	↑	↑↓	↓	↓
410	↑	↑	↓	
450	↑			
510	↑	↑	↓	
590	↑	↑	↓	
680	↑	↑	↓	
730	↑	↓	↓	

Similarities over Infants in Secondary Variables

There were no evident trends in pO_2 values or glucose values among the study subjects. There was great variability in the pO_2 and glucose and number of values obtained with some infants having two measures and others up to six measures. Without continuous sampling, relating the values to temperature observations was impossible.

Two infants had a stable pH throughout the study with no evidence of acidosis. Two infants had a persistent metabolic acidosis throughout the study period, three infants had a metabolic acidosis that improved over time, two infants had a slight acidosis that was compensated, and one infant had an acidosis throughout the study period and was attempting to compensate by using the respiratory system to eliminate CO_2. Metabolic acidosis during the stabilization of extremely low birth weight infants is not unusual because of low temperatures, low blood pressure and poor perfusion. Most infants in this study had low abdominal temperatures for much of the study and because the pH values were measured sporadically, the only conclusion that can be drawn is that metabolic acidosis was common during the stabilization period for these ELBW infants and these ELBW infants had low abdominal temperatures for much of the study period.

Abnormal Values of Heart Rate and Oxygen Saturation in Relationship to Hypothermia

Analyses were conducted to determine at which temperature range (>36.4˚ C or ≤ 36.4˚ C) the heart rate and oxygen saturation for each infant was most stable, that is in the normal range. Normal oxygen saturation range for preterm infants as measured by pulse oximetry should be 92-96%, however can go as high as 100% (Ng, Subhedar, Primhak, & Shaw, 1998; Paky & Koeck, 1995; Poets, 1998 Rey, 2004). For this study, the range of 92-100% was used

as normal oxygen saturation. The upper limit had to be 100% because all study infants were being given room air (21%) at some point in their observation periods. Infants on room air frequently can increase their saturations as high as 100% and the nurse can not decrease their saturation by lowering oxygen below room air or 21%. Because most textbooks define normal heart rate range for the neonate as 100-180 (Blackburn, 2003; Kenner, 2003) and heart rates varied largely across all 10 infants in this study, normal heart rate was defined as the 25th and 75th percentile heart rate values for each infant. Table 4.40 presents the heart range upper and lower limit of normal determined for each study subject.

Table 4.40 The 25th and 75th Percentile for Heart Rate for the Study Infants

Subject #	25th percentile HR	75th percentile HR	Gestation weeks	Birth weight grams
311	121	132	25	550
680	122	135	24	590
450	134	143	25	670
510	134	147	26	510
730	134	145	26	960
170	135	142	25	630
590	139	147	25	710
360	156	166	26	880
410	160	173	25	720
240	162	173	24	680

Only four infants spent more than 50% of their observations without hypothermia (temperature less than 36.4˚ C). All study subjects had oxygen saturations in the normal range more than 50% of their observations and 8 out of 10 infants had more than 70% of their observations in the normal oxygen saturation range.

Table 4.41 Percentage of Observations in the Normal Heart Rate Range for Hypothermic and Nonhypothermic Temperatures for Study Infants

Subject #	% of observation in the normal heart rate range when temperature > 36.4˚ C	% of observation in the normal heart rate range when temperature ≤ 36.4˚ C	Chi square values df=1
170	69.9	41.5	40.78*
240	64.1	28.4	77.91*
311	59.9	55.7	1.23
360	52.9	54.5	0.16
410	44.7	50.8	0.65
450	68.8	48.8	20.90*
510	77.9	43.4	52.78*
590	66.6	30.9	73.10*
680	65.3	46	27.45*
730	51.3	56.4	1.19

* $p < .05$ for chi square of proportion of observations in the normal heart rate range comparing observations at abdominal temperature > 36.4˚ C and ≤ 36.4˚ C

Chi square analyses were used to compare the proportions of observations in the normal and abnormal heart rate range for each infant when their abdominal temperature was greater than 36.4˚ C and less than or equal to 36.4˚ C. Table 4.41 shows the results of these analyses. Six out of the ten study subjects had a statistically significant ($p < .05$) relationship between normal heart rate observations and whether the abdominal temperature was hypothermic or not. Of these six significant relationships, a larger percentage of observations in the normal heart rate range always occurred when temperatures were above 36.4˚ C. Therefore, having non-hypothermic temperature was associated with normal heart rate in this sample.

Chi square analyses were used to compare the proportion of observations in the normal and abnormal oxygen saturation range for each infant when their abdominal temperature was greater than 36.4˚ C and less than or equal to 36.4˚ C. Table 4.42 presents these results. Eight of ten study subjects had significant relationships between the percentage of normal oxygen saturation observations and whether the abdominal temperature was hypothermic or not. However, four infants had more normal oxygen saturations when temperature was greater than 36.4˚ C and four infants had more normal oxygen saturations when temperature was less than or equal to 36.4˚ C. Although the significant relationships between hypothermic or nonhypothermic abdominal temperatures with oxygen saturation were significant, the number of infants with more normal oxygen saturation above or below the cut point of 36.4˚ C did not differ. Therefore, 36.4˚ C may not be the right cut point to predict more normal oxygen saturations. The analyses is also affected by caregivers attempting to keep the oxygen saturation in a normal range by giving oxygen to the infant, therefore abnormal oxygen saturation readings were minimal in the data.

Table 4.42 Percentage of Observations in the Normal Oxygen Saturation Range for Hypothermic and Nonhypothermic Temperatures for Study Infants

Subject #	% of observation in the normal oxygen saturation range when temperature > 36.4˚ C	% of observation in the normal oxygen saturation range when temperature ≤ 36.4˚ C	Chi square values df=1
170	93.3	71.1	50.9*
240	65.8	53.7	9.6*
311	100.0	93.6	18.2*
360	69.5	87.0	28.0*
410	85.5	79.4	1.7
450	60.6	93.9	121.1*
510	74.3	75.3	0.1
590	94.0	86	12.4*
680	90.1	97.2	16.2*
730	54.3	73.8	18.3*

* $p < .05$ for chi square of normal oxygen saturation comparing temperature > 36.4˚ C and ≤ 36.4˚ C

Peripheral Vasoconstriction and Hypothermia

Only one infant (#360) showed true peripheral vasoconstriction using the definition of having an abdominal temperature greater than 2˚ C over the peripheral temperature, which was not influenced by temperature probe problems; 8% of this infant's 1-minute periods exhibited peripheral vasoconstriction. A second infant (#510) had 6% of the temperature

Table 4.43 Mean Abdominal – Peripheral Temperature Difference in ˚ C (AbT-Ft Diff) for Hypothermia/Nonhypothermia, Normal/Abnormal Heart Rate Observations and Oxygen Saturation Observations for Each Study Infant

Infant #	AbT-Ft Diff for observations when AbT > 36.4˚ C	AbT-Ft Diff for observations when AbT ≤ 36.4˚ C	t value	AbT-Ft Diff for observations in normal HR range	AbT-Ft Diff for observations in abnormal HR range	t value	AbT-Ft Diff for observations in normal O_2 saturation range	AbT-Ft Diff for observations below normal O_2 saturation	t value
170	-0.15	-0.91	-8.80*	-0.27	-0.48	-2.40*	-0.28	-0.91	-4.48*
240	-0.09	-0.86	-11.12*	-0.22	-0.38	-3.32*	-0.32	-0.23	2.06*
311	-0.51	-1.30	-14.74*	-0.90	-1.19	-4.25*	-1.00	-1.12	-0.16
360	0.26	0.67	6.33*	0.62	0.53	-1.20	0.60	.51	-0.96
410	-0.10	-1.27	-19.02*	-1.27	-1.09	3.37*	-1.06	-1.43	-7.37*
450	0.58	-0.09	-15.65*	0.31	-0.09	-6.01*	0.92	0.56	4.97*
510	0.16	-0.77	-5.59*	-0.41	-0.62	-1.93	-0.36	-0.84	-5.28*
590	-0.12	-0.85	-13.77*	-0.14	-0.55	-9.55*	-0.28	-0.80	-7.65*
680	-0.43	-0.94	-16.29*	-0.60	-0.85	-6.51*	-0.72	-0.59	3.19*
730	1.08	1.09	0.10	1.09	1.08	-0.19	1.11	1.04	-2.36*

*** $p < .05$ Abt: Abdominal temperature Diff: Difference O_2: Oxygen Ft: Peripheral temperature HR: Heart rate**

observations with peripheral vasoconstriction. However, the abdominal temperature increased greatly for that short period of time and was most likely reading the air temperature instead of the abdominal temperature. The remaining temperature observations for infant #510 had the peripheral temperature higher than the abdominal temperature and were valid temperatures.

For infant # 360, the mean abdominal-peripheral temperature difference was larger for 1-minute periods with an abdominal temperature less than or equal to 36.4˚C than for periods with an abdominal temperature greater than 36.4˚C. The abdominal-peripheral temperature difference was 0.26˚ C for observations of abdominal temperature greater than 36.4˚ C and 0.67˚ C for observations of abdominal temperature less than or equal to 36.4˚ C, as would be expected for peripheral vasoconstriction in response to cold stress.

Because the other eight subjects had less than 2% of their observations with peripheral vasoconstriction, their data were not analyzed to determine if there was more peripheral vasoconstriction when temperatures were less than or equal to 36.4˚ C. Instead, Student's *t*-tests were conducted between the abdominal-peripheral temperature difference for 1-minute periods with abdominal temperature greater than 36.4˚ C and for periods with abdominal temperature less than or equal to 36.4˚C for each infant (Table 4.43). *T*-tests were also conducted between the abdominal-peripheral difference for observations in the normal heart rate range versus observations out of the normal heart rate range, as well as for temperature difference for observations with normal and abnormal oxygen saturation range for each infant.

The mean abdominal-peripheral temperature difference was significantly different when the abdominal temperature was less than or equal to 36.4˚ C compared to when abdominal

temperature was greater than 36.4˚ C in 9 of the 10 infants studied. The difference between the abdominal temperature and peripheral temperature increased such that the peripheral temperature was higher than the abdominal temperature in 8 of the 10 infants when abdominal temperatures were less than or equal to 36.4˚ C when compared to periods when abdominal temperatures were greater than 36.4˚ C. Two of these eight infants had the abdominal temperature higher than the peripheral temperature when abdominal temperature observations were greater than 36.4˚ C, then the peripheral temperature became higher than the abdominal temperature when the abdominal temperature observations were less than 36.4˚ C. In two infants in which the abdominal temperature remained higher than the peripheral temperature, the temperature difference increased when abdominal temperatures were less than or equal to 36.4˚ C compared to periods when abdominal temperatures were greater than 36.4˚ C.

Seven of the ten infants showed a significant difference in the mean abdominal-peripheral difference when observations were in the normal heart rate range for each infant versus out of the normal heart rate range. In 6 out of 10 infants, the abdominal-peripheral temperature differences become larger with the peripheral temperature higher than the abdominal temperature when heart rate was not in the normal range compared to periods when heart rate was in the normal range. Additionally, 8 of 10 infants showed a significant difference in the mean abdominal-peripheral temperature difference when oxygen saturation observations were in the normal range versus below the normal limit. Five of ten infants also had an increase in the abdominal-peripheral temperature difference with peripheral temperature being higher when there were observations below the normal oxygen saturation range compared to when observations were in the normal oxygen saturation range.

Heart Rate and Oxygen Saturation in Relationship to the Decrease in Abdominal Temperature from the 36.4˚ C Cut Point

In order to determine the degree of abnormality in heart rate (extent to which the observation was above or below the normal range) and in oxygenation (extent to which the observation decreased below normal) compared to the extent in which each infant's body temperature was below 36.4˚ C, a Pearson correlation was conducted between observations of abdominal temperature less than or equal to 36.4˚ C and each infant's corresponding heart rate and oxygen saturation data. Degree of abnormality for abdominal temperature was defined as the difference of the observed temperature from 36.4˚C and this analysis was only concerned with temperatures lower than 36.4˚C. For example, if the observed temperature was 35.8˚C, the degree of abnormality for that one minute observational period was 0.6˚C. Degree of abnormality for heart rate was determined as the difference between the observed heart rate and the normal heart rate limits. The normal heart rate levels for each infant were determined by the corresponding 25^{th} and 75^{th} heart rate percentiles. Therefore, if normal heart rate was 136 to 166 and the observed heart rate was 120, the degree of abnormality for that one minute observation period was 16. The normal oxygen saturation level for each infant was oxygen saturation greater than or equal to 92%. The degree of abnormality for oxygen saturation was defined as the difference of the observed oxygen saturation from 92%. For example, if the observed oxygen saturation was 86%, then the degree of abnormality for that one minute observational period was 6%. Analyses was done correlating each one minute observation of abdominal temperature less than or equal to 36.4˚ C with the corresponding heart rate for that observation minute if the heart rate was above or below the normal range and with oxygen saturation for that observation minute if the oxygen saturation

was below the normal range. The observations were included in the analyses if the corresponding temperatures and heart rate or oxygen saturation for each one minute observation period met the abnormal criteria. Therefore, the number of observations meeting the required abnormal criteria and included in the Pearson correlation (n) is denoted on Table 4.44 which presents the results of these analyses.

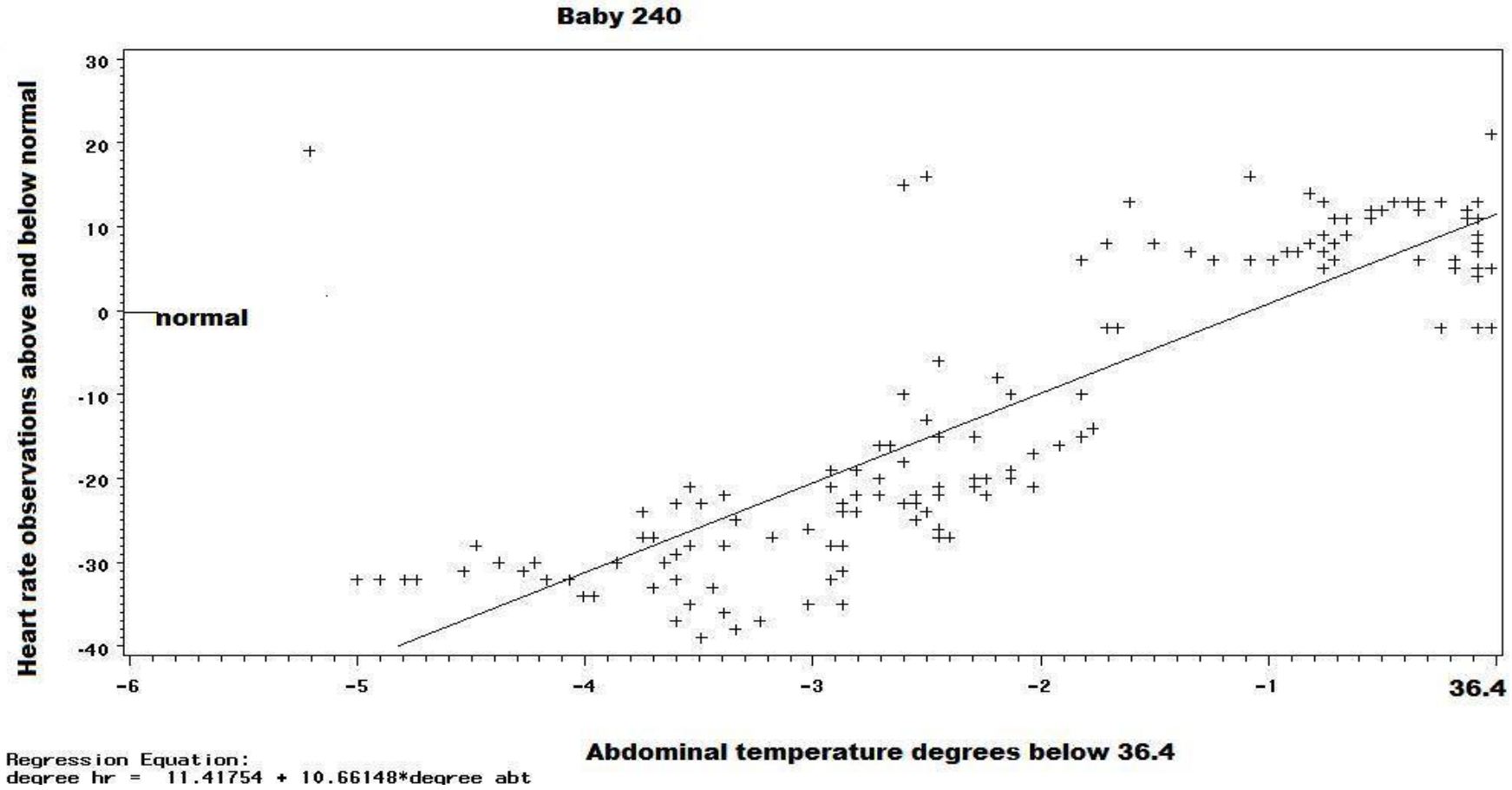
Table 4.44 Pearson Correlations of the Extent of Observations of Abdominal Temperature ≤ 36.4° C and the Degree of Abnormality for Heart Rate and Oxygen Saturation Observations for Study Infants

Subject #	Degree of abnormal heart rate		Degree of abnormal oxygen saturations	
	n	r value	n	r value
170	100	0.26 *	48	0.12
240	156	0.85*	101	0.10
311	201	0.02	29	.07
360	171	0.09	50	0.41*
410	239	0.27*	126	0.00
450	260	0.35*	33	0.04
510	334	-0.45*	144	0.54*
590	134	0.57*	28	-0.18
680	215	0.33*	11	0.81*
730	65	-0.01	39	-0.33*

* $p < .05$

Six out of ten infants had a significant positive ($p < .05$) correlation between the extent of

Figure 4.49 Scatterplot with Regression Line of Observations of Abdominal Temperature ≤ 36.4˚ C with Corresponding Abnormal Heart Rate Observations for Infant 240



r = 0.85 * (p < .05), n= 56

hypothermic (≤ 36.4˚ C) abdominal temperature observations compared to the extent of abnormality in the heart rate (above or below the 25th and 75th percentile heart rate limits for each subject). However, one was in the negative direction (r = -0.45). Figure 4.49 shows the scatterplot of the strongest positive correlation (r = .85) for infant 240 with 156 observations meeting the low temperature and abnormal heart rate criteria. As shown in Figure 4.49, as the infant's abdominal temperature decreased below the cut point of 36.4˚ C (0 point on the x-axis) until approximately 34.4˚ C, the infant's heart rate increased above the upper normal limit. Once the temperature decreased low enough (below 34.4˚ C), the heart rate decreased below the lower normal limit, most likely because the infant was unable to compensate at such a low temperature. Four other infants (# 410, 450, 590, 680) had this pattern with heart rates below the normal limit associated with temperatures decreased below approximately 34.5˚ C (see Appendix V).

Figure 4.50 shows the one infant (#510) that had a negative correlation at the significance level of $p < .05$ with 334 observations and r = -0.45. As this infant's abdominal temperature decreased further below 36.4˚ C (0 point on x-axis), the heart rate increased above the upper limit of 147 (0 point on y-axis) for that infant (#510). This infant was able to compensate well for low temperatures by increasing heart rate which is also shown in Figure 4.50.

One infant (#170) had heart rates lower than the low normal limit for most temperatures less than 36.4˚ C (see Figure 4.51). This infant was not able to increase her heart rate in association with hypothermia. The remaining three infants (#311, 360, 730) did not show a clear relationship between the heart rate data and abdominal temperatures less than or equal to 36.4˚ C.

Four infants had a significant correlation ($p < .05$) between the extent to which the

Figure 4.50 Scatterplot with Regression Line of Observations of Abdominal Temperature ≤ 36.4˚ C with Corresponding Abnormal Heart Rate Observations for Infant 510

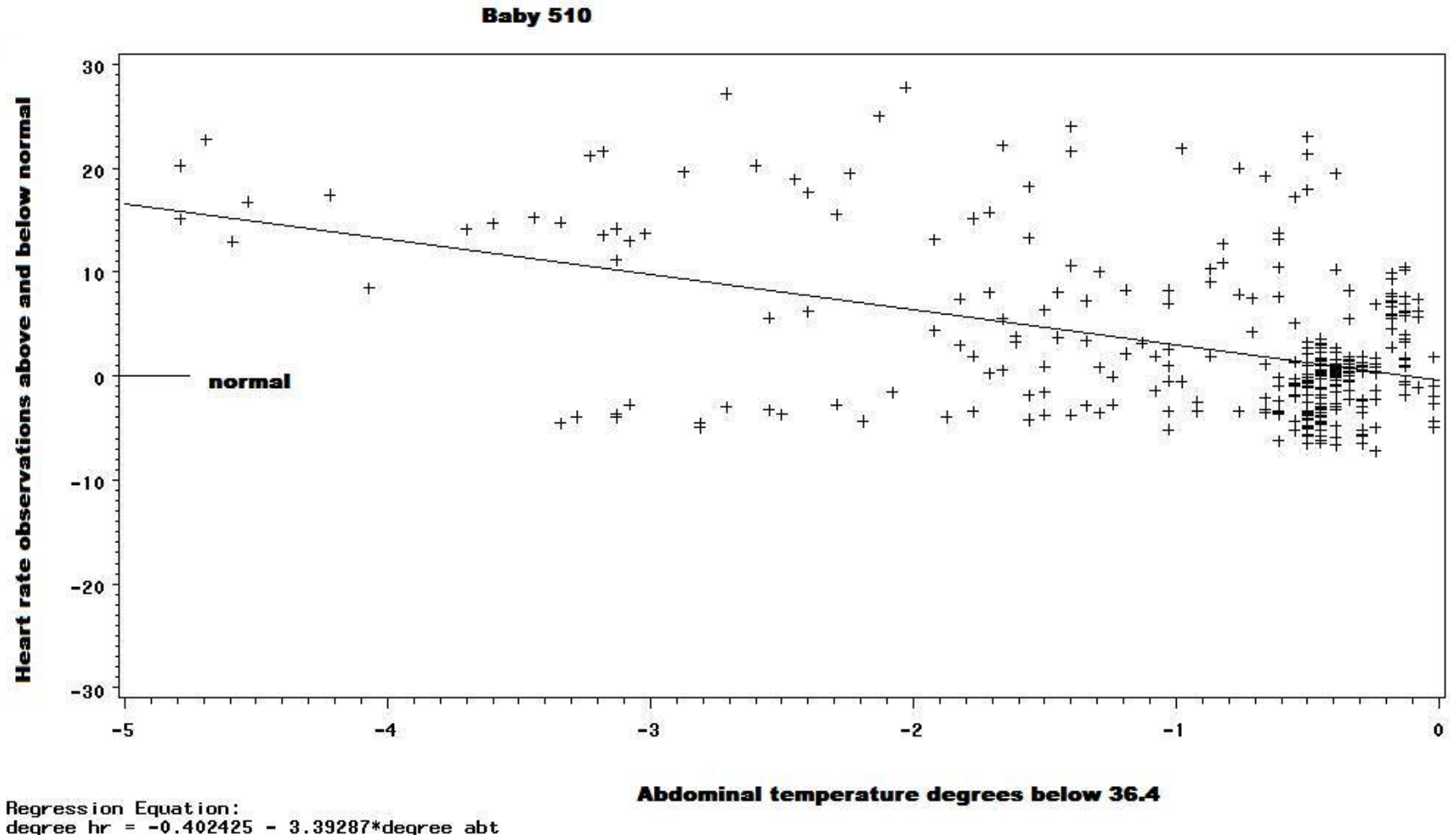
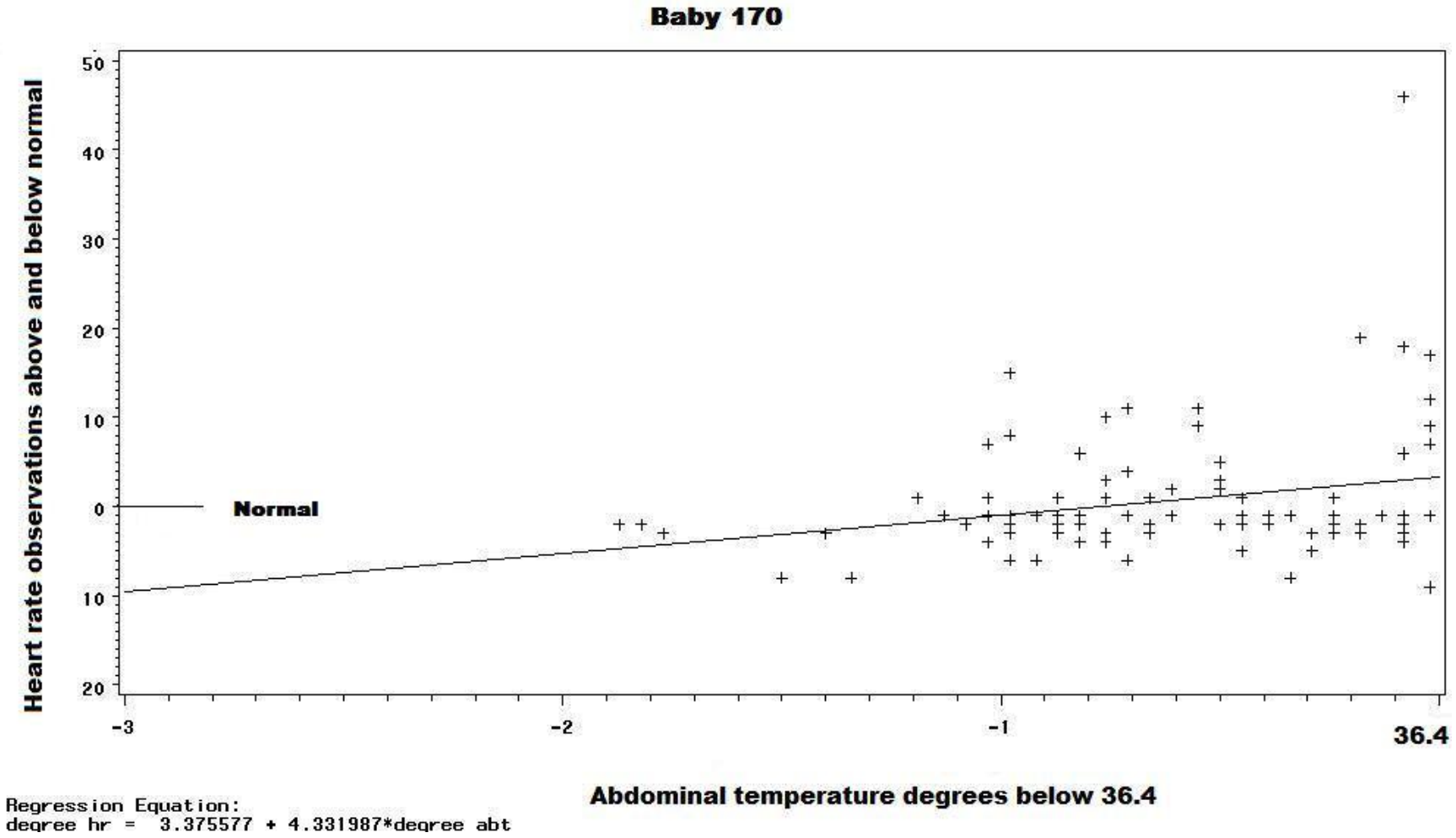


Figure 4.51 Scatterplot with Regression Line of Observations of Abdominal Temperature ≤ 36.4° C with Corresponding Abnormal Heart Rate Observations for Infant 170



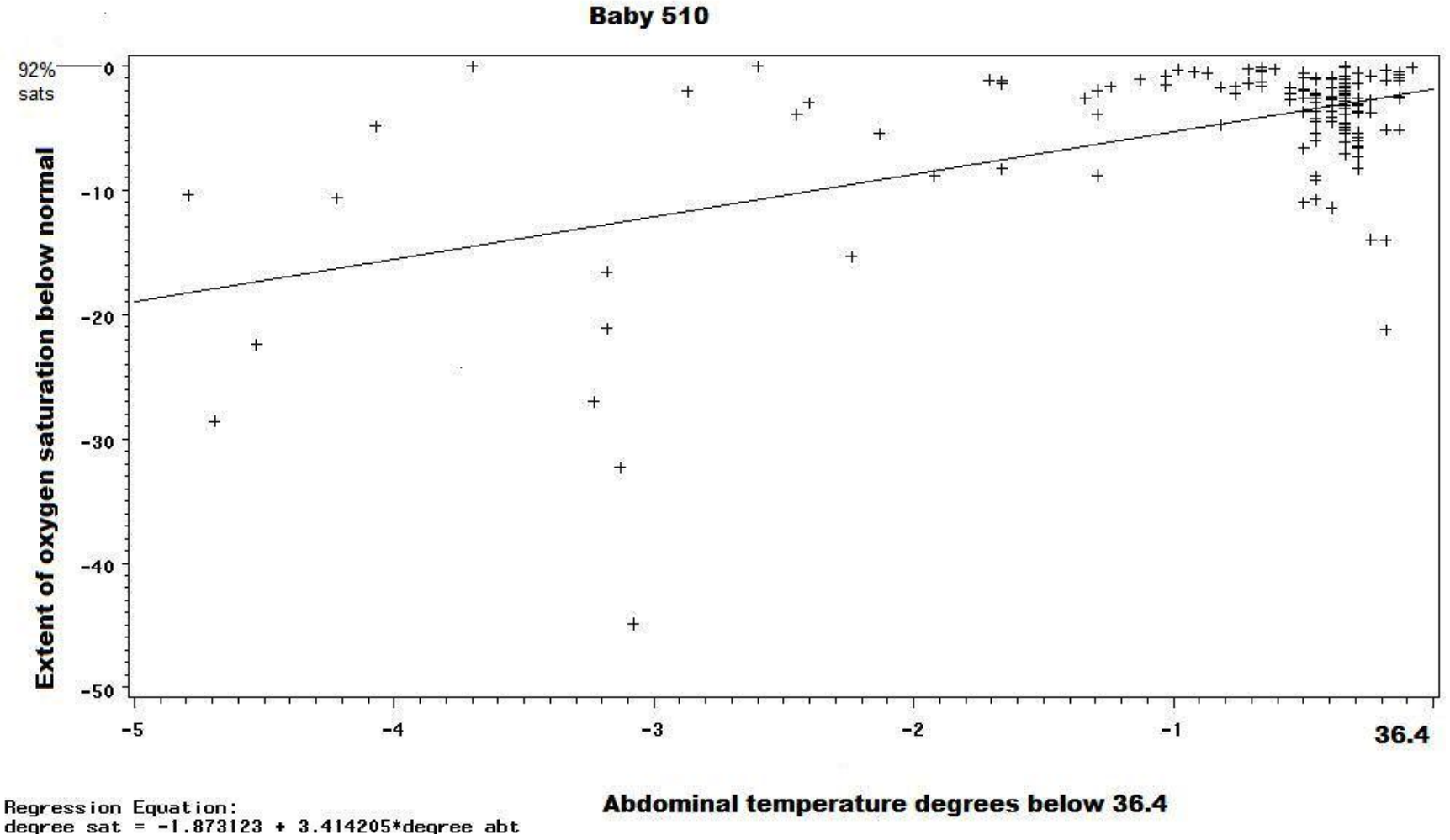
abdominal temperature decreased below 36.4˚ C the degree the oxygen saturations decreased below 92%. Because all of the study subjects were well maintained as to their respiratory status, very few abnormal oxygen saturation observations occurred in the data. Therefore, the observation numbers were low on this analysis and no definite conclusions can be drawn. Only one of the four infants had more than 100 observations of abdominal temperatures less than or equal to 36.4˚ C along with the abnormal oxygen saturations. Figure 4.52 shows the scatterplot for this infant's observations showing that the extent of hypothermia was correlated with the extent of decrease in oxygen saturation for infant 510 with an *r* value of 0.54 (n=144).

Relationship of Abdominal-Peripheral Temperature Difference to the 36.4˚ C Cut Point.

The original research question was whether the amount of time spent in peripheral vasoconstriction was related to the extent to which body temperature was below 36.4˚ C. Because 8 of 10 subjects had less than 2% of their observations defined as peripheral vasoconstriction, this question was answered using the abdominal-peripheral temperature difference. Normally, if peripheral vasoconstriction occurred this difference would be greater than 2˚ C. Most infants had peripheral temperatures greater than their abdominal temperature during the study periods. Therefore, the abdominal-peripheral temperature difference for those infants was negative. Pearson correlations were done to compare the extent of observations of abdominal temperature as they decrease below the cut point less than or equal to 36.4˚ C with the abdominal-peripheral temperature difference to determine if there was a correlation (Table 4.45).

Seven of ten infants had significant correlations between the extent to which their

Figure 4.52 Scatterplot with Regression Line of Observations of Abdominal Temperature ≤ 36.4˚ C with Corresponding Subnormal Oxygen Saturation Observations for Infant 510



abdominal temperature decreased below the cut point of 36.4˚ C and the abdominal-peripheral temperature difference. Four infants (# 360, 450, 590, 730) had a temperature difference between abdominal and peripheral temperatures between 0 and 2˚ C when abdominal temperatures were closer to the 36.4˚ C (see Appendix VI) cut point, mostly between 34.4˚ and 36.4˚ C (see Figure 4.53).

Table 4.45 Pearson Correlations of the Extent of Observations of Abdominal Temperature ≤ 36.4˚ C and the Difference Between Abdominal and Peripheral Temperatures for Corresponding Observations

Subject #	Mean temperature for all observations below AbT ≤36.4˚ C (SD)	Mean AbT-Ft Diff˚C(SD) for observations AbT ≤36.4˚ C	n	r value
170	35.77 (0.46)	-0.35 (0.99)	142	0.03
240	34.60 (1.47)	-0.29 (0.61)	179	0.82*
311	34.64 (2.10)	-1.00 (0.77)	337	-0.35*
360	35.58 (0.57)	0.50 (0.92)	422	0.53*
410	35.06 (0.84)	-1.13 (0.69)	565	0.04
450	34.59 (0.99)	0.07 (0.89)	43	0.71*
510	35.58 (0.81)	-0.52 (1.12)	327	-0.10
590	34.84 (1.08)	-0.32 (0.57)	200	0.32*
680	34.77 (1.22)	-0.71 (0.52)	398	-0.23*
730	36.21 (0.31)	1.08 (0.35)	122	0.54*

* $p < .05$

Figure 4.53 Scatterplot with Regression Line of Observations of Abdominal Temperature ≤ 36.4˚ C with Corresponding Abdominal Peripheral Temperature Difference for Infant 450

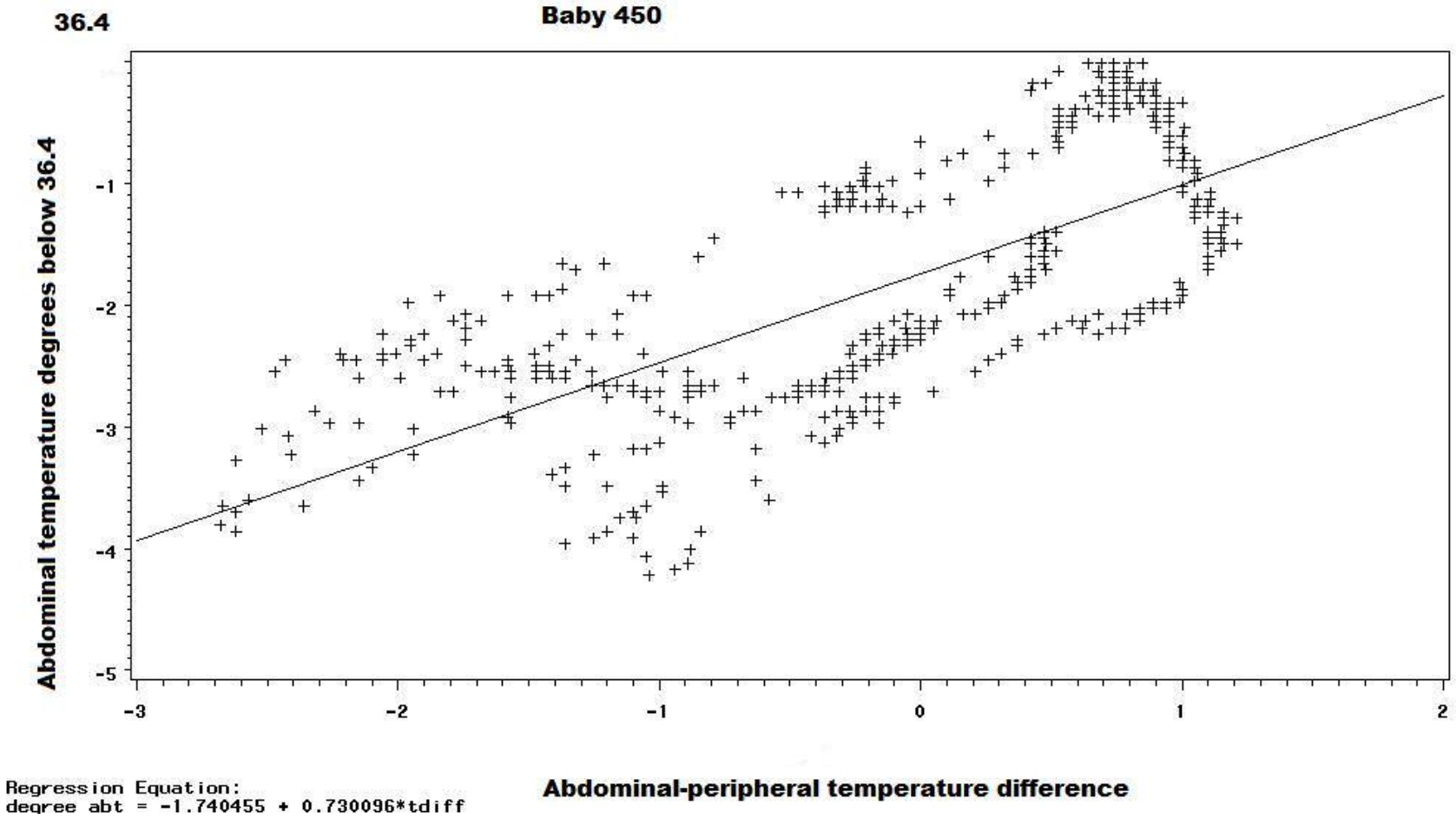
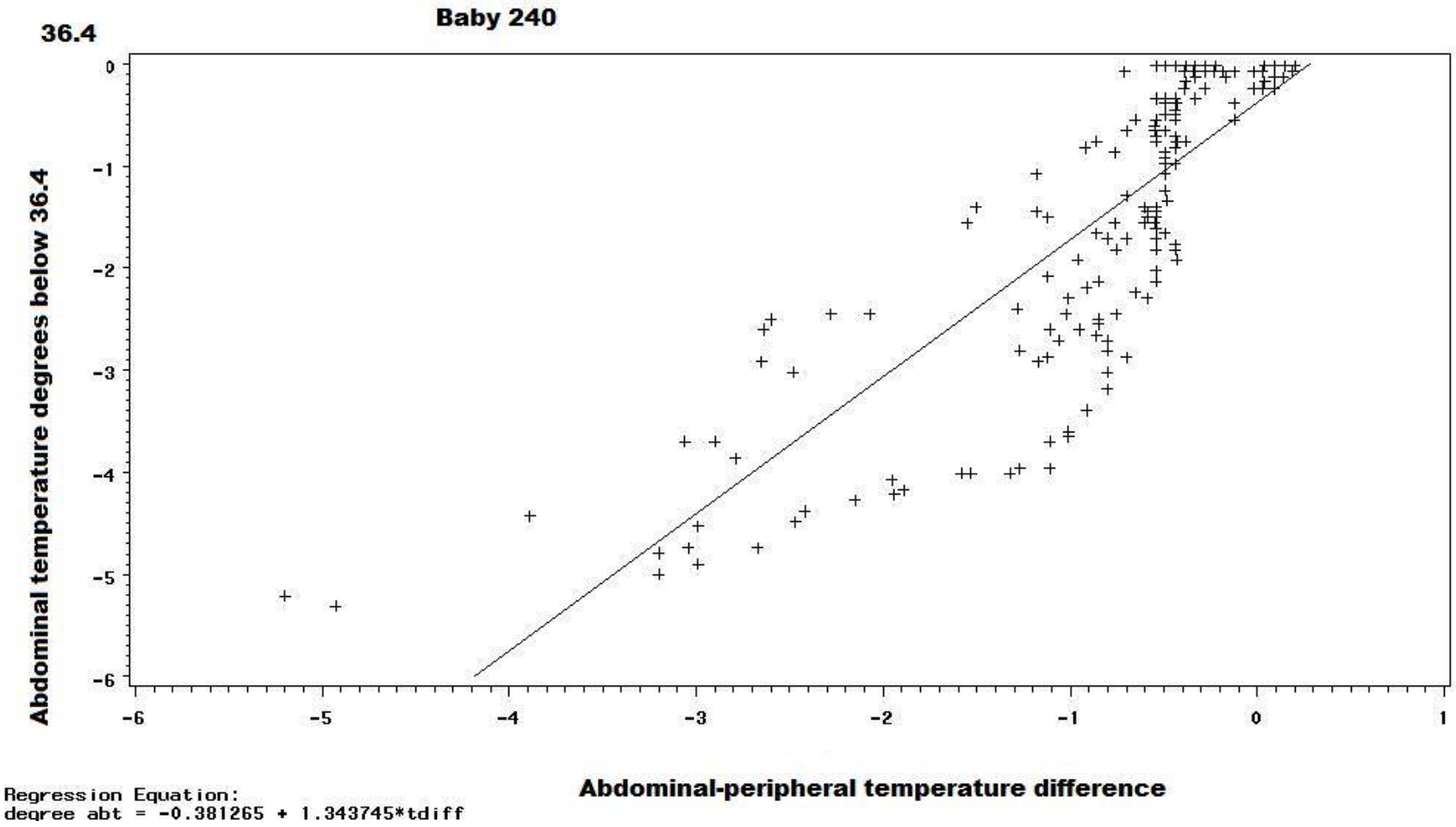


Figure 4.54 Scatterplot with Regression Line of Observations of Abdominal Temperature ≤ 36.4˚ C with Corresponding Abdominal Peripheral Temperature Difference for Infant 240



Also, three infants (240, 360, 450) showed a pattern in which the peripheral temperature was higher than the abdominal temperature at temperatures approximately lower than 34.4˚ C (see Appendix VI) and the difference increased as the abdominal temperature decreased (Figure 4.54).

Optimal Cut-point in Abdominal Temperature As Indicated By Heart Rate

Oxygen saturation data were not used to answer the question, "Is there an optimal cut-point in body temperature where amount of abnormal physiological variable observations are minimized and amount of normal physiological variable observations are maximized?," because the values were confounded due to oxygen delivery to the infant, with most values being in the normal range. Therefore, heart rate data for each subject were used to determine the optimal body temperature to minimize heart rate observations in the abnormal range and maximize heart rate observations in the normal range. Normal heart rate was defined as heart rate observations between the 25^{th} and 75^{th} percentile for each infant because all infants had a wide range in heart rate values. A table was calculated for each infant for abdominal temperatures at 35.5˚- 37.5˚ C and percentage of heart rate observations at the below normal, normal, and above normal ranges with below normal defined as observations below the 25^{th} percentile and above normal defined as observations above the 75^{th} percentile. Percentage of heart rate observations within each heart rate level was plotted on the y-axis, and abdominal temperature observations were rounded to the nearest 10^{th} degree and plotted on the x-axis for each infant. Percentages (see Table 4.45) and graphs (see Figure 4.55) were examined across infants to look for a similar abdominal temperature range that minimized heart rate observations at the below and above normal levels while maximizing normal heart rate

observations.

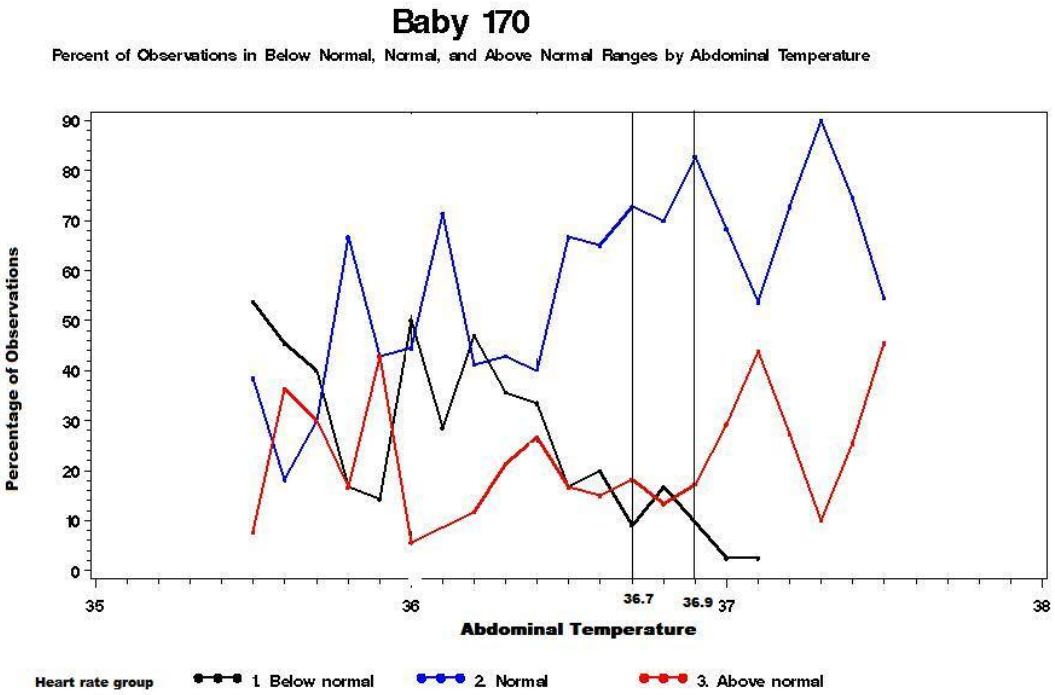
From the results presented in Table 4.45, the optimal abdominal temperature range for infants in this study appears to be between 36.8˚C and 36.9˚ C. In this range, observations for most infants were in the normal range (> 50% of observations for 8 of 10 infants) while minimizing (< 25% of observations in 8 of 10 infants) heart rate observations in the below normal range and above normal range (< 25% of observations in 8 of 10 infants). Visual examination of the graphs in Figure 4.55 gives evidence that the optimal abdominal temperature range for infants in this study was around 36.8˚ C to 37.0˚ C in order to minimize abnormal heart rate observations and to maximize normal heart rate observations.

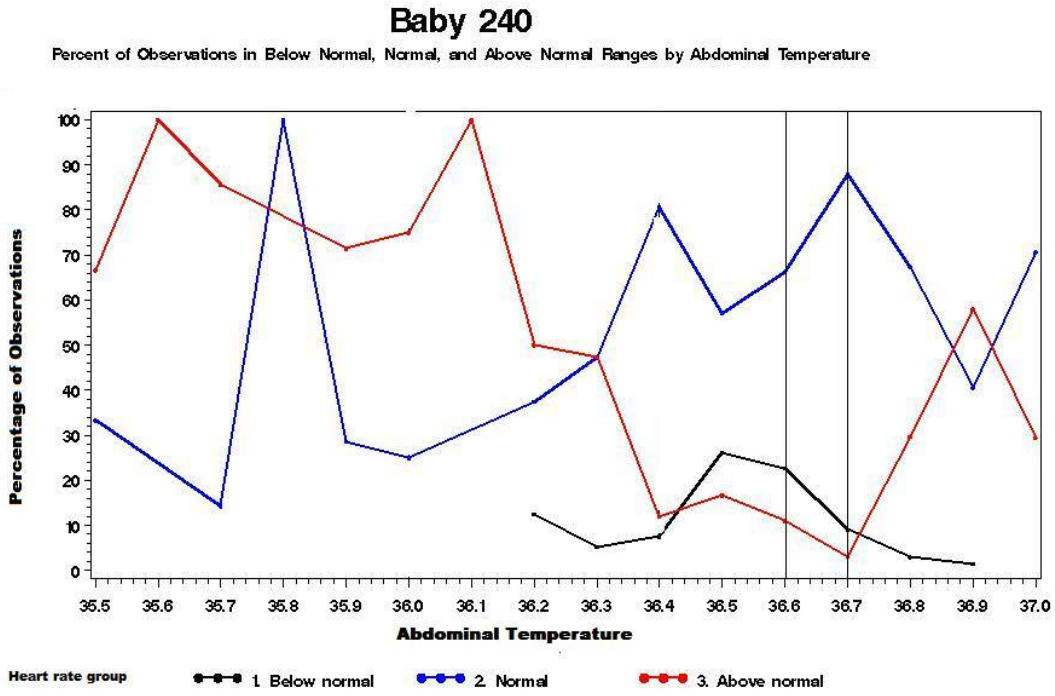
Table 4.45 Percentage of Observations in the Below Normal, Normal, and Above Normal Heart Rate Ranges at Different Abdominal Temperatures for each Infant

Subject # / Heart rate level/Temp	170	240	311	360	410	450	510	590	680	730	Mean
Below Normal	16.7	26.2	42.9	16.7	0	0	7.8	0	0	16.4	12.7
Normal **36.5**	66.7	57.1	57.1	66.7	50	53.3	72.6	73.7	76.1	62.3	63.6
Above Normal	16.7	16.7	0	16.7	50	46.7	19.6	26.3	23.9	21.3	23.8
Below Normal	20	22.7	33.3	0	0	0	0	16.7	1.7	26.6	12.1
Normal **36.6**	65	66.3	61.9	60	0	80	100	58.3	48.8	40.7	58.1
Above Normal	15	11	4.8	40	100	20	0	25	49.6	32.7	29.8
Below Normal	9.1	9.1	23.1	50	0	0	0	37.5	0	35.9	16.5
Normal **36.7**	72.7	87.9	69.2	0	46.7	0	100	50	75	53.9	55.5
Above Normal	18.2	3	7.7	50	53.3	100	0	12.5	25	10.3	28
Below Normal	16.7	3	32	0	0	0	0	22	2.4	31.4	10.8
Normal **36.8**	70	67.3	68	82.4	25	100	100	68.3	75	48.6	70.5
Above Normal	13.3	29.7	0	17.7	75	0	0	9.8	22.6	20	18.8
Below Normal	0	1.5	61.1	0	10	0	0	15.2	0	18.2	10.6
Normal **36.9**	82.8	40.6	33.3	80	90	83.3	100	68.2	80	54.6	71.3
Above Normal	17.3	58	5.6	20	0	16.7	0	16.7	20	27.3	18.2
Below Normal	2.4	0	34.8	13.3	0	12.8	0	9	0	15.8	8.8
Normal **37.0**	68.3	70.6	30.4	80	0	85.11	100	74.4	0	42.1	55.1
Above Normal	29.3	29.4	34.8	6.7	0	2.1	0	16.7	0	42.1	16.1

Heart rate levels:
Below Normal $< 25^{th}$ Percentile
Normal 25^{th}-75^{th} Percentile
Above Normal $> 75^{th}$ Percentile

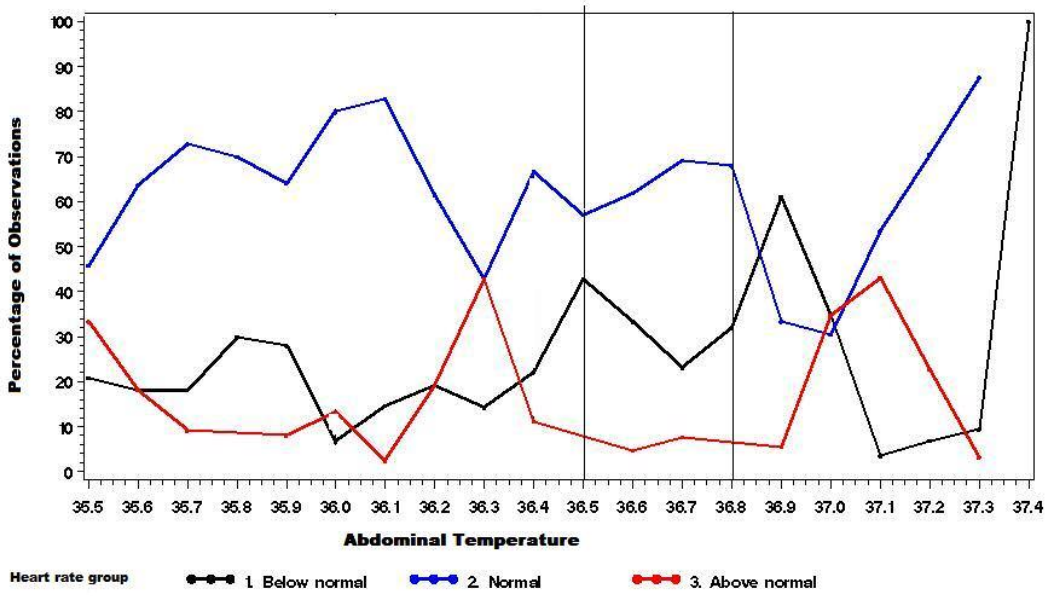
Figure 4.55 Plots of All Infants





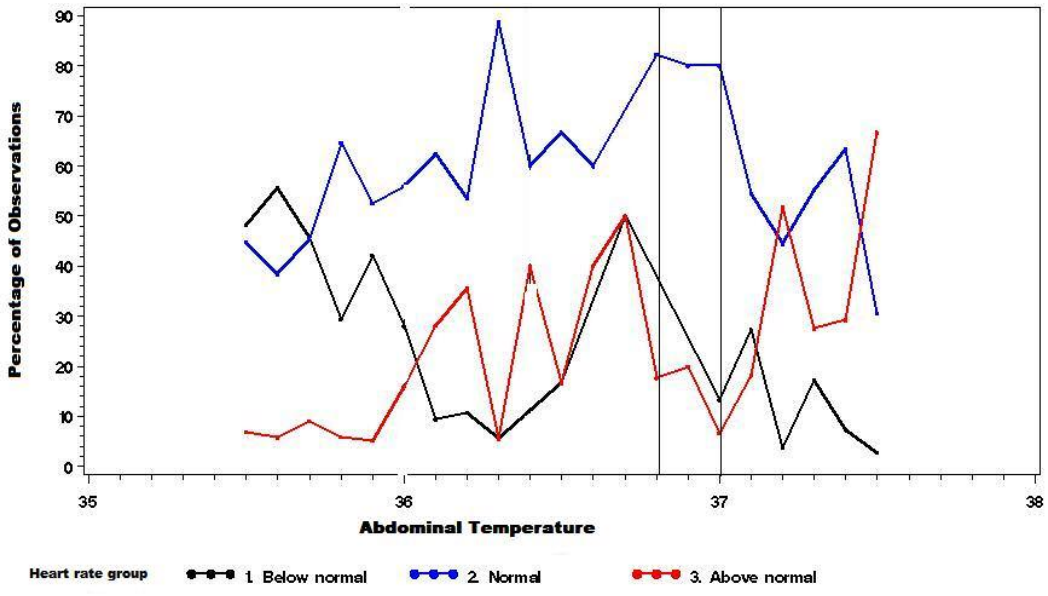
Baby 311

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



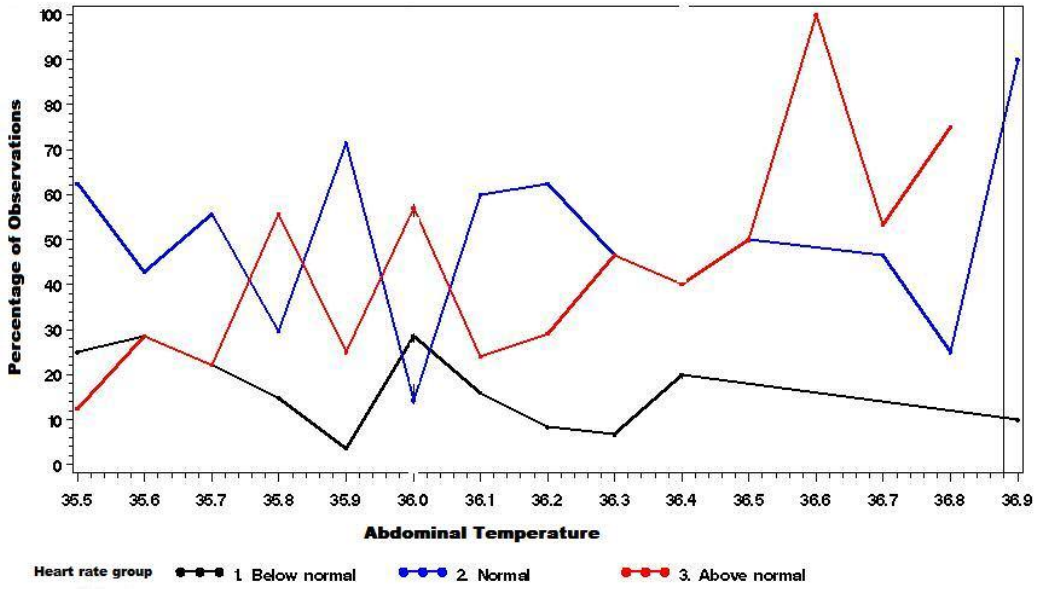
Baby 360

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



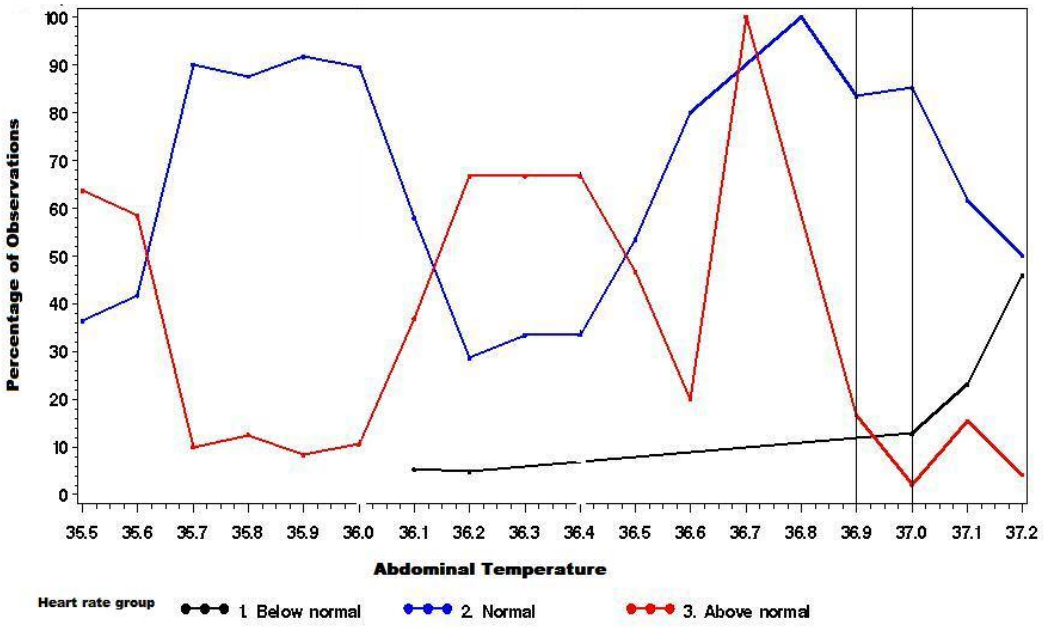
Baby 410

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



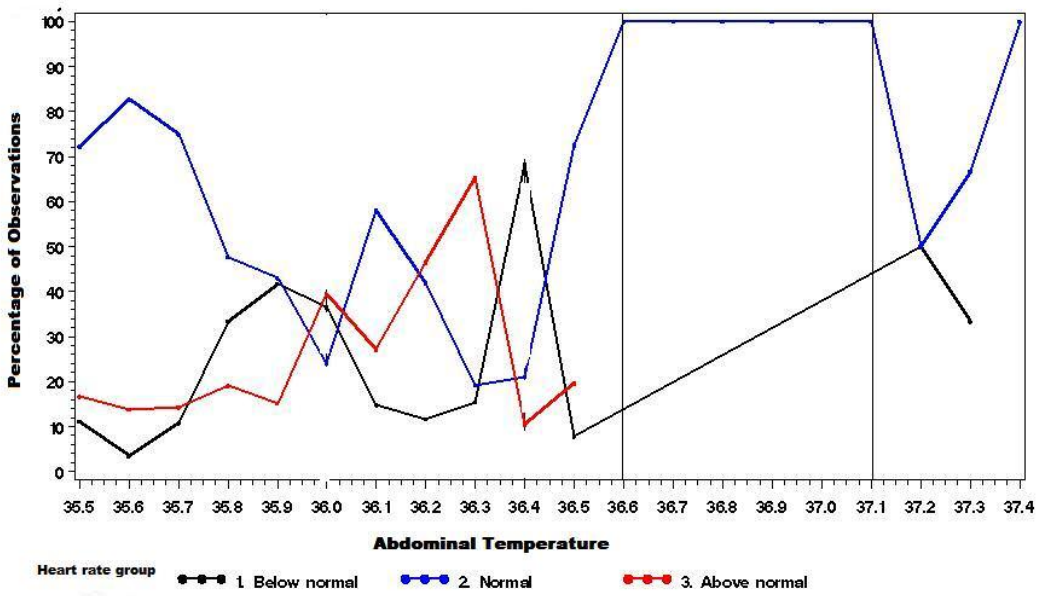
Baby 450

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



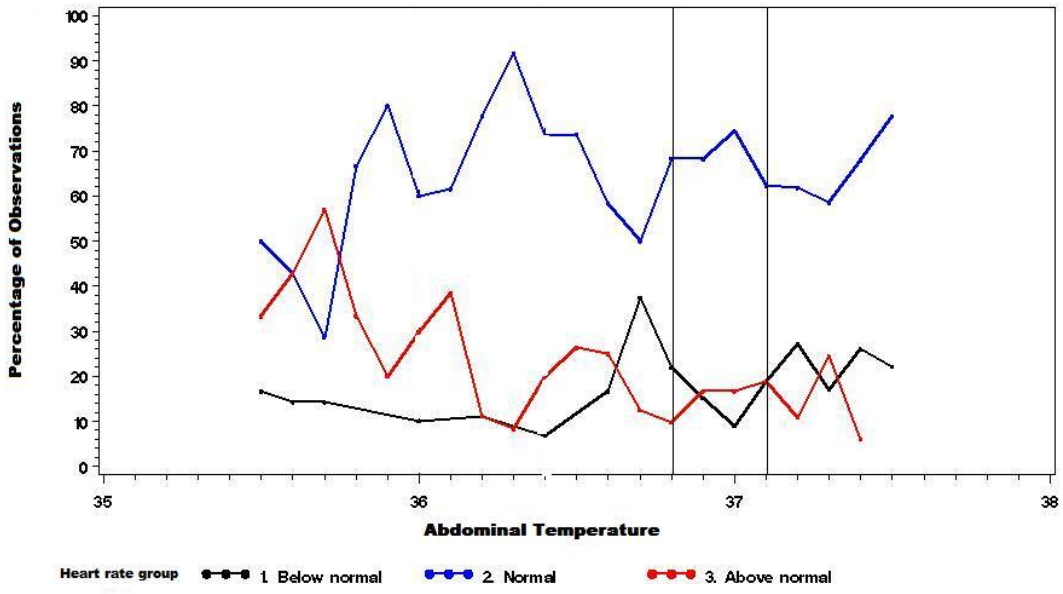
Baby 510

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



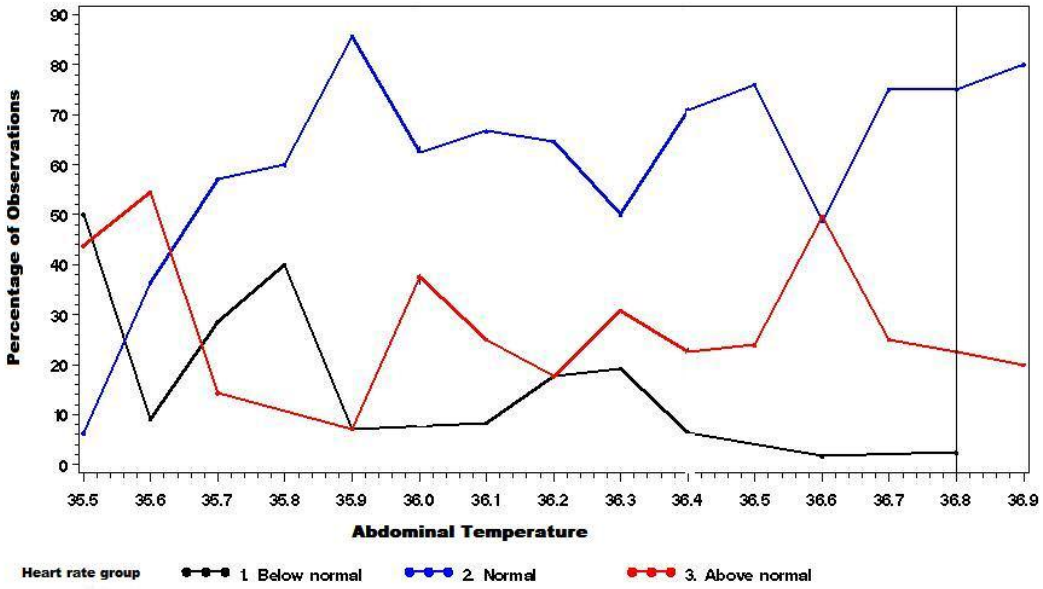
Baby 590

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



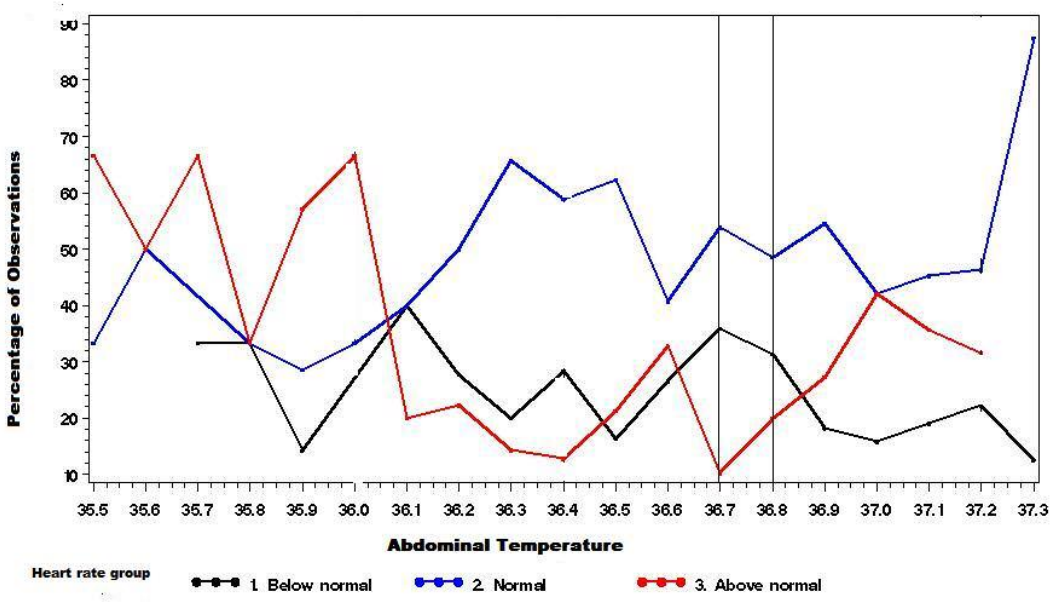
Baby 680

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



Baby 730

Percent of Observations in Below Normal, Normal, and Above Normal Ranges by Abdominal Temperature



CHAPTER FIVE

Discussion

The findings of this study indicated that ELBW infants have high rates of hypothermia (less than 36.4˚ C by traditional definition; American Academy of Pediatrics, 1988). Infants in this study averaged very low abdominal temperatures throughout the 12-hour study period (35.17˚-36.68˚ C). Axillary temperatures recorded as low as 33.0˚ C and were too low to register at times. Temperatures through initial parts of stabilization in the NICU were very low for most infants and 7 of 10 infants averaged hypothermic temperatures throughout the entire 12-hour study period. Extremely low birth weight (ELBW) infants (< 1000 grams at birth) are exposed to many stabilization procedures and cool room temperatures, cold infusions, and cold drapes from birth through the first 12 hours of life. These infants are likely to become very cold because of this exposure. Because ELBW infants have little to no ability to generate heat by non-shivering thermogenesis (Houstek et al., 1993; Lyon et al., 1997), their body temperatures can become very low in response to environmental cold stress. Without the ability to generate heat, these infants can experience morbidity and mortality from such low body temperatures (Buetow & Klein, 1964; Day et al., 1964; Hazan, Maag, & Chessex, 1991; Vohra, Grent, Campbell, Abbott, & Whyte, 1999).

The temperatures of ELBW infants during stabilization easily can decrease as low as 33˚ C even though the infants are placed on radiant warmers. Because ELBW infants are vulnerable to cold stress, knowing the optimal range for the ELBW infant's temperature is important in order to protect the infant from cold stress and organ system insult. However,

very little research has examined this range in ELBW infants. Most of the research on optimal body and environmental temperatures for premature infants was conducted 20-40 years ago, before significant numbers of ELBW infants or ventilated infants survived (Adams et al., 1964; Bruck, 1961; Buetow & Klein, 1964; Day, Caliguiri, Kamenski, & Ehrlich, 1964; Silverman, Fertig, & Berger, 1958; Yashiro, Adams, Emmanouilides, & Mickey, 1973). Results from the current study give evidence on how to optimize temperature control in ELBW infants weighing 550-960 grams during the first 12 hours of life.

Although abdominal and peripheral temperatures were correlated in all infants, peripheral temperatures were higher than abdominal temperatures for the majority of the study period for most infants (7 out of 10). Lyon et al. (1997) found that this phenomenon (peripheral higher than abdominal temperature) seemed to increase with caregiver handling. Association between medical and nursing procedures (repositioning, suctioning, drawing of blood gases, giving intravenous infusions) and an increase in the abdominal-peripheral temperature difference was also seen in the current study for 9 of 10 infants. Seven of these infants exhibited higher peripheral temperatures than abdominal temperatures as in the Lyon et al. (1997) study. The association between caregiver handling and an increased difference between peripheral and abdominal temperatures was most likely due to exposure to cold environmental air during the procedure because the side of the incubator was opened, incubator top was lifted or portholes were opened. Because these infants were cared for in closed incubators with up to 80% humidity and at environmental air temperatures up to 39˚C, any exposure to room air outside the incubator greatly decreased the infants' environmental temperature. Of note, when infants were given intravenous infusions through their umbilical

venous catheter, the fluid probably caused a decrease in abdominal temperature because abdominal temperatures were noted to decrease during these events. In this NICU, intravenous infusions were stored at room temperature which was kept around 22-25˚C, usual for fluid storage in NICUs. Therefore, intravenous fluids were very cold in relation to the warm body temperatures and might have decreased the abdominal temperature because the infants were affected by the cold central infusion.

An increased difference in the peripheral and abdominal temperatures, especially when the peripheral temperature was higher than the abdominal temperature as seen in these study infants was also associated with stress, be it cold exposure or caregiver handling. Stimulation events to the infants were also associated with increases in heart rate and decreases in oxygen saturations based on visual inspection of the printed graphs. An increase in heart rate has been shown to be associated with caregiver procedures to ELBW infants (Grunau et al., 2000).

Lyon et al. (1997) also noted an association between death and the proportion of time that the peripheral temperature was greater than the abdominal temperature. This association may occur because the time the peripheral temperature is higher than the abdominal temperature is time when the infant is cold centrally and because a higher peripheral temperature indicates poor, if any, vasomotor control. Mortality was not followed in the current study since subjects were only studied for the first 12 hours of life. However, future research should examine the relationship between elevated peripheral temperatures and mortality, especially in relationship to stressful events and low temperatures.

The findings of the current study indicated that heart rate was a better indicator of cold stress than oxygen saturation. Heart rates varied for each infant. Therefore, normal heart

rate was defined as the 25th and 75th percentile of each infant. Abdominal temperature was significantly correlated with heart rate in 7 infants and with oxygen saturation in 8 infants. However, the correlations between abdominal temperature and oxygen saturation were as likely to be positive as negative. The two infants who were most unstable, requiring inotropic infusions for hypotension had the strongest correlation between abdominal temperature and heart rate. Both of these infants received Dopamine infusions and one of the infants also received Dobutamine and Epinephrine infusions. These inotropes increase blood pressure, improve cardiac stability, and improve cerebral perfusion (Pellicer et al., 2005). Dopamine has also been shown to release energy from brown fat in rats (Maxwell, Crompton, Smyth, & Harvey, 1985) which may increase heat production. Therefore, the two most unstable infants (having hypotension and hypoperfusion requiring treatment) improved their abdominal temperature as they became more stable, which corresponds with the passing of time in the study period and beginning the inotropic infusions.

Inotropic infusions such as Dopamine and Epinephrine also cause heart rate to increase, however, Dopamine does not cause as much of an increase as Epinephrine (Heckmann, Trotter, Pohlandt, & Linder, 2002; Pellicer et al., 2005). The infant who had the strongest correlation between abdominal temperature and heart rate received Dopamine first then Dobutamine, and finally an Epinephrine infusion (see Figure 4.40). The exact relationship between abdominal temperature and heart rate is not known, however, we speculate the inotropic infusions improved blood pressure and cardiac stability in these two infants resulting in warmer abdominal temperature over the study period secondary to improved central perfusion. Since an increase in heart rate is often seen with stressful events and as a side effect of inotropic infusions and lower abdominal temperatures were seen with

instability and stressful procedures, it would seem appropriate that heart rate and abdominal temperature would be strongly correlated.

A future study could examine aspects of stability in ELBW infants while correlating abdominal temperature and heart rate. In this study, classifications of stability were not defined a priori and dividing the infants based on stability classification was too difficult, except for infants who received inotropic infusions and those who did not.

ELBW infants maintained their heart rate in their own normal range more often when their abdominal temperature was higher than 36.4˚ C. Significantly more observations in the normal heart rate range occurred in 6 infants when their abdominal temperature was greater than 36.4˚ C, the American Academy of Pediatrics (1988) definition for hypothermia. Therefore, the abdominal temperature for ELBW infants needs to be at least 36.4˚C. Not only did maintaining temperature above the hypothermic cut point help keep heart rate in the normal range for these ELBW infants, but decreasing the abdominal temperature further below the hypothermic cut point was associated with moving the heart rate further above or below the normal range. In 7 infants the extent of heart rate abnormality was significantly correlated with the extent to which the abdominal temperature decreased below the hypothermic point. In this study five infants increased their heart rate in association with temperatures between approximately 34.4˚C and 36.4˚ C. Once abdominal temperature decreased below approximately 34.4˚ C, five infants were unable to increase their heart rate in response to the extremely low temperatures and they decreased their heart rate below their normal range. There seems to be a point at which ELBW infants are unable to compensate metabolically for extremely low temperatures and at which they start to deteriorate. Hypothermia has been associated with a fall in systemic arterial pressure, a decrease in

plasma volume, decreased cardiac output, increased peripheral resistance, and metabolic acidosis (Sinclair, 1992). If this condition is left uncorrected, most likely death would ensue. No previous research has examined heart rate, hypothermia and mortality. Further research to explore the connection between heart rate, stress, and low abdominal temperature is needed.

Oxygen saturation was not a good indicator of abdominal temperature in the current study because this measure is confounded by oxygen delivery to the infant. Normal oxygen saturation was defined as greater than 92% for all infants, based on the literature (Ng, Subhedar, Primhak, & Shaw, 1998; Paky & Koeck, 1995; Poets, 1998 Rey, 2004). However, most oxygen saturation observations were normal because it was standard protocol was for caregivers in this NICU to increase oxygen delivery to the infant if oxygen saturation decreased below 85%. Most infants in this study did not require a high amount of oxygen delivery with the ventilator and received 21% oxygen (room air) much of the observation period. Therefore, oxygen saturation data averaged higher than 85%, which is the low acceptable saturation for this NICU and the point where a bedside nurse gave supplemental oxygen. All study subjects had oxygen saturations in the normal range greater than 50% of the time and 8 of 10 had normal oxygen saturations at least 70% of the time according to the textbook normal of 92% that was used as normal in the analyses. All 10 infants had at least 94% of their saturation observations greater than the unit normal of 85%. Abdominal temperature was significantly correlated with oxygen saturation for eight study subjects. However four correlations were in the positive direction and four correlations were in the negative direction. Because caregivers were purposefully keeping oxygen saturations above 85% with additional oxygen delivery to the infant, there was little variation in oxygen

saturation observations. Therefore, having a correlation between abdominal temperature and oxygen saturation and the direction or strength of correlation has little if any meaning. No association was found between the strength of correlation and mean abdominal temperature or demographic characteristics.

The abdominal-peripheral temperature difference for observations differed significantly between normal oxygen saturation and abnormal oxygen saturation. However, little statistical conclusion could be drawn for analyses conducted between temperature and oxygen saturation observations because few abnormal oxygen saturation observations occurred. Oxygen saturation was used as a proxy for oxygen consumption, which may be a much better determinant of heat production. However oxygen consumption can not be measured in infants so small because of extremely low tidal volumes they generate (Gomella, 1994).

Additionally, oxygen saturation may also not be a good determinant of stress because Grunau et al. (2000) did not find a significant relationship between oxygen saturation and caregiver procedures in ELBW infants. These researchers most likely had the same confounding effect of caregivers increasing oxygen delivery to maintain higher oxygen saturations which would yield stable, higher oxygen saturations in ELBW infants, regardless of stress to the infants. Other studies have confirmed that caregiver handling is associated with a decrease in oxygen saturation in infants who are not being given supplemental oxygen (Evans, 1991; Evans et al., 2000; Zahr & Balian, 1995) and when being given supplemental oxygen, caregiver handling results in a brief decrease in oxygen delivery (Peters, 1992). A researcher should plan a priori to record oxygen saturations to correlate with oxygen delivery each minute and examine those observations in relationship to procedures occurring at each

minute in order to analyze oxygen saturation data in relationship to caregiver handling.

Oxygen delivery to the infant is an integral part of the oxygen saturation response to caregiver handling. Older research showed decreased transcutanous pO_2 levels with suctioning (Evans, 1992). However, modern day technology allows continuous oxygen delivery through inline suctioning use (as was used in the NICU for this study), therefore researchers today may not see a statistical difference in oxygen saturations with suctioning due to constant oxygen delivery.

The ELBW infants in this study appeared to be unable to exhibit peripheral vasoconstriction. Only one infant exhibited peripheral vasoconstriction at the traditional definition of an abdominal peripheral temperature difference of greater than 2˚ C (Lyon et al., 1997; Simbrunner, 1995). This was an 880 gram 26-week gestational infant. Seven of infants spent at least 15% of their temperature observations with the peripheral temperature higher than their abdominal temperature. Weight in a premature infant is roughly correlated with gestational age and weight is generally associated with gestational age when the infant is premature, under 1000 grams and appropriate weight for gestational age. Smaller infants (500-710 grams) and the most premature (24-25 weeks gestation) were most likely to have peripheral temperatures 1-2˚ C higher than their abdominal temperature. Mok et al. (1991) showed occasional peripheral vasoconstriction in response to caregiver handling of ELBW infants. However 80% of their sample weighed more than 800 grams. We speculate that the weight at which ELBW infants can exhibit peripheral vasoconstriction is greater than approximately 800 grams which is roughly associated with greater than 26-weeks gestation.

With only one infant exhibiting true peripheral vasoconstriction, our findings confirmed those of Lyon et al. (1997): Infants under 1,000 grams exhibit poor vasomotor control. Lyon

et al. (1997) found that ELBW infants had no ability to exhibit peripheral vasoconstriction, an early response to thermal stress in changing the peripheral temperature to conserve the central body temperature. Horns (2002) found that ELBW infants exhibited peripheral vasoconstriction about 18% of the time when studied from 12-24 hours of age. She studied infants weighing 570-880 grams at birth but did not specify which infants in her sample exhibited peripheral vasoconstriction. Although Horns (2002) studied infants weighing approximately the same as infants in the present study, she studied the infants over 24 hours of age. I examined infants only in the first 12 hours of age and found ELBW weighing less than 800 grams and less than 26-weeks gestation did not exhibit peripheral vasoconstriction, probably because the ability to exhibit peripheral vasoconstriction had not developed yet.

Peripheral vasoconstriction may be related to the chronological ages of the ELBW infants as well as their birth weights and gestational age. Lyon et al. (1997) found that ELBW infants studied on the first day of life showed higher peripheral than abdominal temperatures 18.3% of the time, but this decreased to 4.9% of the time by 5 days of age. We speculate that as the neurologic system develops over the first few days of life, so does the ability for peripheral vasoconstriction. Therefore, as the ELBW infant becomes older chronologically, the peripheral temperature may decrease along with the abdominal temperature as the infant is cold stressed. The peripheral temperature may decrease more than the abdominal temperature, causing an increased abdominal-peripheral temperature difference and movement towards peripheral vasoconstriction. Mok et al. (1991) showed peripheral vasoconstriction in association with caregiver handling environmental cold stress in ELBW infants that were 2-7 days old.

Instead of peripheral vasoconstriction, results of the current study confirm that most

ELBW infants (7 of 10) showed higher peripheral than abdominal temperature for most of the 12-hour transition periods. Nine of ten infants had a significant increase in the abdominal-peripheral temperature difference when abdominal temperatures were less than or equal to 36.4˚ C. Therefore, colder body temperatures caused an increased difference in the peripheral and abdominal temperatures. As body temperature decreased below 36.4˚ C, the smaller more premature infants were most likely to be unable to increase metabolism to generate heat and had very little vasomotor control. Abdominal temperatures decreased in relationship to the inability to generate heat; however, the peripheral temperature stayed elevated, thus increasing the difference between the peripheral and abdominal temperatures.

Peripheral temperatures may have been higher than abdominal temperatures because these extremely premature infants had poor vasomotor control and their foot took on the temperature of the air, similar to a poikilothermic animal (taking on environmental temperature) as noted by Lyon et al. (1997). The foot has a much smaller surface area than the trunk. Therefore, the foot can more easily be more affected by the warm air of the incubator. Abdominal temperature represents an infant's central body temperature or core temperature (Simbrunner, 1995), which most likely becomes colder in association with the cold environmental temperatures to which the infant is exposed to during caregiver handling, nursing, and medical procedures. Because ELBW infants lack the ability to generate heat adequately, their trunks will stay colder longer than their feet and their feet may gain heat more quickly than their trunks when the incubator air temperature is increased.

In addition, the abdominal temperature was kept lower possibly because of colder intravenous fluids that infused through the umbilical venous and arterial lines, straight into the center of the body. Two infants had a decrease in abdominal temperatures associated

with infusion of intravenous fluids through the umbilical venous catheter. Previous research has not documented a decrease in temperature related to cold intravenous fluid infusions in ELBW infants. However, standard protocol for conducting exchange transfusions, whereby an infant's blood is removed slowly while the infant is transfused with new blood, dictates the use of blood warmed to 37° C for infusion (Cloherty & Stark, 1998). To minimize the effects of cold fluids the bedside caretakers need to take the time to warm up fluids for infusion during the first 12 hours of life.

In the current study, most infants were stressed during caregiver handling from either the procedures or exposure to cold during the procedures. Caregiver handling was associated with an increase in the difference between peripheral and abdominal temperature as well as an increase in heart rate. From visual inspection of the graphs, 9 infants exhibited an increased temperature difference between abdominal and peripheral temperatures in association between caregiver handling and clinical stressors. In 7 of 10 infants, this difference was with peripheral temperatures greater than abdominal temperatures. Previous research has shown that the difference in abdominal and peripheral temperatures increase (abdominal temperature higher) with caregiver handling (Horns, 2002; Mok et al., 1991). Lyon et al., 1997 also showed the difference in peripheral and abdominal temperature increased (peripheral temperature higher) with caregiver handling. Additionally, 7 of 10 infants had an increase in heart rate associated with caregiver handling which confirms previous research showing increased heart rate in association with caregiver handling (Grunau et al., 2000; Peters, 1992; Peters,2001; Zahr & Balian, 1995).

No trends were evident trends in the secondary variables of pO_2 and glucose values when compared to temperature trends or demographic characteristics. However, eight infants had

either a persistent metabolic acidosis, improving metabolic acidosis, or a compensated metabolic acidosis generalized from the few pH values collected. Only one infant had a stable pH throughout the study period. Previous research indicated that low body temperatures in neonates during the first few hours of life are associated with metabolic acidosis (Gandy et al., 1964). Because most infants (7 of 10) had low mean abdominal temperatures ($\leq 36.4^{\circ}$ C) and were acidotic, there may be an association with metabolic acidosis and low temperature. Additionally, these study infants appeared to lack the ability to exhibit peripheral vasoconstriction, therefore they could not conserve central heat which may have led to persistent attempts at nonshivering thermogenesis. This inability to generate heat most likely leads to an acidotic condition because of tissue impairment from increased oxygen needs and the build up of lactic acid (Seri, 1998). However, the study was not designed to evaluate acid base balance statistically and results are purely exploratory. A future study should examine blood gas results in relationship to temperature in ELBW infants if the ability exists to collect pH and base deficit data continuously so that statistical analyses can be performed.

In addition, the picture is complicated by the clinical instability of a newly born ELBW infant who often exhibits hypotension, hypovolemia, and hypothermia because of stressful stabilization procedures and lack of fluid infusions until umbilical lines can be placed. All of these conditions also may lead to metabolic acidosis. Future research should examine continuous pH readings in relationship to infant temperature as monitoring equipment becomes available to measure internal arterial blood pH continuously because knowing exactly what the blood pH is doing (increasing or decreasing) in relationship to the increases or decreases of temperature is important. Making assumptions from sporadic pH values in

association with continuous abdominal and peripheral temperature measurements is not possible.

Blood glucose values were recorded to give direction for future research in relationship to temperature in ELBW infant because hypothermia is associated with hypoglycemia (Cowett, 1985). However, the sporadic measures of glucose did not seem to be associated specifically with the trends in temperature. Few measures of blood glucose were obtained in this study and they varied in association with glucose infusions, stress to the infant, acidosis and temperature. Identifying useful information from the glucose values was not possible because of the many factors causing them to fluctuate. Perhaps continuous measurement of blood glucose would be more helpful to determine the relationship of blood glucose to temperature in ELBW infants when the technology becomes available for ELBW infants, especially in the first few hours of stabilization before glucose infusions are adequate. No research studies have used continuous blood glucose measurements and any future research attempting to associate glucose to abdominal temperature would need to consider the effects of glucose infusion to the ELBW infant and use continuous glucose and abdominal temperature measurement.

Study results also indicated that ELBW infant's abdominal temperature should be kept higher than 36.4˚ C. Previous research is not specific as to the point at which normal temperature ends and hypothermia begins in the neonates. The American Academy of Pediatrics specified hypothermia for neonates as 36.4° C in their 1988 guidelines (American Academy of Pediatrics, 1988). Researchers have defined hypothermic cut points to evaluate interventions to reduce hypothermia as 35.0°C (Costeloe et al., 2000), 35.5° C (Thomas, 2003), 35.6° C (Bredemeyer, Reid, & Wallace, 2005), and 36.4° C (Knobel, Wimmer, &

Hobert, 2005;). Thus, there is no clear definition of the hypothermic limit in ELBW infants.

We used the Academy of Pediatrics traditional hypothermia cut point of 36.4˚ C and found that 6 of 10 infants had normal heart rate observations when abdominal temperature was greater than 36.4˚ C. Six of ten infants had a significant correlation between the degree the abdominal temperature was below 36.4˚ C and the extent of the heart rate was above or below the normal range. Nine of ten infants had a significant relationship between the abdominal-peripheral temperature difference and whether temperature was above or below the 36.4˚ C cut point. Seven of ten infants had a significant correlation between the abdominal-peripheral temperature difference and the extent of abdominal temperature decreased below 36.4˚ C. Therefore, a cut point of at least 36.4° should define hypothermia for the ELBW infant. However the cut point may need to be even higher.

Abdominal temperature clearly needs to be kept above 36.4˚ C to minimize heart rate abnormality and decrease the abdominal-peripheral temperature difference. This study found that when abdominal temperature was greater than 36.4˚ C, heart rate was more apt to be in the normal range. The abdominal-peripheral temperature difference was also smaller when the abdominal temperature was greater than 36.4˚ C. In 8 of 10 infants, the abdominal-peripheral temperature difference was larger when abdominal temperature was below 36.4˚ C than when the abdominal temperature was above 36.4˚ C.

However, this traditional cut point of hypothermia may not be enough to minimize abnormalities in physiological variables. This study found the optimal abdominal temperature to minimize abnormal heart rates and maximize normal heart rates in ELBW infants was between 36.8˚ and 37˚ C. Based on early research with infants approximately 29 weeks gestation (Sauer, Dane, & Visser, 1984), current standard of care is that servo control

for abdominal temperature in ELBW infants be set at 36.5º C. However, I believe the range should be increased to 36.8º-37º C. In the current study, heart rate increased above each infant's 75th percentile when abdominal temperature decreased to between 34.4˚-36.4˚ C range and heart rate decreased below the 25th percentile when abdominal temperature decreased lower than approximately 34.4˚ C.

Keeping the heart rate of an ELBW infant in a normal range is important to maintain cardiac output and minimize states of increased or low cardiac output (Guyton, 1971). Many infants did not reach the normal heart rate range until the end of their study period. The first several hours was associated with low abdominal temperatures, and many heart rate fluctuations from normal. Because these study results point towards the need to maintain ELBW infants at a higher abdominal temperature, future research should examine the effects of setting the incubator control temperature to achieve an abdominal temperature between 36.8˚ and 37˚ C. This study could be repeated while randomizing infants into abdominal temperature control groups of 36.8°, 36.9° and 37.0° C to evaluate heart rate and abdominal-temperature difference with these groups.

Limitations of the Study

Because this study had an exploratory design and a sample limited to 10 ELBW infants, it had several limitations. The results of this study should be generalized only with caution beyond this sample because the study took place in one particular NICU with their nurses and attending physicians determining the care for each ELBW infant. Additionally, this small sample did not include a large number of gender, weight, gestation and ethnic combinations. The methods of this study were exploratory and therefore the study will need to be replicated with a larger population of ELBW infants to compare heart rate to abdominal

and peripheral temperature and examine the abdominal-peripheral temperature difference in relationship to clinical events and mortality. Because the sample was held at 10, I was not able to determine the effects of demographic variations in birth weight and gestation for the ELBW infant population. Therefore, a future study could sample a more discrete weight stratification, such as infants falling into 100 gram weight classes between 500 grams and 1000 grams. In this study the smaller infants (500-800) which corresponded with 24-25 weeks gestation, exhibited little if any vasomotor control. Larger infants (800-1000), corresponding to 26 weeks gestation, showed some vasomotor control by attempts at peripheral vasoconstriction. However, this finding is speculation because there were only two infants in the more mature gestation and larger weight division. Therefore, conducting a study with 100 gram weight divisions for analyses using many more subjects would yield valuable information about the minimum size at which infants are able to exhibit peripheral vasoconstriction. Weight is used to roughly correlate with gestational age, however neither measure is absolute. Gestational age estimates can be slightly off by 1-2 weeks according to obstetrical ultrasound or maternal dates. Exact weights do not correlate to gestational age, but by using weight classes and gestational age estimation, extent of prematurity can be approximated. Additionally, a future, larger study will be able to sample many infants in each gestational age class separated by one week differences between 23 and 29 weeks gestational age because the poor vasomotor control may be associated with gestational age as well as chronological age (Lyon et al., 1997). Chronological effects were suggested by Lyon et al. (1997) as the difference between peripheral and abdominal temperatures decreased by 5 days of age.

Using temperature probes on the skin of ELBW infants also led to limitations. Because I

was unable to touch the infant periodically, ascertaining if the temperature probe was adhering to the abdominal skin closely was difficult. The skin probe was covered by a reflective cover. However, the skin of the more premature, newly born ELBW infants is usually gelatinous and thin. Adhesive material does not adhere very well to this skin. Additionally, humidity was added to the incubators for ELBW infants. Because the skin was wet from the humidity, adhesive did not stay on the skin. Occasionally, skin probes lifted off the skin and may have registered air temperature instead of skin temperature. Air temperature was usually at maximum output capability of the incubator with temperatures as high as 39.5˚ C. The peripheral temperature probe did not have problems with the adhesive because the probe was secured with a strip of adhesive duoderm material which was wrapped around the foot and on top of the probe.

A further limitation was measuring oxygenation by the proxy measures of oxygen saturation. This method has not been used in a previous research study and was exploratory. Since oxygen consumption can not be measured in active ELBW infants that are intubated due to low tidal volumes (Gomella, 1994), the methods of this study were limited to using this proxy for oxygenation or oxygen consumption.

Despite these limitations, this study gave valuable information that could be used to design a future, larger study. Heart rate was a good indicator of abdominal temperature; however oxygen saturation should not be used in a future study as this measure was not a good indicator of abdominal temperature. Measuring the abdominal-peripheral temperature difference was valuable and a future study would measure this variable for at least 24 hours, or possibly for 5 days as in the Lyons et al (1997) study, to examine the developmental aspects related to the abdominal-peripheral temperature difference. Perhaps the ability to

exhibit vasomotor control develops as the infant ages over the first few days of life.

Clinical Research in the NICU

Clinical research in the NICU is difficult and has limitations because of the inherit instability of NICU patients. Newly born ELBW infants have many clinical conditions such as respiratory distress syndrome, hypotension, potential for hypovolemia, potential for sepsis from maternal infection, and circulatory and respiratory instability from the transition from fetus to neonate which may confound any physiological variables measured in these infants. In addition, necessary nursing and medical procedures contribute to the instability of the infants' physiologic condition. Any future studies should control as many aspects of the subjects' environment as possible by having a detailed study plan and record any extraneous variables on the data collection sheet that may confound results during analyses (Thomas, 1992). Controlling environmental conditions during clinical research in the NICU is nearly impossible; therefore within subject designs are beneficial because usually the environment is the same for a patient through the study course (Thomas, 1986).

A researcher is an outsider when doing research in the NICU and data collection is always second to the welfare and stability of the infant. Therefore, checking data collection on a subject may be limited in frequency to insure stability of the infant. Data collection monitoring devices also can malfunction due to nursing interference and probes can become unattached. The incubator environment can become altered introducing systematic error into your data collection (Thomas, 1986). Future studies should consider all of these factors a priori with a detailed study plan and a pilot study to check the every aspect of the study plan because this was helpful in my study.

Recommendations for practice

Previous researchers (Costeloe et al., 2000; Horns, 2002; Lyon et al., 1997) have found that ELBW infants exhibited extremely low temperatures during the first few hours of life due to stabilization in the NICU, and this current study confirms that this problem still exists. Thus all nursing and medical care providers need to be cognizant of the ELBW infants' inability to generate heat when exposed to cold environmental temperatures and the propensity of those infants to have abdominal temperatures that decrease to extremely low temperatures during stabilization procedures. We found that many times care was not clustered; one infant was suctioned nine different times in the 12-hour study period along with many other medical and nursing procedures. Providers should take precautions to augment the environmental air to provide warmth during stabilization procedures and attempt to adhere to a minimal stimulation policy for at least the first 12 hours of life. By observing an infant over the 12-hour study period, I noted that routine interventions to augment heat such as keeping porthole covers over portholes, providing humidity as soon as possible to the infant, minimizing time the incubator is open were many times delayed for the entire 12-hour study period. Additionally, most infants had very low abdominal temperatures while umbilical lines were being inserted and this procedure took up to 2 hours. Therefore, I recommend augmenting the environment around the ELBW infant during umibilical line insertion with heat lamps or a warming gel mattress. Providers should also expedite stabilization procedures to minimize exposure to cold environmental temperatures by placing lines as quickly as possible. Abdominal temperature should be controlled minimally at 36.5˚C and results of the current study suggest the control point should be increased to between 36.8° and 37° C. Because abdominal temperature was seen to decrease in

association with fluid infusion through the umbilical catheter, nurses may want to warm intravenous infusions prior to infusing through the umbilical venous or arterial catheters during the first 12 hours of life. This could be achieved by keeping syringes or bags of fluid for a new ELBW infant in the incubator while the incubator is being prewarmed for that infant.

These study results confirm the results of Lyon et al. (1997), which suggested continuous monitoring of the peripheral and abdominal temperature to give valuable clinical information to the healthcare providers as to the stability of the infant. When there is an increased difference between the abdominal and peripheral temperatures, providers should seek the etiology of stress to the infant at that time and attempt to minimize the environmental stressors. Because the first 12 hours of life are a stressful time for ELBW infants and caregiver handling should be kept to a minimum. Stimulation to these infants increases heart rate and abdominal-peripheral temperature difference which indicates stress to the infant.

Directions for Future Research

This study should be replicated with a larger sample population of ELBW infants. Each infant needs to be followed through 5 days of life for data collection and mortality outcomes for these infants through hospitalization should be determined. The first 12 hours are a time of instability, therefore at least an additional 12 hours of data collection would allow the infant to become stable and normalize physiological variables. The additional 4 days would allow for chronological effects to be determined. Some infants in this current study did not become warm until the last 1-2 hours of the study period. Therefore, at least an additional 12-hours of data collection would examine ELBW infants during a time of normalization and warmth. Collecting data over 5 days will give valuable information as to the development of

vasomotor control in infants weighing 500-700 grams. Analyses should be done to correlate the peripheral-abdominal temperature difference with clinical events and mortality in order to investigate the phenomenon of the peripheral temperature being higher than the abdominal temperature further.

In addition, salivary cortisol levels (Morelius, Nelson, & Theodorsson, 2006) should be collected at time periods throughout the study period as cortisol levels increase in association with stressful events (Heckmann, Wudy, Haack & Pohlandt, 1999). Salivary cortisol would be a noninvasive technique to collect cortisol measurements in that a specimen is obtained using a toothpick sized swab which is placed inside the infant's mouth which quickly absorbs saliva for cortisol measurement. By showing an increase in cortisol levels associated with procedures, we can validate stress to the infant during nursing and medical procedures associated with an increase in abdominal-peripheral temperature difference. The increased difference between peripheral and abdominal temperatures may be related to stress instead of exposure to cold environmental air during stressful caregiver procedures.

As technology allows the collection of continuous arterial blood pH levels, pO_2 levels, and continuous blood glucose levels, these variables should be used to validate the physiologic process in response to the ELBW infants' inability to adequately initiate nonshivering thermogenesis. A monitor, Trendcare Neotrend Monitor, on the market prior to the initiation of this study, could measure these variables through a transducer at the end of the umbilical arterial catheter. This monitor was taken off the market because of financial difficulties in production of the monitor and the technology is no longer available. If this technology becomes available again, the variables should be included in a replication of this study. Analyses of continuous variables (pH levels, pO_2 levels, blood glucose values) in relationship

to continuous temperature measurements would be more statistically valid than using continuous temperature measurements and sporadic pH levels, pO_2 levels, and blood glucose levels. Because data points become the "subjects" in a within subject design, an approximately equal number of observations of the variables need to be analyzed, as in this study with 720 observations of abdominal temperature. In order to conduct a *t*-test between abdominal temperature and pH, approximately equal number of pH values compared to abdominal temperature values need to be available. In this study, we were unable to analyze pH levels, pO_2 levels, or blood glucose levels against temperature observational data because there were not enough observations of these variables.

Another future study could examine the effect of warming intravenous fluids on abdominal and peripheral temperatures during the first 12 hours of life. Using cold intravenous fluids is the standard of care in most NICUs including the NICU in which this study was conducted. If the intravenous fluids are prewarmed and kept warm, the constant warm infusion could keep the infant warm centrally and decrease the incidence of low abdominal temperatures such as was seen in this current study. This simple nursing intervention may decrease morbidity and mortality due to an overall increase in abdominal temperature and decrease in abdominal-peripheral temperature difference.

Because morbidity and mortality are high in ELBW infants, especially infants weighing 400-700 grams, further research should examine the relationship of cerebral perfusion to low abdominal temperature and poor vasomotor control. Intraventricular hemorrhage is a possibility in the first week of life for these extremely premature infants (Gardner, 2005) and poor vasomotor control may possibly be linked to an increased incidence of intraventricular hemorrhage. Preterm infants have difficulty in autoregulating their cerebral blood flow and

changes in venous and arterial blood flow can translate into increased cerebral blood pressure resulting in rupture of vessels in the brain and hemorrhage (Goddard-Finegold. & Mizrahi, 1987). A new technology called NIR spectroscopy (Bozkurt et al., 2005) can measure cerebral oxygen saturation and could identify decreased oxygenation to the brain in these infants during the first 12 hours of life. Poor vasomotor control exemplified by an increased peripheral-abdominal temperature difference may be linked to the inability of the ELBW infant to protect the brain from stressful clinical events. Therefore, measuring oxygenation to the brain during the stabilization period for these infants, especially in relationship to low abdominal temperature and abdominal-peripheral temperature difference measures should yield valuable information towards decreasing morbidity.

Appendix I: Study Consent Document

CONSENT DOCUMENT

Small Baby Temperature Study

Title of Research Study: **Physiological Effects of Thermoregulation in Transitional Extremely Low Birth Weight Infants (Small Baby Temperature Study)**
Principal Investigator: Robin B. Knobel, Neonatal Nurse Practitioner
Institution: University of North Carolina at Chapel Hill, School of Nursing and Pitt County Memorial Hospital, Neonatal Nurse Practitioner Dept.
Address:2100 Stantonsburg Rd, Greenville, NC 27834
Telephone #: 252-847-4378

This consent document may contain words that you do not understand. You should ask the study **nurse** to explain any words or information in this consent form that you do not understand.

INTRODUCTION

You have been asked to allow your baby to take part in a research study being conducted by Robin Knobel. This research study will include 10 premature babies weighing less than 2 lbs, 2 ounces who will be watched their first 12 hours of life in the neonatal intensive care unit (NICU). Mothers in labor or fathers with a premature baby expected to be born 12 or more weeks early at Pitt County Memorial Hospital will be asked for permission to include their babies in this study. The baby's temperature, **amount of oxygen in the blood**, blood gases **(blood tested for oxygen and acid)**, blood **sugar**, and heart rate will be studied to help us learn how to best keep premature babies warm. Premature babies weighing under 2 pounds get cold very easily during and shortly after birth in the delivery room and NICU. Previous studies do not tell nurses and doctors exactly how warm these tiny babies need to be. This study will give information that will help us understand what is the best body temperature for these tiny babies during the first 12 hours of life.

PLAN AND PROCEDURES

This study will **study** 10 premature babies, one at a time, from admission to the NICU until 12 hours of age. If your baby is born at least 12 weeks early and weighs less than 1000 grams at birth (2 pounds, 2 ounces), then your baby can be enrolled in this study. Once your baby is placed on a special bed that keeps the baby warm (incubator) in the NICU, the doctors and nurses will begin routine care for your baby as normal. One extra monitor (temperature measuring tool) will be used to measure your baby's foot and stomach temperature. This temperature measuring tool will use two temperature wires to

measure temperature, which will each be placed next to the normal monitor wires on your baby (one on the foot and one next to the incubator wire on the stomach). Nurses and doctors normally measure the amount of oxygen in your baby's blood with a monitor and your baby's heart rate and blood pressure with a separate monitor. These monitor readings (your baby's blood oxygen amount, heart rate and blood pressure) will be recorded from the normal monitors into a laptop computer specifically for this study. The temperature from the stomach and foot will also be recorded into the laptop computer. Your baby will need blood gases (blood tested for oxygen and acid) and blood sugars (blood tested for blood sugar content) as part of his/her normal care, which your baby's doctor or nurse practitioner will order. If your baby has any blood gas results or blood sugar results available during this study, then those results will be recorded into the laptop computer to compare to your baby's temperature. The principal investigator or one of two research assistants will sit at your baby's bedside in the NICU to run the laptop computer and record any time that your baby is touched. They will also record how much oxygen is being given to your baby if your baby is on a ventilator (breathing machine). After the 12 hours of data collection is complete, the extra temperature wires will be removed from your baby's foot and stomach and the temperature monitor removed from your baby's bedside. The principal investigator or research assistant will read your baby's medical chart and record your birth history and your baby's medical history for those first 12 hours on the study data collection sheet. All data will only be identified with a study number assigned to your baby. No names will be used with the study data. Once the 12 hours of data collection is complete and medical history recorded, your baby's participation in this study is finished.

POTENTIAL RISKS AND DISCOMFORTS

It is extremely unlikely that this study could cause any additional risk to your baby above the normal risks for very small babies admitted into an NICU. There is no additional risk to using the study monitor (temperature measuring tool). The wires for the temperature measuring tool will be attached next to the existing skin temperature wire and wire used to read amount of oxygen in the blood which are being applied by the nurses to your baby for usual monitoring while in the NICU. No additional tape is needed on your baby's skin because of using the existing special tape which holds the temperature wire on the skin.

POTENTIAL RELATED RISKS TO SUBJECT

Your baby will have a research assistant, study monitor (temperature measuring tool) and laptop computer next to his/her bed. There is a potential breach of confidentiality in that others in the NICU will know that your baby is participating in a research study because of the extra monitor (temperature measuring tool) and laptop computer. Medical personnel will be able to view the study data while its being collected because they need this data to care for your baby.

POTENTIAL BENEFITS

The study monitor (temperature measuring tool), will offer medical staff two extra temperatures for your baby during the 12 hours of study time to help with the medical care of your baby. This study will also address many unanswered questions about the best body temperature for very small premature babies based on usual monitoring of heart rate, blood oxygen content, blood sugar content and blood acid content. Information from this study will help doctors and nurses determine the best body temperature range for these tiny babies during the first 12 hours of life.

ALTERNATIVE COURSES OF TREATMENT

If you choose not to have your baby take part in this study, he/she will receive normal care in the NICU without the extra study monitor (temperature measuring tool).

SUBJECT PRIVACY AND CONFIDENTIALITY OF RECORDS

To reduce the risk of breach of confidentiality, each enrolled baby will be assigned a study number and all data will be written down with the study number instead of the baby's name. Data collection sheets will use the study number. Downloaded computerized information from the monitors will also be identified with the study number. Only the principal investigator, Robin Knobel, or the research assistants, Carla Ahearn or Betty Nielsen, will have access to the consent forms or study data. The notebook of consent forms and the laptop computer (when not in use at the study bedside) will be locked in Ms. Knobel's locker in the neonatal nurse practitioner's office at Pitt County Memorial Hospital. No individual baby names will be identified in any report or publication about this study. Although every effort will be taken to keep research records private, there may be times when federal or state law requires the disclosure of such records, including the personal information. This is very unlikely, but if disclosure is required, UNC-CH will take all steps allowable by law to protect the privacy of information.

TERMINATION OF PARTICIPATION

Participation in the study will be ended once 12 hours of monitor data are collected (from admission to the NICU to 12 hours of life) and after data is recorded from the medical chart at the end of the 12 hours.

COSTS OF PARTICIPATION

There is no cost to participating in this study.

COMPENSATION AND TREATMENT FOR INJURY

The policies of East Carolina University and/or Pitt County Memorial Hospital and/or University of North Carolina, Chapel Hill do not provide for payment or medical care for research participants because of physical or other injury that result from this research study. Every effort will be made to make the facilities of the School of Medicine and Pitt County Memorial Hospital available for care in the event of injury. You do not give up any legal rights for your baby as a research participant by signing this consent form.

VOLUNTARY PARTICIPATION

Participating in this study is voluntary. If you decide that your baby should not to be in this study after it has already started, you may stop at any time without losing benefits that your baby should normally receive. You may stop your baby's participation at any time you choose without penalty, loss of benefits, or without a causing a problem with your baby's medical care at this institution.

PERSONS TO CONTACT WITH QUESTIONS

The investigators will be available to answer any questions concerning this research, now or in the future. You may contact the investigator, Robin Knobel (principal investigator) at phone numbers 252-847-4378 (days, nights and weekends). If you have questions about your baby's rights as a research subject, you may call the Chair of the University and Medical Center Institutional Review Board at phone number 252-744-2914 (days) and/or the hospital Risk Management Office at 252-847-4584. I understand the study has also been approved by the UNC-Chapel Hill Nursing Institutional Review Board. I may contact this committee at (919) 966-3113 or by email to IRB_subjects@unc.edu any time during this study if I have any questions about my baby's right as a subject in this study.

CONSENT TO PARTICIPATE

I have read all of the above information, asked questions and have received satisfactory answers in areas I did not understand. (A copy of this signed and dated consent form will be given to the person signing this form as the parent authorizing their baby's participation.) The consent form will be maintained for 5 years at the University of North Carolina, Chapel Hill, School of Nursing.

_____ _____

Parent's Name **(PRINT)** **Signature** **Date** **Time**

_____ _____

Guardian's Name **(PRINT)** **Signature** **Date** **Time**

WITNESS: I confirm that the contents of this consent document were orally presented, the parent or guardian indicates all questions have been answered to his or her satisfaction, and the parent or guardian has signed the document.

_____

Witness's Name **(PRINT)** **Signature** **Date**

PERSON ADMINISTERING CONSENT: I have conducted the consent process and orally reviewed the contents of the consent document. I believe the parent understands the research.

_____

Person Obtaining consent **(PRINT)** **Signature** **Date**

_____

Principal Investigator's **(PRINT)** **Signature** **Date**

 Parent's Signature_____ Initials_____

Appendix II: Demographic Data Document

Physiological Effects of Thermoregulation in Transitional ELBW Infants
(PETTE Study)

Study Number _____ DOB _____ Time of Birth _____
Race: White / African American Birth Weight _____ Time of Admission_____
Gestational Age _____ Gender: Male / Female
APGAR Score: _____1 min., _____5 min., _____10 min.
Delivery Mode: vaginal/ c-sect
Resuscitation: ETT: yes / no Epi: yes / no Chest Compressions: yes /no
Placement in Bag: yes / no Time of bag removal: _____

Maternal History:

PNC: yes / no EDC: _____ Singleton / Twin / Triplet
Rubella immune: yes / no Serology: neg / pos Hep B: neg / pos HIV: yes / no / NA
Steroids: yes / no Chorioamnionitis: yes / no Antibiotics: yes / no Maternal temp prior to del: ____
Tocolysis: $MgSO_4$ yes / no other: _____

Disease History in first 12 hours:

RDS: yes / no PDA: yes / no Hypotension: fluid bolus / Inotropic Medications / Hydrocortisone
Antibiotics: Ampicillin / Gentamicin / Cefotaxime

Procedures During first 12 hours and time

_____ ETT	_____ Chest tube	_____ Foley Catheter
_____ UAC	_____ CUS	_____ Needle Aspiration
_____ UVC	_____ PIV	_____ _____
_____ Art line	_____ PICC	_____ _____

CBC: time: _____ WBC _____ Neut %_____ Bands % _____ Plts _____ Hct % _____

Giraffe Isolette: Time of placement on warmer: _____ Manual temp set: _____
Servo temp set: _____ time _____
Servo temp set: _____ time _____
Servo temp set: _____ time _____
Servo temp set: _____ time _____
Time top down on isolette _____Researcher 1:_____time _____
Researcher 2:_____time_____
Anectodal Notes During 12 hours:

_____
_____

Study#

Appendix III: Observer Data Collection Document

Date:
Admit time:

Time	ISC	Air temp	Vent temp	FiO2	pH	BE	pO2	gas sat	humidity	C/S	stimulation	notes
0:01												
0:02												
0:03												
0:04												
0:05												
0:06												
0:07												
0:08												
0:09												
0:10												
0:11												
0:12												
0:13												
0:14												
0:15												
0:16												
0:17												
0:18												
0:19												
0:20												
0:21												
0:22												
0:23												
0:24												
0:25												

Appendix IV: Primary Variable Data for Study Infants

Baby #	Mean	Std Dev	Min	Max
170	36.68	0.713	33.85	37.87
240	36.05	1.245	31.09	37.01
311	35.51	2.030	28.96	38.14
360	36.23	0.935	32.70	38.19
410	35.28	0.993	32.49	37.92
450	35.17	1.333	32.18	37.23
510	35.79	0.878	31.61	38.25
590	36.44	1.167	32.80	37.92
680	35.61	1.304	31.24	36.91
730	36.60	0.343	33.95	37.28

Abdominal temperature (AbT)

Baby #	Mean	Std Dev	Min	Max
170	37.10	0.907	35.12	39.61
240	36.49	0.688	33.55	37.19
311	37.06	1.00	32.13	38.35
360	35.73	1.302	32.91	38.41
410	36.36	0.957	32.91	37.82
450	35.10	0.986	33.17	36.80
510	36.71	0.907	29.44	37.78
590	36.75	0.953	33.17	38.14
680	36.32	1.287	32.96	37.44
730	35.50	0.488	33.53	36.91

Peripheral foot temperature (FT)

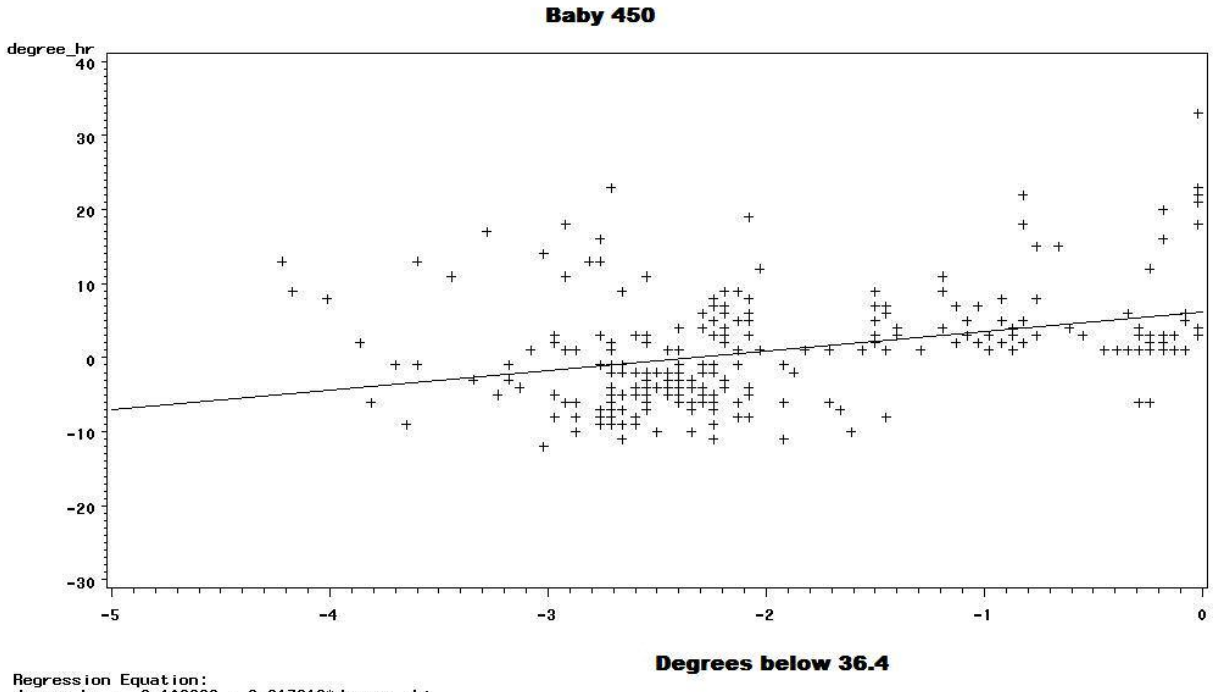
Baby #	Mean	Std Dev	Min	Max
170	139.38	7.533	124	188
240	165.47	13.463	123	194
311	127.54	9.32	104	164
360	161.95	9.294	113	194
410	166.12	10.79	133	192
450	139.38	7.903	106	176
510	141.97	9.480	108	174
590	144.04	7.045	125	164
680	129.10	9.616	106	165
730	140.57	9.652	76	174

Heart Rate (HR)

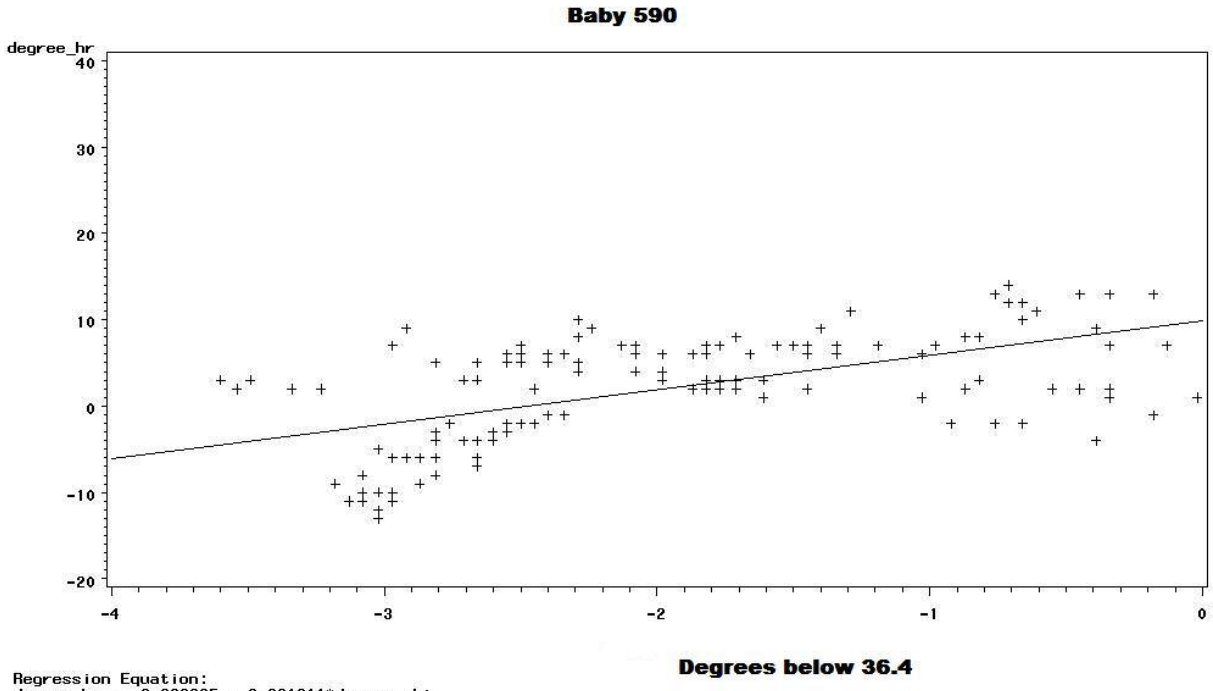
Baby #	Mean	Std Dev	Min	Max
170	93.57	4.364	63	100
240	92.04	3.719	76	100
311	96.42	2.39	80	100
360	93.42	4.250	64	100
410	94.00	4.438	65	100
450	93.79	2.726	74	100
510	94.34	5.563	47	100
590	94.17	3.331	69	100
680	94.53	2.433	72	100
730	91.26	4.403	51	100

Oxygen Saturation (SAT)

Appendix V: Scatterplots of infants with heart rates below normal limit associated with temperatures less than approximately 34.5°C

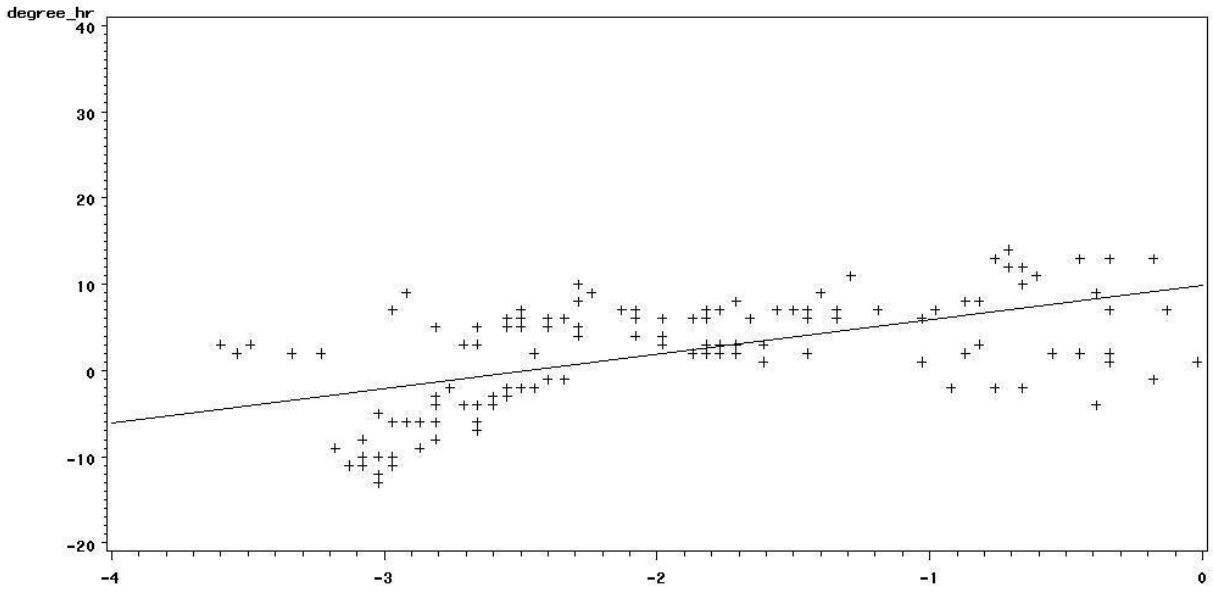


Regression Equation:
degree hr = 6.106693 + 2.617919*degree abt



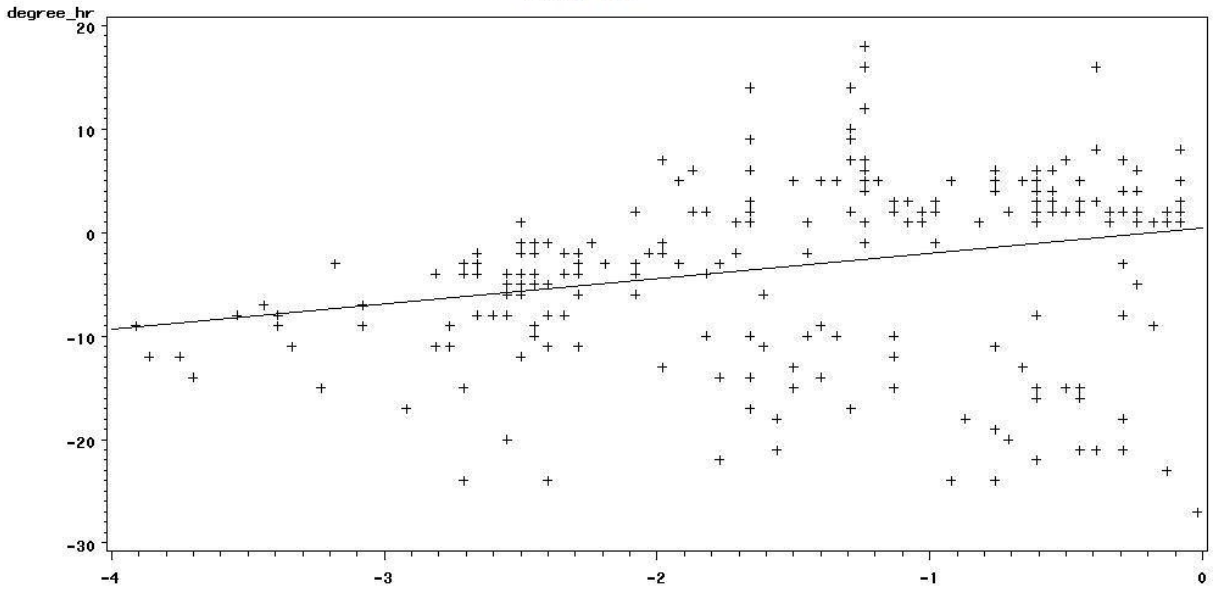
Regression Equation:
degree hr = 9.823665 + 3.981911*degree abt

Baby 590



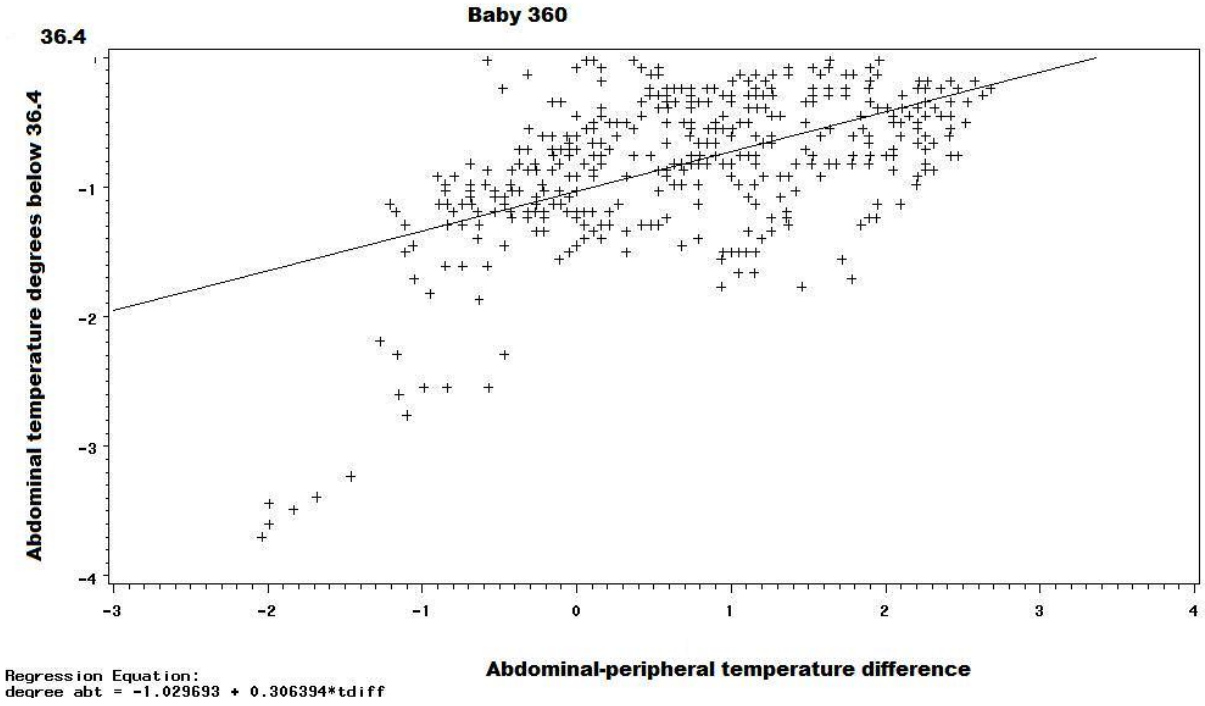
Regression Equation:
degree_hr = 9.823665 + 3.981911*degree_abt

Baby 410

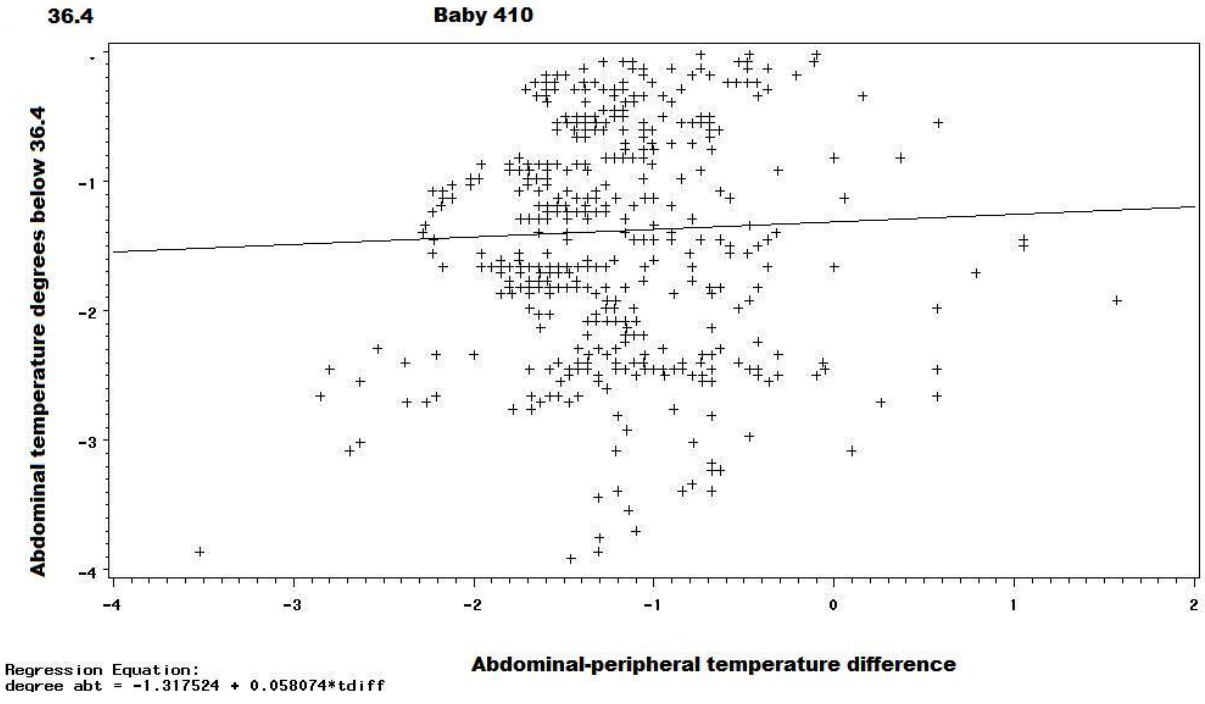


Regression Equation:
degree_hr = 0.446102 + 2.45676*degree_abt

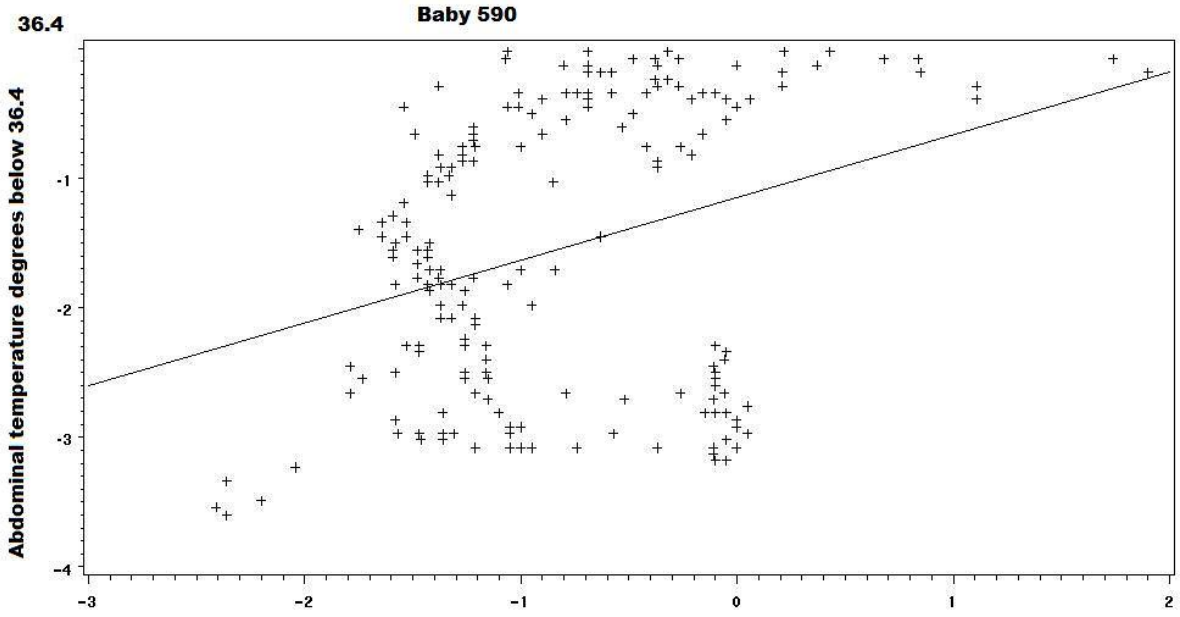
Appendix VI: Scatterplots of infants' difference between abdominal and peripheral temperatures when abdominal temperature < 36.4°C



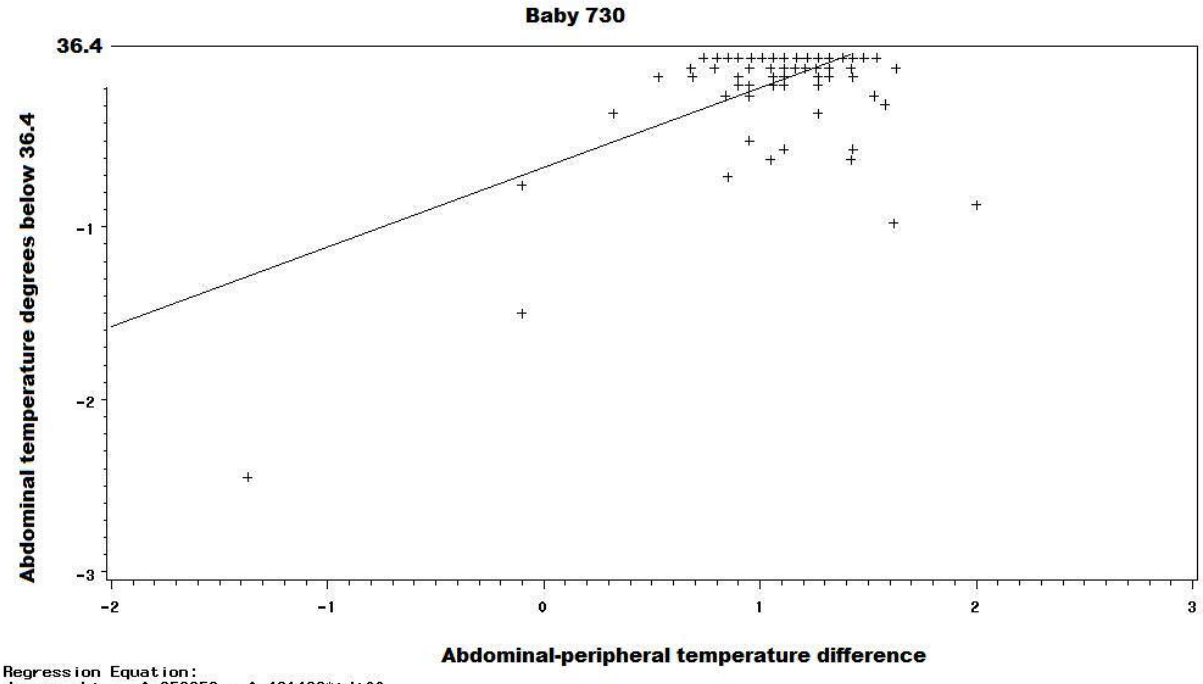
Regression Equation:
degree abt = -1.029693 + 0.306394*tdiff



Regression Equation:
degree abt = -1.317524 + 0.058074*tdiff



Regression Equation:
degree abt = -1.149815 + 0.482832*tdiff



Regression Equation:
degree abt = -0.653853 + 0.461469*tdiff

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