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Neonatal temperature homeostasis and obstetric anesthesia

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NEONATAL TEMPERATURE HOMEOSTASIS AND OBSTETRIC ANESTHESIA

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March 1, 1983
(Date)

NEONATAL TEMPERATURE HOMEOSTASIS

AND

OBSTETRIC ANESTHESIA

A Thesis Submitted to
Yale University School of Medicine
In Partial Fulfillment of the
Requirements for the Degree of
Doctor of Medicine

by

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To my mother,
Maria Guadalupe Lomeli
and
My wife, Ann

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ABSTRACT

The complete hospital records of 97 neonates and their respective mothers were studied to determine the relationship between the ability of neonates to maintain their body temperatures and the antecedent maternal obstetric anesthesia technique. Neonates were dividied into three groups: (1) a control group (N = 30) whose mothers received no anesthesia and had normal spontaneous deliveries (NSD); (2) neonates (N = 31) whose mothers received local infiltration (lidocaine 1%) of the perineum for delivery (LA); and (3) neonates (N = 36) whose mothers received lumbar peridural anesthesia (bupivacaine 0.5%) for labor and delivery (PD). Neonates were further categorized on the basis of parenteral administration of narcotic analgesics during labor, alphaprodine having been administered to 11 mothers (36%) in the NSD group, 11 (35%) in the LA group, and 20 (55%) in the PD group. Recorded data included serial neonatal temperature (rectal) determinations during the first 24 hours of life. For each of the three groups, temperature values were grouped in terms of "time intervals" by dividing the 24 hours into 6 aliquots of 4 hours each and obtaining the mean temperature during that time interval. The first 4 hours following delivery were associated with PD neonatal temperatures that were significantly ($P < 0.05$) higher than those of the corresponding NA and LA neonates. While alphaprodine administration did not affect NSD and LA neonatal temperatures, PD group mothers receiving alphaprodine had neonates whose temperatures were significantly ($P < 0.05$) higher than those of PD neonates whose mothers did not received alphaprodine. Finally, PD mothers had significantly ($P < 0.05$) higher temperatures at the time of delivery than did NSD and LA mothers. These

findings suggest that: (1) immediate postpartum neonatal body temperatures are closely related to the antecedant maternal obstetric anesthesia technique; (2) neonates whose mothers received effective and sustained analgesia (peridural group) experience the least decrease in body temperatures; and (3) early neonatal temperatures may reflect maternal temperatures at birth.

CHAPTER I

INTRODUCTION

Obstetric Anesthesia and Neonatal Thermoregulation

A relationship between obstetric anesthesia and neonatal well-being was first suspected in 1853 when John Snow, Queen Victoria's physician, noted that chloroform appeared to blunt the usual lively behavior of newborn babies (Snow, 1853). Indeed, during the past twenty years, studies have identified the effects of obstetric anesthetic medications on uterine activity, uterine and placental blood flow, maternal and fetal acid-base status, fetal heart rate variability, neonatal respiration and muscular tone, and newborn neurobehavior (Brazelton, 1961; McDonald et al., 1974; Ralston and Shnider, 1978; Yurth, 1982; and Fishburne, 1982).

Decreased neonatal temperatures have been associated with markedly lower survival rates, metabolic acidosis, hypoglycemia, and, in animal studies, may result in profound temporary or permanent developmental deficits (Budin, 1907; Cross et al., 1958; and Klaus et al., 1979). Neonatal temperature regulation is influenced by the sympatho-adrenal system, with catecholamines (CAT) being largely responsible for neonatal brown fat thermogenesis and the shivering reflex. Attempts have been

made to correlate neonatal levels of epinephrine (E) and norepinephrine (NE) with maternal anesthesia (Lagercrantz et al., 1981; and Irestedt et al., 1982). However, studies relating to the effects of obstetric anesthesia on newborn temperature homeostasis are scanty.

Schwartz et al. (1978) remarked that heat loss from the body surface is minimal in the fetus. Heat exchange with the external environment is largely dependent on the placental circulation, which allows the fetus to be in thermal equilibrium with the mother. Experimentally, Abrams et al. (1970) have demonstrated that umbilical artery blood temperature is $0.3^{o}C$ higher than that of the umbilical vein, objective evidence that the fetus transfers heat to the mother via the placenta. Data from various researchers (Wood and Beard, 1964; Adamsons and Towell, 1965; Mann, 1968; Walker and Wood, 1970) have shown that during labor and just prior to delivery, the human fetal temperature is usually about $0.5^{o}C$ above maternal temperature. Further animal studies have revealed that changes in maternal core tempertures are accompanied by parallel changes in fetal temperatures (Assali and Westin, 1962; Abrams et al., 1969; and Morishima et al., 1975).

Neonatal Thermoregulation and Nonshivering Thermogenesis

Heat production by the newborn is mediated by the sympatho-adrenal system and produced largely by nonshivering mechanisms. When delivered, the newborn is out of its protective environment and is faced with a thermal stress, which must be adapted to in order to survive. Because of its small size and relatively high surface area to mass ratio, newborns have an expected heat loss that is about three times that of an adult per

unit body weight (Brück, 1961). Reduced skin thickness and decreased subcutaneous body fat in the neonate also contribute to its inability to conserve heat (Swyer, 1978). Accordingly, unlike the adult, the newborn's temperature fluctuates over a wide range as a function of its environment.

In addition to the tendency to lose heat, the variations in temperature during the first few days of life are also thought to be due to an inefficiency in the effector system when the neonate attempts to thermoregulate (Hensel et al., 1973). In response to heat loss to the environment, the newborn must increase heat production (Brück, 1961; and Hey, 1974) and endogenous warming appears to be accomplished largely by nonshivering thermogenesis.

Most of the work regarding nonshivering thermogenesis and its association with brown adipose tissue has been done in animals and its importance to the human neonate is indirect (Jansky, 1973). Nonshivering thermogenesis is a heat-producing mechanism that liberates chemical energy through metabolism, and does not involve muscular contractions as does shivering. It is believed by many researchers that this metabolic response to cold is mediated by the sympathetic nervous system (Cottle, 1970; and Hardman and Hull, 1970). The release of NE into brown adipose tissue leads to brown fat oxidation and heat production (Hull and Segall, 1965). That CAT are important for the activation of nonshivering thermogenesis is not unexpected, since the sympathoadrenal system appears to play a pivotal role in sustaining homeostasis and in facilitating neonatal adaption (Langercrantz, et al., 1981).

Catecholamines During Labor and Delivery

The influence of obstetric anesthesia and analgesia on maternal-fetal plasma CAT levels has been only recently investigated. Maternal stress, pain, and anxiety have been associated with elevated maternal CAT release. Lederman et al. (1977) noted elevated levels of E and NE in the last two stages of labor and during the immediate postpartum period when compared to levels previously obtained during the third trimester. They remarked that the CAT elevation reflected the "emotional stress concomitant with delivery". In another study (Lederman et al., 1978), a significant correlation was established between stress and anxiety and endogenous plasma E. Shnider and Biehl (1981) examined the effects of an electrical stimulus in pregnant ewes and discovered that plasma NE levels consistently increased over non-stressed levels. More recently, Jones and Greiss (1982) confirmed previous studies that demonstrated elevated maternal CAT concentrations associated with parturition.

By elevating maternal circulating CAT, maternal stress can cause a decrease in uterine blood flow, adversely affecting the fetus. Morishima et al. (1978) exposed pregnant rhesus monkeys to the stress of bright light and reported elevated maternal blood pressure and a decrease in fetal heart rate. Profound hypoxia was demonstrated in those fetuses affected. Fetal hypoxia and acidosis were also noted by Myers (1975) in monkeys following painful maternal stress. In sheep studies, Shnider et al. (1979) and Shnider and Biehl (1981) also described decreased uterine blood flow, associated with elevated maternal CAT levels and maternal hypertension.

The fetus has a functioning sympathoadrenal system and does secrete CAT in response to stressful stimuli. Eliot et al. (1979) reported

elevated plasma NE and E levels after the onset of uterine contractions (3 hours prior to birth) in chronically catheterized fetal sheep. Also using a stressed maternal sheep preparation, Jones and Robinson (1975) found high plasma CAT levels and suggested that hypoxia or acidosis was probably responsible for the amine release. Human neonates have also exhibited increased levels of cord blood CATs in response to normal vaginal delivery (Eliot et al., 1980). Padbury et al. (1982) reported the striking elevations of plasma CAT in umbilical cord blood of babies of mothers who had stressful deliveries. The greatest elevations of plasma NE and E were observed in those neonates whose antepartum fetal heart rate patterns indicated fetal distress. More relevant to this study is work with human neonates, which has revealed elevated urinary CAT shortly after birth in response to cold exposure (Stern et al., 1965; and Schiff et al., 1966).

Several studies (Lederman et al., 1977; Shnider et al., 1979; Shnider and Biehl, 1981; Lagercrantz et al., 1981 and Irestedt et al., 1982) have attempted to demonstrate the benefit to the fetus of preventing or reducing maternal pain and stress. Reducing maternal stress should decrease maternal CAT levels, improve utereroplacental blood flow and cause concomitant lowering of fetal CATs as well.

If certain levels of catecholamines are required for neonatal adaptation at the time of birth, does an increase or a decrease in fetal CAT better prepare a fetus for the extrauterine environment? An indirect approach to answering this question would be to investigate the postpartum effects of obstetric anesthetic agents on neonatal thermoregulation, one facet of neonatal adaptation.

Narcotic Effects on Thermoregulation

Narcotic medication administered to parturients for pain relief during labor can affect thermal regulation in the newborn. Burnard and Cross (1958) noted a hypothermic effect at birth in neonates whose mothers were given meperidine two hours prior to delivery. Alphaprodine is the most commonly used narcotic analgesic in obstetrics, at least in this institution, and is the preferred choice because of diminished incidence of nausea and vomiting when compared with meperidine (Gillam et al., 1958; and Petrie et al., 1978). Although decreases in fetal heart variability (Gillam et al., 1958) and sinusoidal fetal heart patterns (Gray et al., 1978) have been reported with the use of alphaprodine, its effects on neonatal thermoregulation are as yet unexplored.

Purpose of the Study

The purpose of the following study was to determine the relationship between the ability of neonates to maintain their body temperature and the antecedant maternal obstetric anesthesia technique.

CHAPTER II

MATERIAL AND METHODS

Patients

The subjects for this study were selected from the daily obstetrical records of the delivery suite at Yale-New Haven Hospital. The hospital is a 900 bed teaching facility that averages 5,700 obstetrical admissions annually. The hospital is also a high-risk obstetrical and neonatal referral center for most of southern Connecticut. The population served is composed of private practice and clinic patients, as well as patients with pre-paid health plans. The sample population included women who delivered from October through December 1982. The following criteria were used in the initial selection of women and their babies for study:

(1) The mothers of the neonates had to receive either no analgesia, narcotic (alphaprodine) analgesia, peridural analgesia, or infiltration of the perineum with a local anesthetic for their babies to be included.

(2) Infants of healthy parturients with uncomplicated full-term pregnancies who delivered vaginally were considered. Full term pregnancy was defined as a gestational age between 38 and 42 weeks, inclusive. The

gestational age was determined by dates, ultra-sound, and/or by Ballard-Dubowitz scores after birth.

(3) Babies requiring mid-forceps delivery, and those whose mothers had rupture of their amniotic membranes greater than 18 hours were not included.

(4) Newborns with APGAR scores at one and five minutes of less than seven, and newborns of low birth weight (less than 2500 g) were excluded.

(5) Newborns requiring special care after delivery, beyond the ordinary resuscitative and suctioning techniques, were not included in the study. In addition, any newborn admitted to the Newborn Special Care Unit for whatever reason was also excluded. Finally, newborns maintained in an isolette warmer during any of the 24 hour study period were disregarded.

Methods

The records of 152 mother-baby pairs were reviewed. Ninty-seven mother-baby pairs met the study criteria. Information collected (Appendix 1) on the mother included the duration of rupture of amniotic membranes prior to delivery, oral temperature at or near delivery, the type or types of analgesia (if any) administered, and the total dose or doses of analgesic medications administered.

Newborn data (Appendix 1) included the gestational age, sex, weight, length, head circumference, APGAR scores at one and five minutes, and all recorded temperatures during the first 24 hours following delivery (Appendices 2, 3, and 4).

The neonates were divided into 3 groups depending upon the type or lack of antepartum analgesia administered to their mothers. Babies in the normal spontaneous delivery group (NSD, n = 30) were born to mothers

who received no anesthesia prior to delivery. The mothers of infants in the local analgesia group (LA, n = 31) received 1% lidocaine infiltration of the perineum prior to delivery. Finally, neonates in the peridural group (PD, n = 36) were born to mothers who received peridural analgesia during labor and delivery. Alphaprodine was administered to 11 (36%) mothers of babies in the NSD group, to 11 (35%) mothers of babies in the LA group and to 20 (55%) mothers of babies in the PD group.

Mean temperatures of the mothers of neonates in each group at birth and the mean durations of rupture of their amniotic membranes prior to the delivery of their neonates were compared using a two-sided Student's t test. The mean birth weights, lengths, head circumferences, gestational age and APGAR scores at 1 and 5 minutes of newborns in each group were also compared using the same statistical analysis.

The serial temperature determinations of all newborns taken during the first 24 hours of life were recorded. The values were grouped in terms of "time intervals" dividing the first 24 hours after birth into 6 sections of 4 hours each. Calculation of the mean temperature in each time interval for the three groups was accomplished by averaging the temperatures of the respective representative neonates. Comparisons of the mean temperatures of neonates in each group during each time period were then made using two-sided Student's t test.

For each group, the temperature point at time zero (birth) was approximated as the average maternal temperature of babies in the group plus 0.5^{o}C (vide supra). For example, the NSD group had an average maternal temperature at birth of 36.6^{o}C; the neonatal temperature at birth was assumed to be 36.6 + 0.5 or 37.1^{o}C. Because of this

assumption the line connecting the zero time temperature to the first mean recorded temperature is plotted as a dotted line in Figures 1-4.

In order to determine the significance of alphaprodine on newborn temperature regulation, the amount of alphaprodine received by mothers in each of the NSD, LA, and PD groups, and the intervals between maternal alphaprodine administration and the birth of their neonates were first compared using the two-sided Student's t-test. Mean temperatures of infants within each group whose mothers received alphaprodine during labor were then compared with mean temperatures of babies whose mothers had not received alphaprodine during labor.

Lastly, to establish the effect (if any) of maternally administered local anesthetic agent per se on thermoregulation in the newborn, the PD group was further subdivided into 3 subgroups according to the mass of local anesthetic (PDa, 30-65 mg; PDb 67.5-85 mg; PDc 90-180 mg) administered during labor. The mean temperatures of newborns within each subgroup were then compared at each postpartum time interval again using the two-sided Student's t test.

CHAPTER III

RESULTS

Mean (± SD) maternal temperatures at the time of delivery, and the mean (± SD) durations of rupture of amniotic membranes were significantly ($p < 0.05$) different when mothers of the PD group were compared to mothers of neonates in the other two groups (Table I).

When babies of the PD group were compared with babies of the NSD group, the mean (± SD) birthweight of the PD group was significantly ($p < 0.05$) higher than that of the NSD group (Table II). However, there were no significant differences between babies of the LA group versus the PD group in any of the neonatal parameters studied.

There was a significant ($p < 0.05$) difference in neonatal temperatures during the first 4 hours postpartum period when the NSD and PD groups were compared (Table III) (Fig. 1). Neonatal temperatures of babies in these two groups were not significantly different during any other time interval. A significant difference ($p < 0.05$) in neonatal temperatures was also noted when the LA group was compared to the PD group, but again, only during the first 4 hour postpartum period.

The mean (± SD) dose of alphaprodine received by mothers of neonates in the PD group during labor was significantly ($p < 0.05$) higher than the

TABLE I. A comparison of mothers of neonates in each group.

CHARACTERISTIC	GROUPS		
	NSD (N = 30)	LA (N = 31)	PD (N = 36)
TEMPERATURE @ BIRTH (^{o} C, mean ± S.D.)	36.11 ± 0.2	36.66 ± 0.2	36.83 ± 0.2*
TIME MEMBRANE RUPT. TO BIRTH (hrs, mean ± S.D.)	3.1 ± 3.7	4.1 ± 4.9	6.9 ± 4.2*

* Significantly different from NSD and LA groups ($p < 0.05$)

TABLE II. A comparison of physical characteristics of neonates of each study group.

CHARACTERISTICS+	GROUPS		
	NSD (N = 30)	LA (N = 31)	PD (N = 36)
WEIGHT (g)	3415 ± 411	3612 ± 466	3658 ± 530*
LENGTH (cm)	51.3 ± 1.9	51.0 ± 1.7	51.8 ± 2.1
HEAD CIRC (cm)	34.3 ± 1.0	34.3 ± 1.3	33.9 ± 2.6
GEST AGE (wks)	39.8 ± 1.2	40.5 ± 1.0	40.2 ± 1.2
APGAR @ 1 min	8.5 ± 0.8	8.5 ± 0.6	8.7 ± 0.5
APGAR @ 5 min	9.0 ± 0.3	9.1 ± 0.4	9.0 ± 0.5

+ = Mean ± standard deviation
* PD vs NSD group, significant at $p < 0.05$

TABLE III. A comparison of temperatures (^{o}C, mean $\pm$ SD) of newborns in each group during each postpartum time period.

POSTPARTUM TIME PERIOD (hrs)	VARIABLE	GROUPS NSD	LA	PD	COMPARISON* NSD vs LA	NSD vs PD	LA vs PD
0 - 4	T (C^{o})	36.49	36.59	36.79			
	S.D.	0.47	0.37	0.43	NS	$P < 0.05$	$P < 0.05$
	N+	35	35	39			
4 - 8	T (C^{o})	36.69	36.71	36.73			
	S.D.	0.27	0.27	0.36	NS	NS	NS
	N	29	17	23			
8 - 12	T (C^{o})	36.71	36.81	36.77			
	S.D.	0.27	0.23	0.27	NS	NS	NS
	N	7	14	20			
12 - 16	T (C^{o})	36.79	36.77	36.77			
	S.D.	0.25	0.24	0.26	NS	NS	NS
	N	14	18	21			
16 - 20	T (C^{o})	36.83	36.88	36.91			
	S.D.	0.24	0.13	0.24	NS	NS	NS
	N	16	15	15			
20 - 24	T (C^{o})	36.81	36.91	36.88			
	S.D.	0.27	0.19	0.29	NS	NS	NS
	N	28	32	28			

* = Statistical significance was made using a two-sided Student's t-test. No significance is abbreviated as NS.

+ = N is the number of temperature recordings of newborns within each group during each postpartum time period.

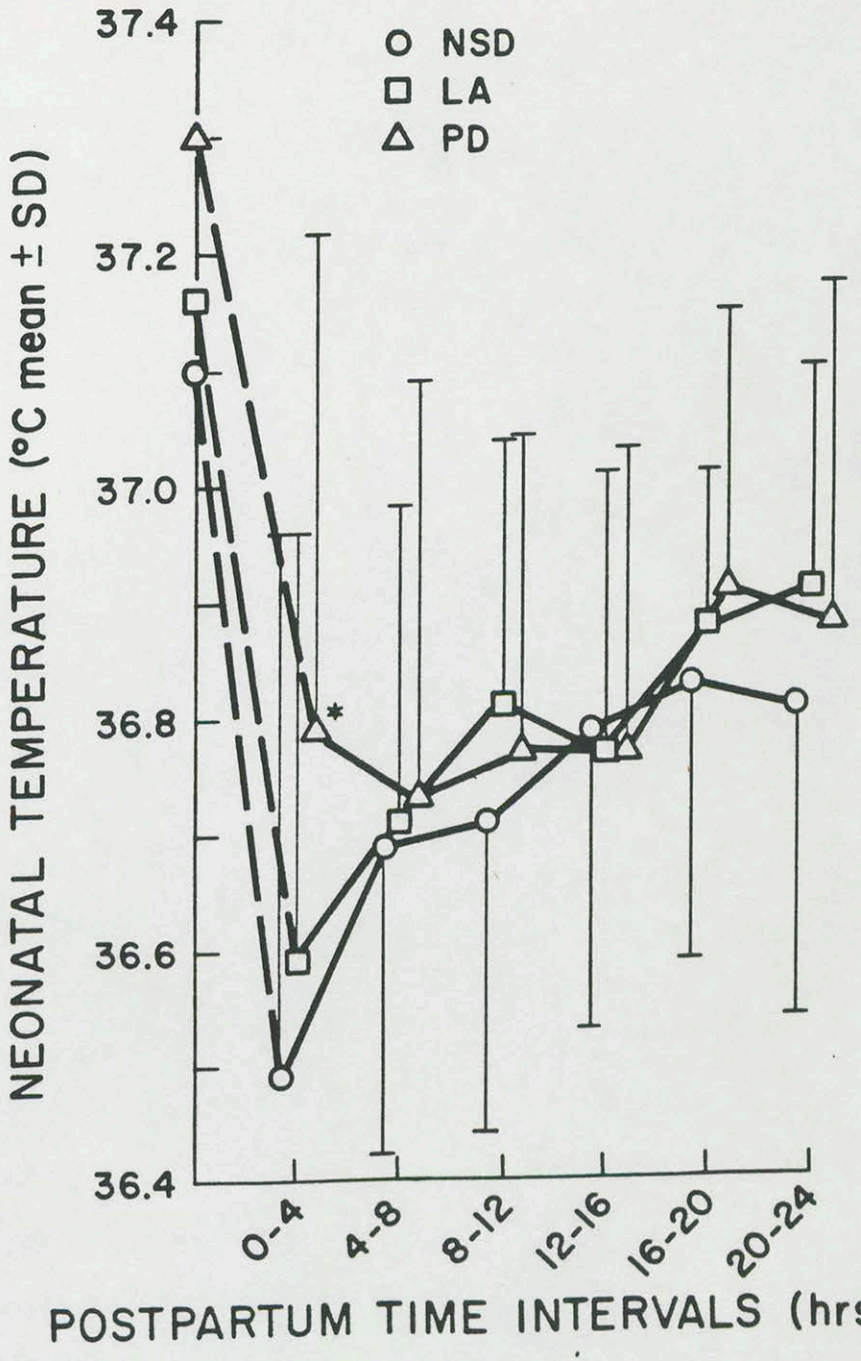


Figure 1. Mean (± SD) temperature (^{o}C) of neonates in the NSD, LA and PD groups during each postpartum time period studied. * indicates significant ($P < 0.05$) differences between mean temperatures of PD group babies when compared to both NSD and LA babies during the first 4 hour postpartum period.

dose administered to mothers of babies in the NSD group (Table IVA). However, there was no significant difference in the amount of alphaprodine administered to mothers who had received peridural block during labor versus mothers of newborns in the LA group.

The time interval between alphaprodine administration and birth was significantly ($p < 0.01$) longer in mothers of neonates in the PD group than in mothers of babies in either the NSD or LA groups (Table IVB).

When NSD group neonates whose mothers received alphaprodine during the last two hours of labor were compared to NSD group neonates whose mothers did not, no significant difference in mean ($\pm$ SD) temperature during the first 24 postoperative hours was noted (Table V) (Fig. 2). Likewise, the mean ($\pm$ SD) temperatures of the neonates in the LA group whose mothers received alphaprodine during labor were not significantly different from those neonates whose mothers did not receive alphaprodine (Table VI) (Fig. 3).

However, within the PD group, neonates of mothers who received alphaprodine during labor had significantly ($p < 0.05$) higher mean ($\pm$ SD) temperatures during the first 4 hour postpartum study period and the last (20-24 hour) postpartum period than did neonates whose mothers received a peridural block alone (Table VII) (Fig. 4).

When neonates within the PD group, subgrouped according to the mass of local anesthetic administered to mother, were compared, no significant differences in their mean ($\pm$ SD) temperatures were noted during any postpartum time period (Table VIII).

TABLE IVA. Comparison of total dosage (mean mg ± SD) of alphaprodine administered to mothers of neonates in each group.

GROUP	ALPHAPRODINE DOSE	SIGNIFICANCE*
NSD	mg (mean) = 28.2 S.D. = 6.0 N+ = 11	
LA	mg (mean) = 30.9 S.D. = 9.2 N = 11	NS
PD	mg (mean) = 32.5 S.D. = 4.4 N = 20	NS P < 0.05

TABLE IVB. A comparison of time (hours, mean ± SD) between the maternal administration of alphaprodine and the birth of neonates in each group.

GROUP	TIME INTERVAL	SIGNIFICANCE
NSD	hours (mean) = 1.8 S.D. = 1.1 N = 11	
LA	hours (mean) = 2.1 S.D. = 0.9 N = 11	NS
PD	hours (mean) = 5.0 S.D. = 1.7 N = 20	P < 0.01 P < 0.01

* = Statistical significance was made using a two-sided Student's t-test. No significance is abbreviated as NS.

+ = N is the number of mothers of neonates in each group who received alphaprodine.

TABLE V. A comparison of the temperatures (^{o}C, mean $\pm$ SD) of newborns (n = 19) in the NSD group whose mothers received no alphaprodine during labor vs newborns (n = 11) whose mothers did receive alphaprodine.

POSTPARTUM TIME PERIOD (hrs)	VARIABLE	SUBGROUPS NSD	SUBGROUPS NSD PLUS ALPHAPRODINE	COMPARISON* NSD VS NSD PLUS ALPHAPRODINE
0 - 4	T (C^{o})	36.50	36.47	
	S.D.	0.53	0.34	NS
	N+	23	12	
4 - 8	T (C^{o})	36.73	36.65	
	S.D.	0.28	0.26	NS
	N	16	13	
8 - 12	T (C^{o})	36.71	—	
	S.D.	0.27	—	—
	N	7	0	
12 - 16	T (C^{o})	36.79	36.80	
	S.D.	0.27	0.17	NS
	N	11	3	
16 - 20	T (C^{o})	36.78	36.90	
	S.D.	0.17	0.39	NS
	N	10	6	
20 - 24	T (C^{o})	36.78	36.85	
	S.D.	0.32	0.18	NS
	N	17	11	

* = Statistical significance was determined using a two-sided Student's t-test. No significance is abbreviated as NS.
+ = N is the number of temperature recordings of newborns in each subgroup during each time period.

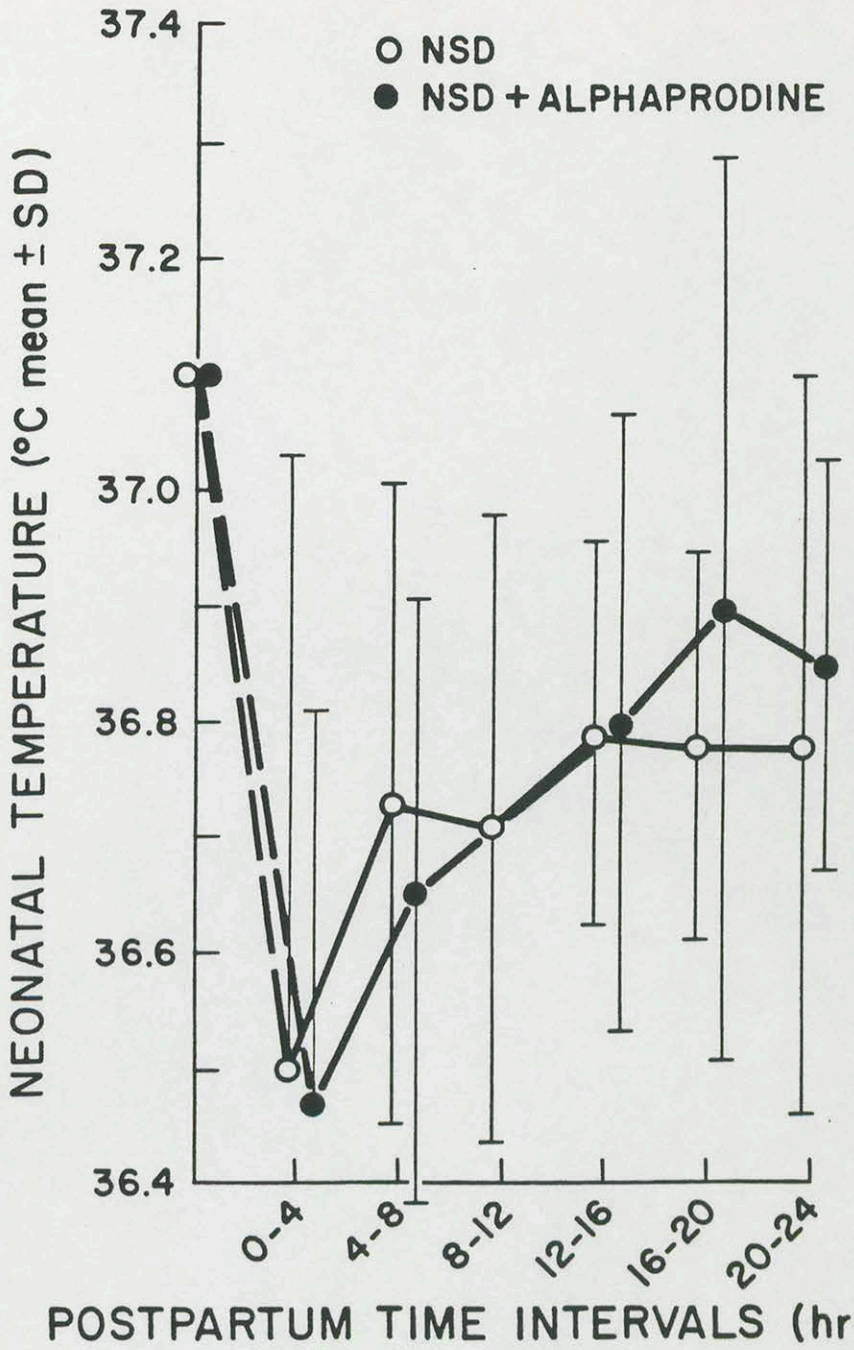


Figure 2. Mean (± SD) temperature (^{o}C) of neonates in the NSD group whose mothers received alphaprodine during labor (n = 11) vs those whose mothers did not (n = 19). There was no significant difference between neonates during any post partum time period studied.

TABLE VI. A comparison of the temperatures (^{o}C, mean ± SD) of newborns (n = 20) in the LA group whose mothers did not receive alphaprodine during labor vs newborns (n = 11) whose mothers did receive alphaprodine.

POSTPARTUM TIME PERIOD (hrs)	VARIABLE	SUBGROUPS LA	SUBGROUPS LA PLUS ALPHAPRODINE	COMPARISON* LA VS. LA PLUS ALPHAPRODINE
0 - 4	T (C^{o})	36.56	36.65	
	S.D.	0.32	0.44	NS
	N+	21	14	
4 - 8	T (C^{o})	36.65	36.77	
	S.D.	0.33	0.21	NS
	N	8	9	
8 - 12	T (C^{o})	36.80	36.83	
	S.D.	0.17	0.39	NS
	N	10	4	
12 - 16	T (C^{o})	36.71	36.88	
	S.D.	0.26	0.13	NS
	N	12	6	
16 - 20	T (C^{o})	36.85	36.95	
	S.D.	0.12	0.13	NS
	N	11	4	
20 - 24	T (C^{o})	36.90	36.92	
	S.D.	0.21	0.18	NS
	N	19	13	

* = Statistical significance was determined using a two-sided Student's t-test. No significance is abbreviated as NS.

+ = N is the number of temperature recordings of newborns in each subgroup during each time period.

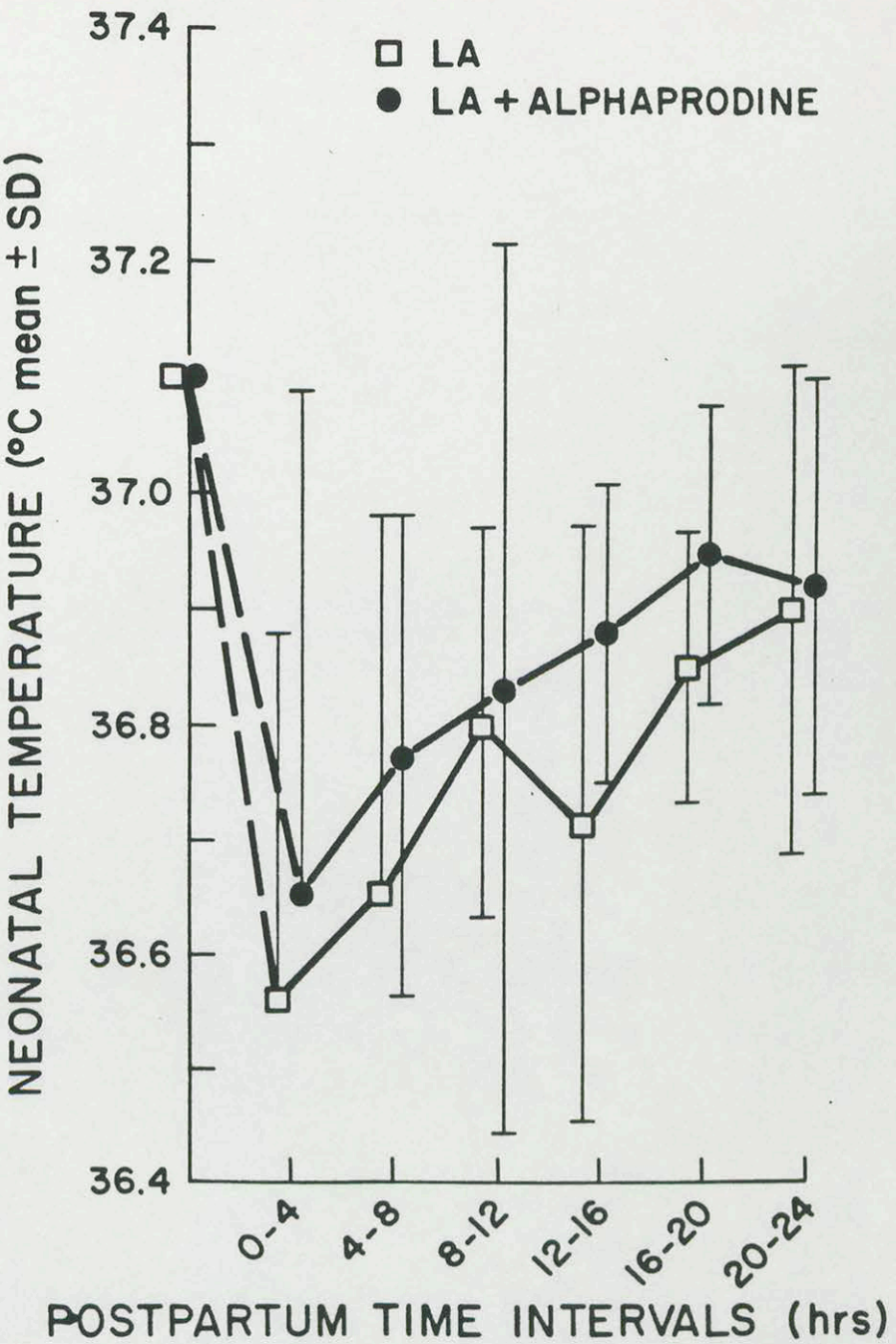


Figure 3. Mean (± SD) temperature (^{o}C) of neonates in the LA group whose mothers received alphaprodine during labor (n = 11) vs those whose mothers did not (n = 20). There was no significant difference between the neonates during any postpartum time period studied.

TABLE VII. A comparison of the temperatures (^{o}C, mean ± SD) of newborns (n = 16) in the PD group whose mothers did not receive alphaprodine during labor vs newborns (n = 20) whose mothers did receive alphaprodine.

POSTPARTUM TIME PERIOD (hrs)	VARIABLE	SUBGROUPS PD	SUBGROUPS PD PLUS ALPHAPRODINE	COMPARISON* PD VS. PD PLUS ALPHAPRODINE
0 - 4	T (C^{o})	36.62	36.93	
	S.D.	0.38	0.42	$P < 0.05$
	N+	17	22	
4 - 8	T (C^{o})	36.58	36.83	
	S.D.	0.42	0.29	NS
	N	9	14	
8 - 12	T (C^{o})	36.68	36.86	
	S.D.	0.31	0.20	NS
	N	10	10	
12 - 16	T (C^{o})	36.79	36.75	
	S.D.	0.22	0.30	NS
	N	10	11	
16 - 20	T (C^{o})	36.87	36.95	
	S.D.	0.26	0.24	NS
	N	7	8	
20 - 24	T (C^{o})	36.73	36.98	
	S.D.	0.22	0.28	$P < 0.05$
	N	11	17	

* = Statistical significance was determined using a two-sided Student's t-test. No significance is abbreviated as NS.

+ = N is the number of temperature recordings of newborns in each subgroup during each time period.

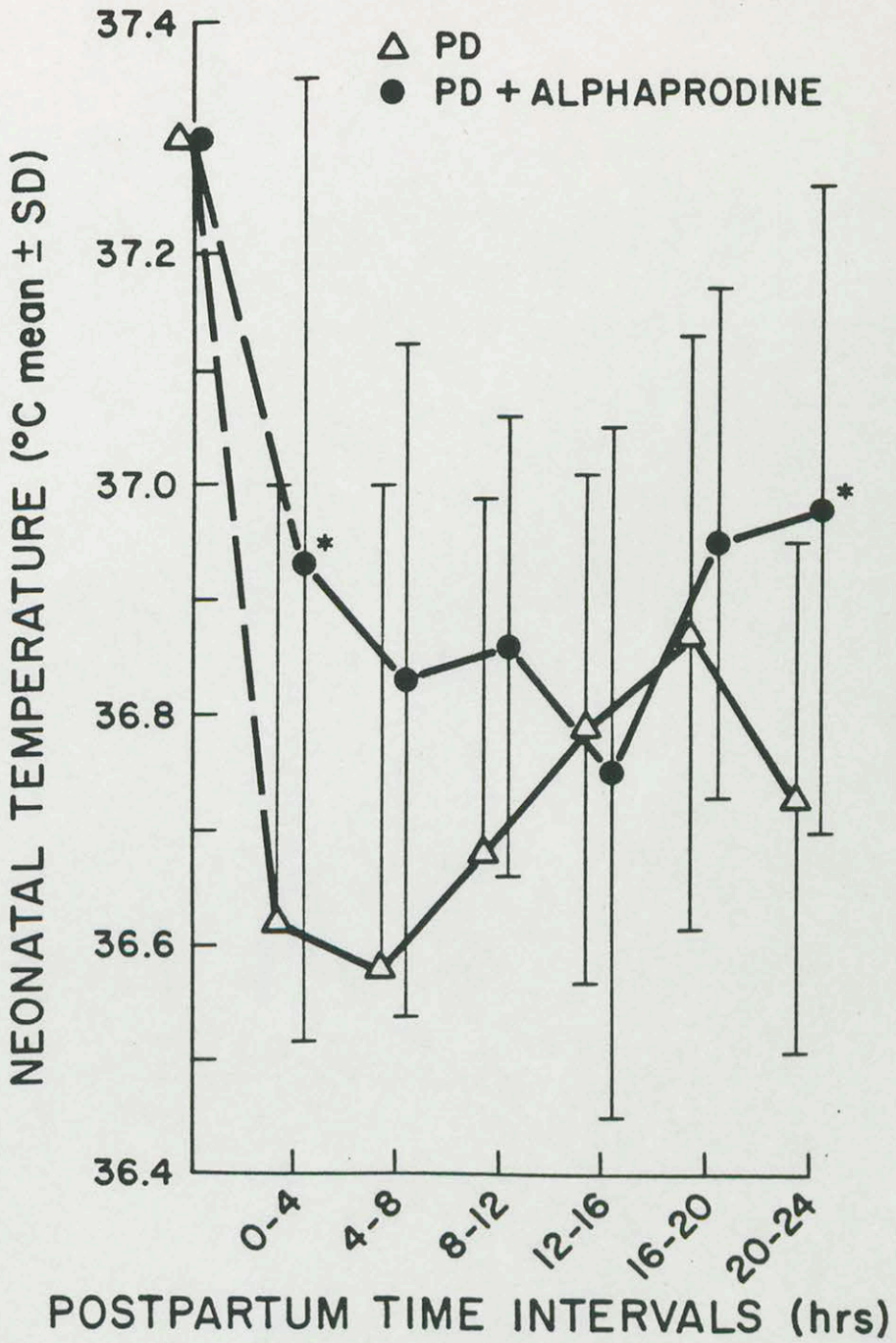


Figure 4. Mean (± SD) temperature (^{o}C) of neonates (n = 20) in the PD group whose mothers received alphaprodine during labor versus those whose mothers did not (n = 16). * indicates that neonates whose mothers received alphaprodine had significantly ($P < 0.05$) higher mean temperatures during the first 4 hour postpartum time period and the 20-24 hour postpartum time period than did babies whose mothers received peridural analgesia alone.

TABLE VIII. A comparison of temperatures (^{o}C, mean ± SD) of thirty six neonates whose mothers received peridural anesthesia with 0.5% bupivacaine. Neonates are divided into subgroups according to the dose of bupivacaine administered.

POSTPARTUM PERIOD TIME (hrs)	VARIABLES		SUBGROUPS PDa 30 to 65 mg 0.5% bupivacaine	PDb 66 to 85 mg 0.5% bupivacaine	PDc 86 to 180 mg 0.5% bupivacaine	COMPARISON PDa vs PDb vs PDc
0 - 4	T (^{o}C)	=	36.73	36.83	36.82	
	S.D.	=	0.41	0.38	0.52	NS
	N+	=	11	12	14	
4 - 8	T (^{o}C)	=	36.64	36.87	36.68	
	S.D.	=	0.39	0.36	0.37	NS
	N	=	9	7	5	
8 - 12	T (^{o}C)	=	36.81	36.68	36.79	
	S.D.	=	0.24	0.22	0.33	NS
	N	=	7	5	8	
12 - 16	T (^{o}C)	=	36.86	36.63	36.76	
	S.D.	=	0.32	0.24	0.21	NS
	N	=	8	6	5	
16 - 20	T (^{o}C)	=	36.93	36.82	37.00	
	S.D.	=	0.31	0.20	0.28	NS
	N	=	3	5	6	
20 - 24	T (^{o}C)	=	36.77	36.68	37.00	
	S.D.	=	0.23	0.15	0.30	NS
	N	=	6	8	11	

* = Statistical significance was determined using two-sided Student's t-test. No significance is abbreviated as NS.

+ = N is the number of temperature recordings of newborns in each subgroup during postpartum time period.

CHAPTER IV

DISCUSSION

Maternal and Neonatal Parameters

Maternal temperature increases during labor had been attributed to the release of metabolic heat resulting from uterine contractions. This belief was explored by Marx and Loew (1975), who studied the tympanic temperatures of eleven women during parturition and reported that maternal temperatures did increase with successive contractions throughout labor. In animal studies, however, core temperatures have been found to decrease during intrapartum courses (Littledike et al., 1979; and Ruppenthal and Goodlin, 1981). In an attempt to clarify this inconsistency, Goodlin and Chapin (1982) studied 50 women and monitored their temperatures from various sites during labor and delivery. They reported lower temperatures in women who received no analgesia as compared with women who received epidural anesthesia, paracervical block, or narcotic analgesics. Those authors concluded that the pain of parturition results in hyperventilation and sweating, thus increasing heat loss and tending to cause a decrease in core temperature.

Mothers of the PD group were found to have significantly higher mean temperatures than mothers of both the LA and NSD groups. Accordingly,

the results of the present study confirm Goodlin and Chapin's (1982) findings. In contrast, the temperatures of the LA mothers did not differ significantly from those of the NSD group. However, this is not surprising as local infiltration of the perineum was usually performed only during the final moments of labor when delivery was imminent. Until that time, the LA parturients had been managed in a manner similar to that of the NSD mothers, i.e., with no significant intervention to alleviate pain. This management was in marked contrast to that of the PD mothers who were usually administered their regional anesthesia well in advance of delivery and "labored" pain free.

A further interesting study of maternal temperatures during labor was reported by Ruppenthal and Goodlin (1982). These authors found that laboring monkeys manifested a decrease in body temperature approximately 90 minutes prior to delivery. In contrast to Goodlin and Chapin's earlier work, they observed that this fall in body temperature was not associated with either hyperventilation or perspiration during labor. They were also unable to demonstrate any fluctuations in maternal temperatures in association with uterine contractions. Unfortunately, a group comparable to the PD mothers was not studied by these latter investigators and whether effective pain relief would have resulted in higher temperature is purely speculative.

The time from rupture of amniotic membranes to birth was found to be significantly longer in mothers of the PD group when compared to NSD and LA group mothers. There was no significant difference between the durations of ruptured membranse in mothers of the latter two groups. In one study by Falconer and Powles (1982), nine patients who received a peridural block were found to have a longer second stage of labor, as

well as lower circulating catecholamines, when compared to eleven non-peridural patients. These observations were attributed to the abolition of the desire to push by the peridural patients. A previous study (Rolly, 1981) also reported prolonged second stages of labor after peridural analgesia, resulting from either blunted reflex urges to bear down, or decreases in muscle function. Therefore, that the PD group mothers experienced a longer duration of ruptured membranes is not unexpected. The reason for studying the duration of rupture of membranes is its relationship to amniitis, with associated maternal fever and newborn sepsis. It is generally believed that amniitis is uncommon unless amniotic membranes have been ruptured for more than 12 hours. Although mothers of the PD newborns did experience a significantly longer duration of ruptured membranes than did NSD and LA group mothers, the mean duration of 6.9 $\pm$ 4.2 hours (mean $\pm$ SD) is well below the duration which might be associated with amniitis and maternal fever. It is unlikely, then, that the higher maternal temperature of mothers in the PD group was the result of infection secondary to prolonged rupture of their amniotic membranes. Therefore, although the mean duration of ruptured membranes in mothers of the PD group was statistically significantly longer, it was probably not of clinical significance.

The neonates of the PD group were found to have a statistically significant higher mean weight when compared to the NSD group. While body weight becomes important when convective, radiative, evaporative, and conductive heat losses to a cold environment are calculated (Swyer, 1978), it is difficult to estimate the clinical significance of a mean weight difference of less than 0.25 kg between the groups. Since the babies of all three groups had mean weights well above the weight of 2.5

kg thought to be critical for newborn thermoregulation (Schwartz et al., 1978; and Sweet, 1979), it is unlikely that the higher mean temperature of the PD group during the first four hour postpartum study period was due to their greater body weights.

Neonatal Temperatures After Birth

Retrospective data collection for this study revealed that newborn temperatures are not routinely taken at birth. Rather, well babies remain with their mothers in labor and delivery rooms for variable periods of time (usually 1-4 hours). Only after admission to the nursery is the newborn's first temperature taken. All maternal temperatures, at or near birth, are recorded. Because fetal temperatures at birth have been shown to correlate with maternal temperatures, maternal temperatures at birth can be used to interpolate newborn temperatures. As noted earlier (Goodlin and Chapin, 1982), maternal and fetal temperatures were shown to be higher at delivery when the pain of parturition has been adequately treated. The present study also found that mothers who received effective antepartum analgesia (peridural block) had higher temperatures at birth. In a sense both maternal and fetal temperatures then become a function of the efficacy, or lack, of antepartum maternal analgesia.

No difference was noted in neonatal temperatures between the LA and NSD groups during the entire 24 hours study period. The PD group, on the other hand, had significantly higher mean temperatures during the first four hours after birth when compared to both the NSD and LA groups.

CATs are necessary for newborn non-shivering thermogenesis. Babies born to mothers who have experienced painful, stressful parturition can be expected to have higher circulating CATs at birth (Lederman et al.,

1977; Shnider et al., 1979; Lagercrantz et al., 1981; Irestedt et al., 1982; Jones and Greiss, 1982; Padbury et al., 1982; and Falconer and Powles, 1982) than babies whose mothers were unstressed during labor. It was postulated that newborns in the NSD group, because of higher circulating CATs would more rapidly respond to cold stress and display higher temperatures than PD group neonates.

That neonatal birth temperatures are reflective of maternal temperatures at birth complicates interpretation of the data. While it may still be true that neonates with elevated catecholamines have better primed adaptive mechanisms, including an activated non-shivering thermogenic systems, the lack of response (i.e. hypothermia) by unprepared sympathoadrenal adaptive systems may not be seen in newborns of unstressed mothers if these babies are delivered with higher birth temperatures than babies of stressed mothers. While some confusion exists in the interpretation of early postpartum data, evidence in support of the importance of CATs for adaptive purposes might still be seen in the observation that mean temperatures in the NSD and LA groups increased during the period from the first four hour postpartum period to the second four hour period, whereas the mean temperatures of neonates of the PD group, presumably less capable of adaptation, decreased during the same postpartum period.

It is suggested then, by this author, that early (0-4 hours) newborn temperatures are related to the antecedant maternal obstetric anesthesia technique and reflective of maternal temperatures at birth, while later temperatures are more dependent upon adaptive mechanisms.

Eliot et al. (1980) observed that neonatal catecholamines remain elevated over normal adult resting levels for the first three hours of

life and then fall by 12 to 48 hours to levels similar to resting adult values. This schedule appears to be applicable to the results of the present study. Neonatal temperatures in the NSD and LA groups increased and stabilized along with the neonatal temperatures of the PD group after the first four hours after birth. The temperatures of all neonates then remained stable during the remainder of the twenty-four hour study period.

Effect of Narcotics

The effects of the narcotic alphaprodine (Nisentil) on the fetus and neonate are not as well documented as are the effects of meperidine and morphine. The effect of alphaprodine on neonatal thermoregulation has not been specifically studied.

Neonatal depression following the use of narcotics for obstetric analgesia is dose related, and a function of the maternal drug administration to delivery time interval (Brooks and Ngeow, 1982). Within the last two hours of labor, mothers of neonates in the NSD and LA groups received approximately 30 mg of alphaprodine. The maternal and fetal pharmacokinetics of alphaprodine are such that neonatal neuroaxial levels of alphaprodine should have been near peak at the time of birth (Shnider and Levinson, 1981). The lack of effect of alphaprodine on newborn temperature in these two groups may be due to one of the following reasons. First, 30 mg of alphaprodine may represent too small a maternal dose to achieve sufficient fetal drug levels to affect newborn thermoregulation. Emich (1955) noted little nonthermoregulatory newborn depression when maternal alphaprodine doses were kept below 40 mg.

Second, alphaprodine, even in moderate doses, and unlike morphine, may not affect thermoregulation in the newborn.

In contrast to the lack of associated changes in newborn temperatures noted in NSD and LA group newborns whose mothers received alphaprodine, babies in the PD group whose mothers received alphaprodine prior to peridural analgesia did have significantly higher mean temperatures during the first and last 4 hour postpartum periods than did babies whose mothers received peridural analgesia alone. Alphaprodine was administered to PD group mothers an average of five hours prior to delivery. One might predict from the analysis of the pharmacokinetics of alphaprodine that most of the narcotic would have been metabolized and/or excreted after five hours, and certainly by 25 hours. While alphaprodine metabolites might be implicated as the active molecules responsible for the higher temperatures observed in the babies whose mothers received peridural analgesia plus alphaprodine, a similar effect would be expected at some time during the 24 hour study period in the NSD and LA groups whose mothers received alphaprodine.

The higher mean temperatures of babies whose mothers received alphaprodine as well as peridural analgesia are not easily explained, especially considering the extremes of the study period in which they occured. Whether a sinergistic response exists between local anesthetic and narcotic molecules contains the neuroaxis has, to this mother's knowledge, not been explored.

Bupivacaine Dosage

Local anesthetic molecules, because of their physiochemical properties, are able to diffuse across maternal blood-brain and placental

barriers with little difficulty. Even bupivacaine, which is highly ionized and bound to maternal proteins does attain significant fetal blood levels (Belfrage et al., 1975a; Belfrage et al., 1975b; Hyman and Shnider, 1971; Reynolds et al., 1973; and Bromage, 1979). Because local anesthetic molecules depress conduction in all excitable tissues, fetal brain can be a target organ of circulating local anesthetic molecules. Indeed, newborn neurobehavioral changes, although transient, have been observed in babies whose mothers received epidural analgesia carbocaine or lidocaine (Scanlon et al., 1974).

To properly investigate the effect of antepartum peridural analgesia on newborn thermoregulation, consideration should also be given to the possibility that dysfunctional thermal adaptation may result from a direct effect of local anesthetic molecules on thermoregulatory centers of the brain, as well as to indirect effects of peridural analgesia, i.e. maternal sympathetic blockade and pain relief. Since fetal blood and brain concentrations of local anesthetic mirror maternal blood concentrations, any adverse response in the neonate should be maternally dose dependent. To further investigate the presence of a dose related response to local anesthetic agents, the PD group neonates in this study were divided into three subgroups according to the dose of bupivacaine administered to their mothers during labor. No significant differences in mean temperatures were noted in any subgroup during any postpartum time interval studied. This would indicate that, at least in moderate doses, maternally administered bupivacaine does not have a direct molecular effect on newborn thermoregulatory centers.

Conclusions

The following conclusions are suggested by the results in this study:

1. Neonatal temperatures fall dramatically following delivery but stabilize within three to four hours after birth. The immediate postpartum period is characterized by neonatal body temperatures that are closely related to the antecedant maternal obstetric anesthesia technique.

2. Neonates whose mothers received effective and sustained analgesia (peridural group) experience the least decrease in body temperatures.

3. The reason for the blunted hypothermic response appears to be that PD group babies begin at higher birth tempertures, reflective of higher maternal temperatures.

4. A direct effect of peridural analgesia on newborn thermoregulation, either secondary to the technique, or the local anesthetic agent itself has not been demonstrated.

5. The narcotic alphaprodine, when used along and in the doses employed, does not appear to affect neonatal thermoregulation following maternal administration. There may exist a synergistic effect of alphaprodine and peridural analgesia on newborn thermoregulation.

APPENDIX 1

MATERNAL AND NEONATAL DATA COLLECTION SHEET

MOTHER

Unit No._____ EDC_____ Blood type_____

Name_____ Age_____ G___P___Ab___LC_____

Birth date_____ Rupture of membranes_____

Date of admission_____

VITAL SIGNS: Wt._____ Ht._____ BP_____ P_____ Temp_____ (@ delivery)

ANESTHESIA: Type_____ Total dose_____

Anesthesia time_____

Meds in last 4 hours (name, dosage, time):_____

_____

_____

DELIVERY: ( ) Singleton ( ) Twins

( ) Vaginal_____

( ) Cesarean_____

COMPLICATIONS: ( ) of pregnancy_____

_____

( ) of labor & delivery_____

_____

* *

BABY

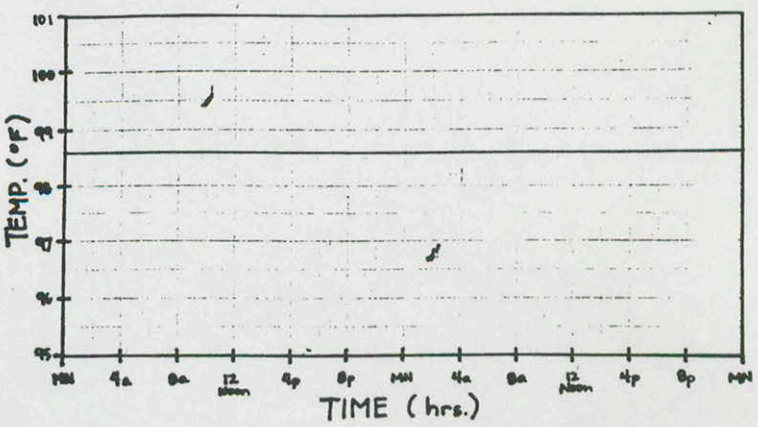
Name_____ Sex____ Birth date_____ Time_____

Birth wt._____ Length_____ HC_____

Gestational age:_____ SGA AGA LGA APGARS_____

Time	Temp

(B = @ birth, N = @ nursery)



APPENDIX 2

TEMPERATURE OF NEONATES IN THE NSD GROUP*

FILE NSD1	TIME(1)=1.33	TEMP(1)=36.4
	TIME(2)=17.33	TEMP(2)=37.5
	TIME(3)=23.33	TEMP(3)=36.8
FILE NSD2	TIME(1)=1.38	TEMP(1)=37.3
	TIME(2)=7.55	TEMP(2)=37
	TIME(3)=15.55	TEMP(3)=37
	TIME(4)=23.55	TEMP(4)=37
FILE NSD3	TIME(1)=1.75	TEMP(1)=37.5
	TIME(2)=7.5	TEMP(2)=36.8
	TIME(3)=7.75	TEMP(3)=36
	TIME(4)=19.75	TEMP(4)=36.7
	TIME(5)=21.75	TEMP(5)=35.9
	TIME(6)=27.25	TEMP(6)=36.3
FILE NSD4	TIME(1)=4.42	TEMP(1)=36.8
	TIME(2)=10.42	TEMP(2)=36.5
	TIME(3)=16.42	TEMP(3)=36.8
	TIME(4)=28.42	TEMP(4)=37
FILE NSD5	TIME(1)=1.17	TEMP(1)=37
	TIME(2)=7.17	TEMP(2)=36.8
	TIME(3)=22.17	TEMP(3)=36.8
	TIME(4)=24.17	TEMP(4)=37.2
FILE NSD6	TIME(1)=1.1	TEMP(1)=36.5
	TIME(2)=6.6	TEMP(2)=36.6
	TIME(3)=20.1	TEMP(3)=36.8
	TIME(4)=23.6	TEMP(4)=36.6
FILE NSD7	TIME(1)=.33	TEMP(1)=35.2
	TIME(2)=5.5	TEMP(2)=37
	TIME(3)=8	TEMP(3)=36.8

*Note: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 2 (continued)

FILE NSD8	TIME(1)=1.37	TEMP(1)=36.5
	TIME(2)=3.2	TEMP(2)=37.2
	TIME(3)=9.2	TEMP(3)=37.2
	TIME(4)=15.2	TEMP(4)=37.4
	TIME(5)=27.2	TEMP(5)=37
FILE NSD9	TIME(1)=1.2	TEMP(1)=36
	TIME(2)=4.7	TEMP(2)=36.8
	TIME(3)=18.7	TEMP(3)=36.6
	TIME(4)=23.7	TEMP(4)=36.7
	TIME(5)=28.7	TEMP(5)=37
FILE NSD10	TIME(1)=2.45	TEMP(1)=35.3
	TIME(2)=5.28	TEMP(2)=36.6
	TIME(3)=23.28	TEMP(3)=36.8
FILE NSD11	TIME(1)=1.45	TEMP(1)=36.1
	TIME(2)=3.95	TEMP(2)=36.7
	TIME(3)=6.95	TEMP(3)=36.5
	TIME(4)=15.2	TEMP(4)=36.6
	TIME(5)=22.95	TEMP(5)=36.7
FILE NSD12	TIME(1)=1.5	TEMP(1)=37
	TIME(2)=6.5	TEMP(2)=36.7
	TIME(3)=17.75	TEMP(3)=36.8
	TIME(4)=23.5	TEMP(4)=37
FILE NSD13	TIME(1)=1.25	TEMP(1)=36.4
	TIME(2)=4.75	TEMP(2)=37
	TIME(3)=9.75	TEMP(3)=36.5
	TIME(4)=22.75	TEMP(4)=36.6
	TIME(5)=26.75	TEMP(5)=36.8
FILE NSD14	TIME(1)=1.37	TEMP(1)=35.8
	TIME(2)=4.37	TEMP(2)=36.8
	TIME(3)=15.87	TEMP(3)=36.7
	TIME(4)=19.87	TEMP(4)=36.6
	TIME(5)=26.87	TEMP(5)=37

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 2 (continued)

FILE NSD15	TIME(1)=1.5	TEMP(1)=36.6
	TIME(2)=4.25	TEMP(2)=36.9
	TIME(3)=16	TEMP(3)=37
	TIME(4)=22.25	TEMP(4)=36.8
FILE NSD16	TIME(1)=.1	TEMP(1)=36.5
	TIME(2)=3.02	TEMP(2)=36.8
	TIME(3)=6.52	TEMP(3)=36.8
	TIME(4)=24.52	TEMP(4)=36.8
FILE NSD17	TIME(1)=1.27	TEMP(1)=36.3
	TIME(2)=5.02	TEMP(2)=36.7
	TIME(3)=7.77	TEMP(3)=36.8
	TIME(4)=14.52	TEMP(4)=36.7
	TIME(5)=29.02	TEMP(5)=36.8
FILE NSD18	TIME(1)=1.9	TEMP(1)=36.6
	TIME(2)=4.9	TEMP(2)=36.6
	TIME(3)=6.9	TEMP(3)=36.5
	TIME(4)=15.4	TEMP(4)=36.8
FILE NSD19	TIME(1)=1.5	TEMP(1)=36.6
	TIME(2)=8.17	TEMP(2)=36.6
	TIME(3)=15.67	TEMP(3)=36.9
	TIME(4)=30.17	TEMP(4)=37
FILE NSD20	TIME(1)=.7	TEMP(1)=35.8
	TIME(2)=6.53	TEMP(2)=36
	TIME(3)=7.53	TEMP(3)=36.6
	TIME(4)=14.53	TEMP(4)=36.7
	TIME(5)=19.03	TEMP(5)=36.8
	TIME(6)=26.03	TEMP(6)=36.8
FILE NSD21	TIME(1)=1.77	TEMP(1)=35.5
	TIME(2)=2.27	TEMP(2)=36.3
	TIME(3)=3.27	TEMP(3)=36.6
	TIME(4)=8.27	TEMP(4)=37
	TIME(5)=15.27	TEMP(5)=36.8
	TIME(6)=18.52	TEMP(6)=36.8
	TIME(7)=25.27	TEMP(7)=37

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 2 (continued)

FILE NSD22	TIME(1)=.83	TEMP(1)=36.3
	TIME(2)=5.33	TEMP(2)=37
	TIME(3)=12.83	TEMP(3)=36.8
	TIME(4)=16.83	TEMP(4)=37.1
	TIME(5)=21.83	TEMP(5)=36.8
FILE NSD23	TIME(1)=2	TEMP(1)=36.2
	TIME(2)=5	TEMP(2)=37.2
	TIME(3)=19	TEMP(3)=36.6
	TIME(4)=27.5	TEMP(4)=37
FILE NSD24	TIME(1)=.75	TEMP(1)=36.2
	TIME(2)=2.25	TEMP(2)=36.6
	TIME(3)=14.75	TEMP(3)=36.8
	TIME(4)=18.25	TEMP(4)=36.6
FILE NSD25	TIME(1)=1.8	TEMP(1)=36.8
	TIME(2)=5.05	TEMP(2)=37
	TIME(3)=19.05	TEMP(3)=37
	TIME(4)=22.55	TEMP(4)=36.8
	TIME(5)=29.05	TEMP(5)=37.2
FILE NSD26	TIME(1)=1.32	TEMP(1)=36.8
	TIME(2)=6.82	TEMP(2)=36.7
	TIME(3)=13.48	TEMP(3)=37
	TIME(4)=21.32	TEMP(4)=37.1
	TIME(5)=30.82	TEMP(5)=37
FILE NSD27	TIME(1)=.72	TEMP(1)=36.3
	TIME(2)=5.97	TEMP(2)=36.5
	TIME(3)=17.97	TEMP(3)=36.7
	TIME(4)=28.97	TEMP(4)=36.6
FILE NSD28	TIME(1)=1.73	TEMP(1)=36.8
	TIME(2)=8.73	TEMP(2)=36.6
	TIME(3)=13.48	TEMP(3)=36.6
	TIME(4)=18.73	TEMP(4)=36.8

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 2 (continued)

FILE NSD29	TIME(1)=1.27	TEMP(1)=36.4
	TIME(2)=4.1	TEMP(2)=36.5
	TIME(3)=10.1	TEMP(3)=36.6
	TIME(4)=14.85	TEMP(4)=36.3
	TIME(5)=21.1	TEMP(5)=36.5
FILE NSD30	TIME(1)=1.25	TEMP(1)=36.5
	TIME(2)=4.5	TEMP(2)=36.8
	TIME(3)=16.5	TEMP(3)=36.8
	TIME(4)=21	TEMP(4)=37.2
	TIME(5)=28.5	TEMP(5)=36.8

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 3

TEMPERATURE OF NEONATES IN THE LA GROUP*

FILE LA1	TIME(1)=2.98	TEMP(1)=36.2
	TIME(2)=5.23	TEMP(2)=37
	TIME(3)=6.48	TEMP(3)=36.5
	TIME(4)=20.48	TEMP(4)=36.8
	TIME(5)=24.23	TEMP(5)=37
FILE LA2	TIME(1)=1.83	TEMP(1)=36
	TIME(2)=9.33	TEMP(2)=37
	TIME(3)=13.33	TEMP(3)=36.6
	TIME(4)=19.33	TEMP(4)=36.8
	TIME(5)=33.33	TEMP(5)=36.8
FILE LA3	TIME(1)=1.1	TEMP(1)=37
	TIME(2)=10.1	TEMP(2)=37
	TIME(3)=15.1	TEMP(3)=36.8
	TIME(4)=20.1	TEMP(4)=36.8
	TIME(5)=28.1	TEMP(5)=37.3
FILE LA4	TIME(1)=1.7	TEMP(1)=36.5
	TIME(2)=6.7	TEMP(2)=36
	TIME(3)=9.87	TEMP(3)=37
	TIME(4)=20.7	TEMP(4)=36.5
	TIME(5)=25.2	TEMP(5)=37
FILE LA5	TIME(1)=1.75	TEMP(1)=36.8
	TIME(2)=5	TEMP(2)=36.6
	TIME(3)=12	TEMP(3)=36.7
	TIME(4)=25	TEMP(4)=36.8
FILE LA6	TIME(1)=3.02	TEMP(1)=37.2
	TIME(2)=10.02	TEMP(2)=36.8
	TIME(3)=24.02	TEMP(3)=36.8
FILE LA7	TIME(1)=.87	TEMP(1)=36.5
	TIME(2)=8.87	TEMP(2)=36.8
	TIME(3)=14.37	TEMP(3)=37
	TIME(4)=19.87	TEMP(4)=37
	TIME(5)=29.87	TEMP(5)=37

*NOTE: Time is given in hours after birth and temperature in ^{0}C.

APPENDIX 3 (continued)

FILE LA8	TIME(1)=1.48	TEMP(1)=36.8
	TIME(2)=2.57	TEMP(2)=36.2
	TIME(3)=10.57	TEMP(3)=36.8
	TIME(4)=21.07	TEMP(4)=37
	TIME(5)=26.57	TEMP(5)=36.8
FILE LA9	TIME(1)=1	TEMP(1)=36.8
	TIME(2)=5	TEMP(2)=37
	TIME(3)=13.25	TEMP(3)=37.2
	TIME(4)=18	TEMP(4)=37
FILE LA10	TIME(1)=1.68	TEMP(1)=36
	TIME(2)=4.68	TEMP(2)=36.8
	TIME(3)=13.68	TEMP(3)=37.2
	TIME(4)=21.18	TEMP(4)=36.8
	TIME(5)=26.68	TEMP(5)=36.8
FILE LA11	TIME(1)=2	TEMP(1)=36.8
	TIME(2)=12	TEMP(2)=36.6
	TIME(3)=18	TEMP(3)=36.8
	TIME(4)=22.25	TEMP(4)=37
FILE LA12	TIME(1)=.8	TEMP(1)=36.3
	TIME(2)=7.3	TEMP(2)=36.9
	TIME(3)=20.3	TEMP(3)=37
	TIME(4)=25.8	TEMP(4)=36.8
FILE LA13	TIME(1)=1.42	TEMP(1)=36.2
	TIME(2)=4.42	TEMP(2)=36.6
	TIME(3)=14.42	TEMP(3)=37
	TIME(4)=22.67	TEMP(4)=37
	TIME(5)=29.41	TEMP(5)=36.7
FILE LA14	TIME(1)=.32	TEMP(1)=36.5
	TIME(2)=2.82	TEMP(2)=36.4
	TIME(3)=4.82	TEMP(3)=37
	TIME(4)=6.82	TEMP(4)=36.8
	TIME(5)=20.32	TEMP(5)=37
	TIME(6)=24.07	TEMP(6)=36.7

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 3 (continued)

FILE LA15	TIME(1)=1.67	TEMP(1)=36.7
	TIME(2)=7.67	TEMP(2)=36.6
	TIME(3)=12.92	TEMP(3)=36.3
	TIME(4)=27.42	TEMP(4)=36.7
FILE LA16	TIME(1)=1.67	TEMP(1)=37
	TIME(2)=4.08	TEMP(2)=37
	TIME(3)=13.08	TEMP(3)=36.8
	TIME(4)=20.08	TEMP(4)=37
	TIME(5)=28.08	TEMP(5)=37
FILE LA17	TIME(1)=2	TEMP(1)=36.2
	TIME(2)=12	TEMP(2)=36.8
	TIME(3)=16.25	TEMP(3)=36.8
	TIME(4)=23	TEMP(4)=37.2
FILE LA18	TIME(1)=2.03	TEMP(1)=36.8
	TIME(2)=15.87	TEMP(2)=36.5
	TIME(3)=23.87	TEMP(3)=36.8
FILE LA19	TIME(1)=2.17	TEMP(1)=36.6
	TIME(2)=4.17	TEMP(2)=36.5
	TIME(3)=16.17	TEMP(3)=36.7
	TIME(4)=21.42	TEMP(4)=37
	TIME(5)=27.17	TEMP(5)=37.2
FILE LA20	TIME(1)=1.33	TEMP(1)=36.5
	TIME(2)=14.33	TEMP(2)=36.8
	TIME(3)=18.33	TEMP(3)=36.9
	TIME(4)=23.33	TEMP(4)=37.1
FILE LA21	TIME(1)=3.37	TEMP(1)=36.8
	TIME(2)=8.37	TEMP(2)=36.8
	TIME(3)=19.87	TEMP(3)=37
	TIME(4)=23.87	TEMP(4)=37

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 3 (continued)

FILE LA22	TIME(1)=1.58	TEMP(1)=36.7
	TIME(2)=5.33	TEMP(2)=36.6
	TIME(3)=11.33	TEMP(3)=36.7
	TIME(4)=18.33	TEMP(4)=37
	TIME(5)=31.33	TEMP(5)=36.8
FILE LA23	TIME(1)=.85	TEMP(1)=36.8
	TIME(2)=14.35	TEMP(2)=37
	TIME(3)=17.85	TEMP(3)=37
	TIME(4)=23.85	TEMP(4)=37.2
FILE LA24	TIME(1)=1.52	TEMP(1)=36.5
	TIME(2)=4.27	TEMP(2)=36.7
	TIME(3)=11.27	TEMP(3)=36.8
	TIME(4)=19.27	TEMP(4)=36.8
	TIME(5)=29.02	TEMP(5)=37
FILE LA25	TIME(1)=2.55	TEMP(1)=36.3
	TIME(2)=4.55	TEMP(2)=37
	TIME(3)=17.55	TEMP(3)=36.7
	TIME(4)=21.05	TEMP(4)=37.2
	TIME(5)=28.05	TEMP(5)=37
FILE LA26	TIME(1)=1.65	TEMP(1)=36
	TIME(2)=8.32	TEMP(2)=36.6
	TIME(3)=15.32	TEMP(3)=36.5
	TIME(4)=23.32	TEMP(4)=36.5
FILE LA27	TIME(1)=2.03	TEMP(1)=36.7
	TIME(2)=12.28	TEMP(2)=36.6
	TIME(3)=16.03	TEMP(3)=36.8
	TIME(4)=18.03	TEMP(4)=36.8
FILE LA28	TIME(1)=1.42	TEMP(1)=37.4
	TIME(2)=3.25	TEMP(2)=37.4
	TIME(3)=8.75	TEMP(3)=37.2
	TIME(4)=25.25	TEMP(4)=37.2

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 3 (continued)

FILE LA29	TIME(1)=1.75	TEMP(1)=36.6
	TIME(2)=9.5	TEMP(2)=36.5
	TIME(3)=13.5	TEMP(3)=36.6
	TIME(4)=20.5	TEMP(4)=36.8
	TIME(5)=33.5	TEMP(5)=37
FILE LA30	TIME(1)=1.28	TEMP(1)=36
	TIME(2)=3.78	TEMP(2)=36.8
	TIME(3)=7.78	TEMP(3)=36.5
	TIME(4)=10.78	TEMP(4)=36.3
	TIME(5)=20.78	TEMP(5)=36.7
	TIME(6)=24.78	TEMP(6)=36.8
FILE LA31	TIME(1)=1.63	TEMP(1)=36.8
	TIME(2)=8.63	TEMP(2)=37
	TIME(3)=12.88	TEMP(3)=36.8
	TIME(4)=18.63	TEMP(4)=37.1
	TIME(5)=32.63	TEMP(5)=36.8

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 4

TEMPERATURE OF NEONATES IN THE PD GROUP*

FILE PD1	TIME(1)=1.78	TEMP(1)=36.5
	TIME(2)=10.03	TEMP(2)=37.2
	TIME(3)=15.28	TEMP(3)=37
	TIME(4)=30.28	TEMP(4)=36.5
FILE PD2	TIME(1)=1.82	TEMP(1)=36.5
	TIME(2)=9.32	TEMP(2)=36.8
	TIME(3)=14.57	TEMP(3)=37
	TIME(4)=22.57	TEMP(4)=37
FILE PD3	TIME(1)=2.5	TEMP(1)=36.6
	TIME(2)=9.5	TEMP(2)=36.5
	TIME(3)=14.5	TEMP(3)=36.4
	TIME(4)=20.5	TEMP(4)=36.5
FILE PD4	TIME(1)=1.45	TEMP(1)=36.6
	TIME(2)=4.95	TEMP(2)=36.5
	TIME(3)=10.45	TEMP(3)=36.6
	TIME(4)=24.45	TEMP(4)=36.8
FILE PD5	TIME(1)=2.53	TEMP(1)=37.6
	TIME(2)=4.03	TEMP(2)=37.6
	TIME(3)=16.03	TEMP(3)=36.8
	TIME(4)=20.03	TEMP(4)=36.8
	TIME(5)=28.03	TEMP(5)=36.8
FILE PD6	TIME(1)=1.47	TEMP(1)=36.5
	TIME(2)=3.47	TEMP(2)=37.2
	TIME(3)=10.47	TEMP(3)=36.6
	TIME(4)=21.47	TEMP(4)=36.8
	TIME(5)=26.72	TEMP(5)=37
FILE PD7	TIME(1)=1.82	TEMP(1)=36.3
	TIME(2)=9.07	TEMP(2)=36.5
	TIME(3)=14.32	TEMP(3)=36.5
	TIME(4)=28.32	TEMP(4)=36.8

*NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 4 (continued)

FILE PD8	TIME(1)=1.73	TEMP(1)=37
	TIME(2)=8.73	TEMP(2)=37
	TIME(3)=15.73	TEMP(3)=37
FILE PD9	TIME(1)=1.93	TEMP(1)=37.5
	TIME(2)=4.93	TEMP(2)=36.7
	TIME(3)=13.93	TEMP(3)=36.5
	TIME(4)=19.93	TEMP(4)=36.8
	TIME(5)=31.93	TEMP(5)=36.8
FILE PD10	TIME(1)=2.55	TEMP(1)=37.2
	TIME(2)=7.47	TEMP(2)=36.7
	TIME(3)=13.47	TEMP(3)=36.8
	TIME(4)=27.97	TEMP(4)=36.8
FILE PD11	TIME(1)=1.7	TEMP(1)=36.5
	TIME(2)=5.45	TEMP(2)=36.7
	TIME(3)=15.95	TEMP(3)=36.8
	TIME(4)=22.95	TEMP(4)=37
	TIME(5)=26.95	TEMP(5)=37.3
FILE PD12	TIME(1)=2.55	TEMP(1)=36.2
	TIME(2)=7.05	TEMP(2)=36.4
	TIME(3)=19.05	TEMP(3)=36.7
	TIME(4)=25.05	TEMP(4)=36.5
FILE PD13	TIME(1)=2.45	TEMP(1)=36.9
	TIME(2)=4.62	TEMP(2)=36.4
	TIME(3)=11.87	TEMP(3)=37
	TIME(4)=20.12	TEMP(4)=37
	TIME(5)=27.62	TEMP(5)=37.5
FILE PD14	TIME(1)=1.57	TEMP(1)=36.8
	TIME(2)=5.57	TEMP(2)=36.9
	TIME(3)=13.57	TEMP(3)=36.6
	TIME(4)=18.57	TEMP(4)=36.8
	TIME(5)=29.57	TEMP(5)=36.6

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 4 (continued)

FILE PD15	TIME(1)=1.92	TEMP(1)=37.1
	TIME(2)=9.75	TEMP(2)=36.8
	TIME(3)=14	TEMP(3)=37
	TIME(4)=18	TEMP(4)=37
	TIME(5)=20.25	TEMP(5)=36.6
FILE PD16	TIME(1)=2.03	TEMP(1)=37
	TIME(2)=6.53	TEMP(2)=36.8
	TIME(3)=15.53	TEMP(3)=36.9
	TIME(4)=18.78	TEMP(4)=36.8
	TIME(5)=26.53	TEMP(5)=37.2
FILE PD17	TIME(1)=1.75	TEMP(1)=37.3
	TIME(2)=5.83	TEMP(2)=37.1
	TIME(3)=10.83	TEMP(3)=37
	TIME(4)=15.83	TEMP(4)=37.4
FILE PD18	TIME(1)=1.53	TEMP(1)=37
	TIME(2)=5.03	TEMP(2)=37.3
	TIME(3)=10.03	TEMP(3)=36.5
FILE PD19	TIME(1)=2.4	TEMP(1)=36
	TIME(2)=4.9	TEMP(2)=36
	TIME(3)=5.9	TEMP(3)=36
	TIME(4)=8.9	TEMP(4)=36.5
	TIME(5)=18.4	TEMP(5)=36.6
	TIME(6)=24.9	TEMP(6)=36.8
FILE PD20	TIME(1)=1.82	TEMP(1)=36.7
	TIME(2)=5.52	TEMP(2)=37
	TIME(3)=12.27	TEMP(3)=36.3
	TIME(4)=24.27	TEMP(4)=36.5
FILE PD21	TIME(1)=1.38	TEMP(1)=36.7
	TIME(2)=6.38	TEMP(2)=36.8
	TIME(3)=14.88	TEMP(3)=36.6
	TIME(4)=20.38	TEMP(4)=36.9

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 4 (continued)

FILE PD22	TIME(1)=2.02	TEMP(1)=37
	TIME(2)=4.02	TEMP(2)=36.8
	TIME(3)=7.77	TEMP(3)=36.6
	TIME(4)=16.02	TEMP(4)=37.2
	TIME(5)=22.52	TEMP(5)=37
FILE PD23	TIME(1)=.98	TEMP(1)=36.4
	TIME(2)=14.48	TEMP(2)=36.8
	TIME(3)=18.73	TEMP(3)=37.4
	TIME(4)=24.98	TEMP(4)=37
FILE PD24	TIME(1)=1.37	TEMP(1)=37
	TIME(2)=6.28	TEMP(2)=36.8
	TIME(3)=14.28	TEMP(3)=36.5
	TIME(4)=26.78	TEMP(4)=36.5
FILE PD25	TIME(1)=1.25	TEMP(1)=36.3
	TIME(2)=3.5	TEMP(2)=36.6
	TIME(3)=6.75	TEMP(3)=36.6
	TIME(4)=21.25	TEMP(4)=36.6
	TIME(5)=25.75	TEMP(5)=36.5
FILE PD26	TIME(1)=1.15	TEMP(1)=36.8
	TIME(2)=1.98	TEMP(2)=36.5
	TIME(3)=14.98	TEMP(3)=36.6
	TIME(4)=18.98	TEMP(4)=37.1
	TIME(5)=25.98	TEMP(5)=36.8
FILE PD27	TIME(1)=1.47	TEMP(1)=37.9
	TIME(2)=11.3	TEMP(2)=37
	TIME(3)=20.3	TEMP(3)=37
	TIME(4)=26.3	TEMP(4)=37.2
FILE PD28	TIME(1)=1.56	TEMP(1)=36.7
	TIME(2)=8.98	TEMP(2)=36.8
	TIME(3)=15.48	TEMP(3)=37

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 4 (continued)

FILE PD29	TIME(1)=1.27	TEMP(1)=36.5
	TIME(2)=7.27	TEMP(2)=37
	TIME(3)=12.02	TEMP(3)=36.8
	TIME(4)=30.2	TEMP(4)=36.7
FILE PD30	TIME(1)=2.48	TEMP(1)=37.2
	TIME(2)=4.73	TEMP(2)=36.6
	TIME(3)=9.98	TEMP(3)=36.8
	TIME(4)=18.48	TEMP(4)=37.2
	TIME(5)=25.98	TEMP(5)=37.5
FILE PD31	TIME(1)=1.52	TEMP(1)=37
	TIME(2)=11.02	TEMP(2)=36.5
	TIME(3)=17.02	TEMP(3)=37
	TIME(4)=28.02	TEMP(4)=37.5
FILE PD32	TIME(1)=1.43	TEMP(1)=37.2
	TIME(2)=5.43	TEMP(2)=36.7
	TIME(3)=13.93	TEMP(3)=36.8
	TIME(4)=23.43	TEMP(4)=36.7
	TIME(5)=29.43	TEMP(5)=36.6
FILE PD33	TIME(1)=1.5	TEMP(1)=36
	TIME(2)=9.83	TEMP(2)=36.2
	TIME(3)=15.33	TEMP(3)=36.9
	TIME(4)=27.33	TEMP(4)=36.8
FILE PD34	TIME(1)=2.78	TEMP(1)=36.9
	TIME(2)=11.28	TEMP(2)=37
	TIME(3)=17.78	TEMP(3)=36.8
FILE PD35	TIME(1)=2.08	TEMP(1)=36.2
	TIME(2)=6.25	TEMP(2)=36.8
	TIME(3)=10.75	TEMP(3)=37.1
	TIME(4)=16.75	TEMP(4)=37

NOTE: Time is given in hours after birth and temperature in ^{o}C.

APPENDIX 4 (continued)

FILE PD36	TIME(1)=1.83	TEMP(1)=37.1
	TIME(2)=11.75	TEMP(2)=37
	TIME(3)=18.25	TEMP(3)=36.5
	TIME(4)=31.75	TEMP(4)=36.7

NOTE: Time is given in hours after birth and temperature in ^{o}C.

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